THIRD EDITION

Rosado-de-Christenson Martmez-Jimenez





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Diagnostic Imaging Oliveration



Diagnostic Imaging

THIRD EDITION

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DIAGNOSTIC IMAGING: CHEST, THIRD EDITION

ISBN: 978-0-323-79663-7 Inkling: 978-0-323-79664-4

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Library of Congress Control Number: 2021944546

Printed in Canada by Friesens, Altona, Manitoba, Canada



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Dedications

To my wonderful family – Paul, Jennifer, Heather, David, Mike, and Juniper, for your unconditional love and support. You are everything to me.

MLR

To Isabela and Lucas. You are simply the best. Just keep smiling and remember that monsters were never under the bed.

SMJ

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Preface

We proudly present the 3rd edition of *Diagnostic Imaging: Chest*. It is hard to believe that 9 years have elapsed since the publication of the 2nd edition. I am immensely grateful to the Elsevier team for giving me the opportunity to, once again, serve as lead author of this work, and to my good friend, colleague, and practice partner, Dr. Santiago Martínez-Jiménez, for serving as co-lead author.

The 3rd edition is similar to the 2nd in both style and appearance, with a succinct, bulleted text format and image-rich depictions of a large number of cardiothoracic diseases. The content is organized based on both anatomic location and category of disease. The work is enhanced by a wealth of new material that includes:

- 13 updated and illustrated section introductions that set the stage for the specific diagnoses that follow
- Updated sections that define and illustrate thoracic imaging terminology, including many entities from the Fleischner Society glossary of terms, as well as classic signs in chest imaging
- An updated section on posttreatment changes in the thorax and the effects of novel therapies that include surgery, radiotherapy, chemotherapy, immunotherapy, and ablation procedures
- New chapters on emerging diseases, including coronavirus disease-2019 (COVID-19) and e-cigarette or vaping product use-associated lung injury (EVALI)
- A total of 344 chapters supplemented with updated material and references
- In all, 2,640 images and 2,536 online-only images that include radiographic, CT, MR, and PET/CT images, as well as gross photographs and photomicrographs where appropriate
- Updated graphics that illustrate the anatomic/pathologic basis of various imaging abnormalities

We were fortunate to recruit a world-class team of authors who delivered meticulously researched content in all areas of thoracic imaging, including both seasoned authors from the 2nd edition and promising early-career cardiothoracic radiologists destined to lead this project in the future. We were privileged to work with Terry W. Ferrell, MS, an outstanding lead editor whose suggestions and edits enhanced each and every chapter, and with Lane R. Bennion, MS, a gifted medical illustrator whose artistry greatly enriched the imaging content. We gratefully acknowledge the tireless work of the Elsevier production staff, who sustained us through each step of the work. Finally, we express our heartfelt gratitude to Karen E. Concannon, PhD, senior manager of content, for her enthusiastic leadership and thoughtful guidance through the entire process.



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Diagnostic Imaging Clock Clock



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Introduction

Chest diseases are prevalent worldwide, and heart disease, malignant neoplasms, and chronic lower respiratory disease are among the top four causes of death in the United States. Chest diseases can be categorized based on anatomic location as affecting the airways, lungs, pleura, mediastinum, chest wall, or diaphragm. Each of these regions may be involved by developmental abnormalities, neoplasms, or infections. Additionally, idiopathic, inflammatory, connective tissue, autoimmune, and lymphoproliferative disorders may also affect the chest. The ventilatory and respiratory functions of the lungs and airways provide a portal for exposure to a variety of inhalational diseases, some of which are related to the patient's environment and occupation. Thoracic diseases may also be categorized based on their physiological effects as obstructive or restrictive abnormalities. Finally, the various organs and anatomic regions of the chest may be affected by traumatic or iatrogenic conditions.

Clinical Presentation

Patients with chest disease often present with chest pain, dyspnea, &/or cough, which may arise acutely or be chronic. Systemic complaints may include malaise, fatigue, and weight loss. Patients with thoracic malignancy may present because of systemic effects of the neoplasm unrelated to metastatic disease or with symptoms related to systemic metastases.

Assessment of Chest Disease

An understanding of the patient's chief complaint and past medical and surgical history is of foremost importance, including relevant habits, such as cigarette smoking, use of prescription or illicit drugs, and environmental or occupational exposures. It is important to determine the patient's immune status, as altered immunity may result in a variety of infectious, inflammatory, and neoplastic conditions. The physical exam may provide important clues to the diagnosis and is complemented by laboratory and pulmonary function tests.

Imaging plays a pivotal role in the assessment of patients with thoracic complaints and is frequently obtained during the initial evaluation. Thus, radiologists often impact patient management by identifying abnormalities and providing a focused differential diagnosis and management recommendations. In selected cases, the radiologist may perform image-guided tissue sampling of specific lesions or provide definitive treatment with various thoracic interventions (e.g., drainage of fluid collections, ablation procedures).

Thoracic Imaging

Chest Radiography

The chest radiograph is frequently the initial imaging study obtained on patients with chest complaints but may also be obtained in asymptomatic subjects as part of a physical exam or a preoperative evaluation. It allows assessment of the airways, lungs, cardiovascular system, pleura, diaphragm, and chest wall osseous structures and soft tissues. Chest radiographic interpretation is challenging because of the broad range of densities produced by the superimposition of the various thoracic organs and tissues and the subtlety of many abnormalities. Thus, accurate interpretation requires an in-depth knowledge of imaging anatomy, impeccable imaging technique, and optimal viewing and working conditions. Additional challenges relate to the population referred for imaging, including patients with large body habitus, severe dyspnea, or inability to understand or follow technologist's instructions.

PA and lateral chest radiography: Ambulatory patients are imaged with orthogonal posteroanterior (PA) and lateral chest radiographs, which allow identification and anatomic localization of abnormalities. Optimal imaging is obtained in the upright position, at full inspiration, without motion or rotation, and with minimal superimposition of upper extremities, head, neck, or scapulae. PA refers to the posteroanterior direction of the x-ray beam as it traverses the patient to expose the image receptor. Source-image distance (SID) is 72 in., and a high kilovoltage technique (120-150 kVp) is used. Lateral radiography is obtained with the patient's left side closest to the image receptor.

Bedside (portable) chest radiography: Neonates and infants, debilitated and unstable patients, and those who have sustained major trauma or are seriously ill or bed-ridden undergo portable anteroposterior (AP) chest radiography, in which the x-ray beam traverses the patient anteroposteriorly using a SID of 40 in. and relatively low kilovoltage techniques with resultant magnification of anterior structures and decreased image sharpness. Portable chest radiography plays an important role in the evaluation of medical life support devices and the identification of complications of their use.

Decubitus radiography is occasionally used to evaluate pleural effusion or pneumothorax. **Apical lordotic** radiography (formerly used to evaluate the lung apices) is rarely used today. **Inspiratory and expiratory chest radiography** for identification of pneumothorax is also rarely used, as it has been shown that it does not improve pneumothorax visualization while effectively doubling radiation dose.

Computed Tomography

Computed tomography (CT) is easily and expeditiously performed. It allows accurate anatomic localization and characterization of radiographic abnormalities and may help detect additional abnormalities that may enable a diagnosis and a management course.

As the growth of multidetector CT utilization has resulted in a substantially increased radiation dose to the population, radiologists and vendors continue to implement dose reduction measures. It is postulated that up to 2% of future cancers will be linked to the increased utilization of medical imaging. Thus, radiologists should actively communicate with and educate referring physicians and work with them toward reducing the number of unnecessary studies. Electronic decision support systems that use evidence-based guidelines and appropriateness criteria have helped reduce the number of inappropriate studies.

Radiologists can take additional measures to reduce dose with the use of shielding, tube current modulation, and adaptive statistical iterative reconstruction techniques. As it has been shown that the radiation dose during CT imaging is directly proportional to tube current, the reduction of tube currenttime product (mAs) can achieve low-dose chest CT studies that preserve satisfactory image quality. Low-dose CT imaging techniques should be used routinely in small patients and in those who will receive serial CT examinations, such as young patients imaged for restaging of malignancy and those imaged for the evaluation of indeterminate lung nodules or diffuse infiltrative pulmonary diseases. **Unenhanced chest CT**: Evaluation of the lungs and airways does not require the use of intravenous contrast. Unenhanced chest CT is ideally suited for lung cancer screening, identifying intralesional calcifications, and assessing indeterminate nodules, diffuse infiltrative lung diseases, and airways diseases.

Contrast-enhanced chest CT: Administration of intravenous contrast is mandatory for vascular imaging and the assessment of hilar lymphadenopathy. Contrast is also valuable in the assessment of thoracic malignancy, as it may help identify and characterize tumors surrounded by atelectasis or consolidation. CT aortography is mandatory for excluding traumatic vascular injury and pulmonary thromboembolism. Acute aortic syndromes are evaluated with both unenhanced and enhanced aortic CT in order to diagnose intramural hematoma.

Post processing: Image reformation in various planes (coronal, sagittal, oblique) helps determine the distribution of lung disease. Because some diseases involve the lung diffusely, while others exhibit a predilection for the upper lung zones or lung bases, recognizing the pattern of distribution allows the radiologist to provide a reasonable differential diagnosis. For example,

lymphangioleiomyomatosis (LAM) and pulmonary Langerhans cell histiocytosis (PLCH) both manifest with pulmonary cysts. However, LAM affects the lung diffusely, while PLCH characteristically spares the lung bases. In addition, since neoplasms may grow in all directions, multiplanar imaging may allow documentation of craniocaudad growth of a tumor that appears stable on axial imaging.

Maximum-intensity projection (MIP) and minimumintensity projection (minIP) images: MIP images retain the relative maximum value along each ray path, preferentially display contrast-filled and higher attenuation structures, and allow detection of subtle lung nodules and evaluation of vascular structures. minIP images display the minimum value along the ray paths and are useful in the assessment of the airways, emphysema, and air-trapping.

Volume and surface rendering: These techniques do not always add value to diagnostic interpretation but are often greatly appreciated by referring physicians. Volume-rendering techniques can provide a 3D image display of vascular anatomy. Surface-rendered displays are ideally suited for depiction of tubular structures, such as the airways, and are employed in performing virtual bronchoscopy, which mimics the airway luminal visualization achieved on bronchoscopy.

High-resolution CT (HRCT): HRCT is the modality of choice for evaluating diffuse infiltrative lung disease. It uses a narrow slice width (1-2 mm) and a high spatial resolution image reconstruction algorithm. The ability to analyze diffuse lung involvement in relation to the anatomy of the secondary pulmonary lobule allows accurate and reproducible disease characterization and the formulation of an appropriate differential diagnosis.

Magnetic Resonance Imaging

Magnetic resonance (MR) imaging is routinely employed in the evaluation of the cardiovascular system and is the modality of choice for the assessment of myocardial perfusion and ventricular and valve function. MR helps evaluate locally invasive thoracic tumors, particularly to identify invasion of cardiovascular structures and to evaluate the brachial plexus in cases of Pancoast tumor. MR is particularly valuable in the noninvasive evaluation of the abnormal thymus and allows the distinction of thymic hyperplasia from thymic neoplasia.

Positron Emission Tomography

Positron emission tomography (PET) and combined PET/CT are invaluable in the staging of patients with malignancy. PET and CT images obtained in a single imaging session are fused into a co-registered image that allows correlation of abnormal metabolic activity with CT abnormalities. It is the imaging modality of choice for staging and restaging lymphoma and other malignancies. Areas of abnormal metabolic activity following treatment can be localized and targeted for tissue sampling. Normal increased metabolic activity may be seen in certain anatomic regions (e.g., the interatrial septum corresponding to brown fat deposition). False-positive PET/CT studies may occur in infectious or inflammatory processes, and false-negative studies may occur in indolent malignancies.

Ventilation-Perfusion Scintigraphy

Ventilation-perfusion (V/Q) scintigraphy has been largely replaced by CT pulmonary angiography (CTPA) in the evaluation of pulmonary thromboembolism, although CTPA and V/Q scintigraphy have similar positive predictive values. CTPA is superior in the evaluation of patients with evidence of lung disease on radiography and has the advantage of demonstrating alternate etiologies for the patient's symptoms.

However, a growing body of literature supports performing perfusion scintigraphy instead of CTPA in the setting of pregnancy, provided that chest radiographs are normal, and in cases in which an alternative diagnosis is not suspected. CTPA may yield indeterminate results in pregnant patients due to physiologic hemodilution of contrast and interruption of contrast by unopacified blood from the inferior vena cava. It should be noted that CTPA delivers a higher radiation dose to the maternal breast when compared to V/Q scintigraphy. Appropriate measures (e.g., hydration) must be taken to decrease the radiation dose to the fetus in pregnant patients undergoing V/Q scintigraphy.

Approach to Chest Imaging

Chest radiographs are the most frequent imaging studies performed in most practices and possibly the most challenging to interpret. Identification of a radiographic abnormality must be correlated with its localization to a specific anatomic compartment in order to provide a differential diagnosis. Identification of associated findings, such as lesion calcification or cavitation, lymphadenopathy, &/or pleural effusion, enables the formulation of a focused differential diagnosis. Comparison to prior studies is of paramount importance as documentation of stability generally supports a benign diagnosis.

Communication of imaging findings to the referring physician is typically accomplished via the radiologic report. Radiologists must strive to produce concise, clear, and unambiguous reports that "answer the question" and include a description of the abnormality, the differential diagnosis, the most likely diagnosis, and management recommendations that may include advanced imaging (e.g., CT, HRCT, MR, scintigraphy, etc.), a course of treatment, tissue sampling, or emergent medical/surgical intervention. Critical and unexpected findings must be promptly communicated to the appropriate member of the healthcare team.

Introduction

Advancements in diagnostic imaging are not limited to evolving technology or the introduction of novel state-of-theart imaging equipment but have also impacted the way radiologists view and interpret images and the manner of completing radiologic reports. Picture archiving and communication systems (PACS) permit inexpensive storage of large image data sets, which are easily accessed by radiologists and referring physicians for interpretation and consultation. Radiologists readily access comparison images and prior reports in order to document change or stability of imaging abnormalities. Speech recognition technology allows the expeditious generation of radiologic reports that can be reviewed for accuracy prior to their release. The availability of electronic medical records provides access to timely relevant clinical and laboratory data that enhances interpretation and the formulation of a focused differential diagnosis.

The wide availability of viewing stations has also impacted communication between radiologists and clinicians, an interchange that frequently occurs via secure electronic mail or by telephone. In fact, face-to-face communication between clinicians and radiologists has greatly diminished with the unfortunate consequence of lessening the opportunity to ask for additional medical history that may not be available on the requisition or electronic medical record.

In today's practice, the radiologic report is the principal method used by radiologists to communicate diagnostic imaging findings. Although unexpected critical abnormalities should always be verbally communicated to a member of the healthcare team, most abnormal findings are communicated via the radiology report. In addition, increased transparency in healthcare has made imaging reports accessible to patients, which generates additional challenges for radiologists as they strive to simplify and clarify the report language and impression. Thus, radiologists must strive to generate concise, clear, and unambiguous reports that not only contain relevant findings but also include focused differential diagnoses and specific recommendations for further imaging &/or future management.

The Proper Language

As imaging specialists, we must strive to use proper and correct language in both verbal communications and in our reports. For example, the phrase "chest x-ray" may be forever ingrained in colloquial communications in spite of the fact that it is an incorrect descriptor of the imaging study. As x-rays are invisible, a radiologist does not interpret a chest x-ray but rather a chest radiograph. Likewise, modern radiologists rarely review or interpret films or analog images given the ubiquitous nature and broad utilization of PACS that allow interpretation of soft copy images.

Infiltrate is a term formerly used to describe any pulmonary opacity produced by airspace &/or interstitial disease on chest radiography or computed tomography (CT). In medicine, the word "infiltrate" is used to describe the accumulation in tissue of either abnormal or excess normal substances. The use of this term is controversial, has various meanings, is imprecise in its implications, and is no longer recommended for the description of chest imaging abnormalities. Instead, the term "opacity" with the addition of appropriate descriptors (airspace, reticular, nodular) is preferred.

Terminology of Thoracic Imaging

In recent years, thoracic imaging has undergone immense growth and technological advancement. Thoracic CT and highresolution computed tomography (HRCT) allow identification and characterization of subtle abnormalities that were previously seen only by anatomists and pathologists. Today, the radiologist can thoroughly analyze pulmonary abnormalities with respect to the underlying units of lung structure, such as the secondary pulmonary lobule and the pulmonary acinus. The ability to correlate imaging abnormalities with the anatomic portion of the lung affected allows the radiologist to make confident diagnoses of diseases, such as pulmonary fibrosis, sarcoidosis, interstitial edema, and emphysema. In fact, thoracic imagers play an integral role in the multidisciplinary diagnosis of interstitial lung disease and adenocarcinoma of the lung. In addition, the growing field of quantitative lung imaging may allow radiologists to contribute to the noninvasive assessment of the entire lung in the setting of diffuse lung diseases and correlate those findings with abnormalities of pulmonary function.

Thoracic imagers are able to evaluate a series of complex imaging abnormalities affecting the thorax and to work in conjunction with clinical colleagues toward an expeditious diagnosis and course of management. The protean and complex findings identified on chest CT and HRCT, along with advances in our understanding of lung diseases, mandate the consistent use of correct terminology for the description of abnormalities. In 2008, the Fleischner Society published the glossary of terms recommended for thoracic imaging reporting, a lexicon that reflects the emergence of new terms and the obsolescence of others.

The Fleischner glossary is not only a list of proper terminology in thoracic imaging but also includes definitions and illustrations of anatomic locations in the thorax, signs in thoracic imaging, specific disease processes (such as emphysema and rounded atelectasis), and the many interstitial pneumonias.

Pneumonia is defined as inflammation of the airspaces and interstitium. The term is predominantly used to denote an infectious process of the lung. The diagnosis may be made clinically or may be proposed by the radiologist based on the correlation of imaging findings with the clinical history. However, the term "pneumonia" is also used for a number of noninfectious pulmonary disorders related to inflammation and fibrosis (e.g., the idiopathic interstitial pneumonias).

Summary

The use of clear and concise terminology facilitates communication with other radiologists, clinicians, and increasingly with patients. Interpretation of thoracic imaging studies requires knowledge of imaging anatomy and the utilization of correct descriptors of imaging abnormalities. In many instances, the description of an abnormality allows the radiologist to suggest the correct diagnosis and formulate the appropriate next step in patient management.

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Approach to Illustrated Terminology

Bacterial Pneumonia





Nonspecific Interstitial Pneumonia

(Left) PA chest radiograph of a 54-year-old man with cough, fever, and leukocytosis shows a right upper lobe consolidation located above the horizontal fissure and, therefore, involving the anterior segment of the right upper lobe. (Right) Lateral chest radiograph of the same patient shows consolidation in the right upper lobe anterior and posterior segments. Based on the radiographic and clinical findings, the final impression was right upper lobe pneumonia. In this case, the term pneumonia refers to

Usual Interstitial Pneumonia



Chronic Eosinophilic Pneumonia



(Left) Axial HRCT of an 83year-old woman with idiopathic pulmonary fibrosis shows a usual interstitial pneumonia (UIP) pattern of fibrosis characterized by basilar predominant subpleural honeycomb cysts arrayed in layers. (Right) Axial NECT of a patient with nonspecific interstitial pneumonia (NSIP) shows patchy, basilar, ground-glass opacities and mild traction bronchiectasis \rightarrow . Noninfectious diffuse fibrotic lung diseases form part of the spectrum of idiopathic

interstitial pneumonias.

Lipoid Pneumonia



(Left) Axial NECT of a patient with chronic eosinophilic pneumonia shows peripheral subpleural ground-glass opacities \blacksquare . This description is preferred over the term "infiltrate," although this noninfectious disease is characterized by alveolar and interstitial eosinophilic infiltration. (Right) Composite image with axial CECT in lung (left) and soft tissue (right) window shows multifocal consolidations with intrinsic fat attenuation \square , representing exogenous lipoid pneumonia secondary to mineral oil aspiration.

Acinar Nodules

KEY FACTS

TERMINOLOGY

- Acinar nodule (accumulation of pathologic material in pulmonary acinus)
 - Clustered, rounded, poorly-defined opacities
 - Typically multifocal
 - Size: 5-8 mm in diameter
- Acinus
 - Largest lung unit in which all airways participate in gas exchange
 - Structural lung unit distal to terminal bronchiole
 - Supplied by 1st-order respiratory bronchioles
 - Contains alveolar ducts and alveoli
 - o Size: 6-10 mm in diameter
- Secondary pulmonary lobule
 - Contains 3-25 acini

IMAGING

- Radiography
 - Multifocal, ill-defined, small, rounded opacities

• CT/HRCT

Multifocal ground-glass or part-solid nodular opacities
5-8 mm in size

PATHOLOGY

- Etiology
 - o Infection
 - o Aspiration
 - o Edema
 - o Hemorrhage
 - Pulmonary vasculitis
 - Pulmonary contusion
 - o Lung cancer: Invasive mucinous adenocarcinoma

DIAGNOSTIC CHECKLIST

- Sputum analysis for diagnosis of infection
- Diagnosis of vasculitis or malignancy may require bronchoscopic or open lung biopsy
- History of blunt trauma in pulmonary contusion

(Left) Axial NECT of a patient who presented with fever and cough shows bronchopneumonia characterized by acinar nodules \supseteq manifesting as multifocal, rounded, illdefined, ground-glass and part-solid right upper lobe nodules. (Right) Axial NECT of a patient with a moderate hiatus hernia (not shown) and aspiration bronchiolitis shows left lower lobe acinar nodules manifesting as rounded nodular consolidations 🖂 surrounded by ground-glass opacity halos 🔁.





(Left) Axial CECT of a patient with hemoptysis and pulmonary hemorrhage shows multifocal ground-glass acinar opacities 🔁 adjacent to medial nodular opacities that exhibit the crazy-paving sign *⊡*. The former correspond to alveolar hemorrhage within pulmonary acini. (Right) Coronal CECT of a patient with multicentric invasive mucinous adenocarcinoma shows multifocal, bilateral lower lobe consolidations and right upper lobe heterogeneous, part-solid acinar nodules with intrinsic lucencies 🔁.





KEY FACTS

TERMINOLOGY

- Air bronchogram
 - Definition: Visualization of air-filled bronchi within background of opacified lung parenchyma
 - o Implies patency of proximal airways
 - Central obstruction is unlikely
 - May occur in confluent interstitial disease
- Bronchi not normally visible in outer 1/3 of lung

IMAGING

- Radiography
 - Air-filled branching lucencies representing patent bronchi
 - Surrounding airspace disease
 - Indicates intrapulmonary location of abnormality
- CT
 - Air-filled branching tapering bronchi
 - Surrounding consolidated lung parenchyma

TOP DIFFERENTIAL DIAGNOSES

• Pulmonary interstitial emphysema

PATHOLOGY

- Alveolar filling with pus, edema fluid, blood, tumor
- Etiologies
 - Pneumonia: Infectious, lipoid, aspiration
 - o Neoplasms
 - Lung cancer; particularly lepidic adenocarcinoma
 - Lymphoma
 - o Alveolar edema
 - o Alveolar hemorrhage
 - Fibrosis: Radiation, sarcoidosis

DIAGNOSTIC CHECKLIST

- Consolidation with air bronchograms in a febrile patient is consistent with pneumonia
- Consolidations in adults should be followed to radiographic resolution to exclude underlying malignancy





(Left) PA chest radiograph of a patient with right upper lobe pneumonia shows a dense consolidation with an intrinsic air bronchogram \blacksquare , the presence of which excludes a central obstructing lesion. Nevertheless, consolidations in adults should be followed to complete resolution to exclude underlying malignancy. (Right) Coronal CECT of a patient with pneumonia shows a dense right upper lobe consolidation with an intrinsic air bronchogram \supseteq that manifests as branching lucencies within the consolidated lung.





(Left) Axial NECT of a patient with pneumonia shows a lingular consolidation with an intrinsic air bronchogram *⇒* manifesting as branching airfilled tubular lucencies within surrounding airspace disease. (Right) Axial NECT of a patient with chronic cough and exogenous lipoid pneumonia shows heterogeneous consolidations in the middle and right lower lobes and a middle lobe air bronchogram \square A variety of alveolar filling disease processes may produce air bronchograms on imaging.

Air-Trapping

KEY FACTS

TERMINOLOGY

- Air-trapping
 - Air retention in lung distal to airway obstruction shown on expiratory CT

IMAGING

- Radiography: Lung hyperlucency on expiration
- CT
 - o Inspiration
 - Normal lung is homogeneously lucent
 - Mosaic attenuation: Patchwork of regions of different attenuation
 - Expiration
 - Increased attenuation of normal lung
 - Air-trapping: Sharply-defined geographic foci of lower attenuation; follow outlines of secondary pulmonary lobules; affects > 25% of lung volume; not limited to lower lobe superior segments or lingular tip
 - Lobular air-trapping in < 3 adjacent lobules is normal

PATHOLOGY

- Etiologies
 - Constrictive bronchiolitis: Peribronchiolar fibrosis of membranous and respiratory bronchioles
 - Infection, chronic rejection in transplantation, connective tissue disease, inhalational lung disease, hypersensitivity pneumonitis, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia
 - Cellular bronchiolitis: Tree-in-bud nodules + mosaic attenuation
 - Infection, aspiration, respiratory bronchiolitis, follicular bronchiolitis, panbronchiolitis
 - o Asthma
 - Endoluminal foreign body or neoplasm

DIAGNOSTIC CHECKLIST

• Consider expiratory HRCT in patients with mosaic attenuation or suspected constrictive bronchiolitis

(Left) Composite image with axial HRCT of a patient with constrictive bronchiolitis obtained in inspiration (top) and expiration (bottom) shows areas of expiratory airtrapping that manifest as geographic areas of hyperlucent lung 🛃. (Right) Composite image with axial HRCT on inspiration (left) and expiration (right) of a patient with constrictive bronchiolitis shows inspiratory mosaic attenuation and expiratory air-trapping with decreased vascularity. Suspected airtrapping is confirmed on expiratory CT imaging.





(Left) Axial NECT of a patient with hypersensitivity pneumonitis shows multiple foci of hyperlucent lung 🔁 due to expiratory air-trapping. In patients with hypersensitivity pneumonitis, areas of air-trapping may be accentuated by surrounding normal lung and ground-glass opacity foci. (Right) Axial NECT of a patient with a central partially obstructing carcinoid tumor shows hyperlucency \implies of the visualized left lower lobe secondary to obstruction by the tumor and resultant airtrapping.





Airspace

KEY FACTS

TERMINOLOGY

Airspace

- Gas-containing portions of lung: Respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli
- Excludes purely conducting airways
- Airspace disease: Increased airspace opacity
 Air loss (atelectasis); air replaced by fluid, pus, blood, cells, fat, and other substances

IMAGING

- Radiography
 - Consolidation, mass, nodule; focal or multifocal, may be heterogeneous
- CT
 - Airspace consolidation: Increased lung attenuation, obscuration of normal structures
 - o Mass
 - o Nodule
 - Solid or subsolid

PATHOLOGY

- Etiologies
 - o Pneumonia
 - Bacterial, viral, fungal
 - AspirationAlveolar edema
 - Alveolar hemorrhage
 - Alveolar nemornagi
 Alveolar proteinosis
 - Neoplastic: Lung cancer, lymphoma, metastasis
 - Inflammation/fibrosis
 - Sarcoidosis, eosinophilic pneumonia, organizing pneumonia, lipoid pneumonia, vasculitis, interstitial lung disease, drug toxicity, radiation pneumonitis/fibrosis

DIAGNOSTIC CHECKLIST

 Consider myriad etiologies of airspace filling in differential diagnosis of airspace disease in patient without signs or symptoms of infection





(Left) Graphic demonstrates the airspaces of the lung, which are composed of the small airways that participate in gas exchange (respiratory bronchiole 🛃, alveolar duct \blacksquare , and alveolar sac) and the alveoli \square and excludes purely conductive airways. (Right) PA chest radiograph of a patient with interstitial edema shows interlobular septal thickening, perihilar haze, and focal airspace opacity \implies in the right lower lobe due to alveolar filling with edema fluid.





(Left) PA chest radiograph of a patient with fever and cough demonstrates pneumonia manifesting with extensive airspace consolidation in the left upper and lower lobes with intrinsic air bronchograms \implies . Pulmonary infection is a common etiology of airspace disease. (Right) Axial NECT of a patient with subacute (nonfibrotic) hypersensitivity pneumonitis shows innumerable small subsolid airspace nodules 🛃 in a centrilobular distribution. This nodular form of airspace disease is also referred to as acinar nodules.

Architectural Distortion

KEY FACTS

TERMINOLOGY

Architectural distortion

- Abnormal displacement of bronchi, vessels, fissures, or septa secondary to diffuse or localized retractile fibrosis
- Characteristically related to interstitial fibrosis

IMAGING

• Radiography

- Reticular opacities; nodular and mass-like opacities
 Volume loss
- Hilar displacement related to volume lossBronchiectasis related to volume loss
- **CT**
 - Abnormal displacement of pulmonary vessels and bronchi associated with pulmonary fibrosis
 - Reticular opacities with interlobular septal thickening and intralobular lines
 - Traction bronchiectasis, honeycombing
 - o Cicatricial atelectasis; may be nodular or mass-like

PATHOLOGY

- Interstitial fibrosis, honeycombing
- Etiologies
 - Fibrosing interstitial lung disease (e.g., idiopathic pulmonary fibrosis, fibrotic nonspecific interstitial pneumonia)
 - End-stage sarcoidosis
 - Radiation-induced fibrosis
 - o Pneumoconiosis
 - Chronic (fibrotic) hypersensitivity pneumonitis
 - Sequela of infection (e.g., tuberculosis, COVID-19)
 - Sequela of acute respiratory distress syndrome

DIAGNOSTIC CHECKLIST

- Architectural distortion is an irreversible process that denotes fibrosis
 - Usually associated with volume loss, reticulation, traction bronchiectasis/bronchiolectasis, and honeycombing

(Left) Coronal NECT of an 87year-old man with idiopathic pulmonary fibrosis shows basilar and subpleural reticulation, architectural distortion and honeycombing, and a CT pattern consistent with usual interstitial pneumonia (UIP). (Right) Composite image with PA chest radiograph (left) and coronal CECT (right) of a 66year-old woman with chronic sarcoidosis shows upper lobe volume loss and upper lung zone predominant peribronchovascular fibrosis and architectural distortion typical of end-stage disease.











KEY FACTS

TERMINOLOGY

• Bulla

- Definition: Air-containing space > 1 cm
- o Surrounded by thin wall < 1 mm thick
- o Subpleural location; largest at lung apex
- Associated with emphysema: Typically paraseptal but also centrilobular
- Bleb
 - Definition: Small gas-containing space within visceral pleura or subpleural lung measuring < 1 cm
 - Difficult distinction between bleb and bulla, as both are peripherally located
 - Term has also been used to describe air-containing space
 1 cm

IMAGING

- Radiography
 - Thin-walled lucency (typically apical)
 - o May mimic solid lesion when fluid-filled

• CT

- Peripheral subpleural air-filled space
- Thin smooth walls
- Typically multifocal
- Thick walls, intrinsic fluid, air-fluid levels, or soft tissue should suggest secondary infection but may also relate to hemorrhage or neoplasm

PATHOLOGY

- Paraseptal/centrilobular emphysema
- Acute respiratory distress syndrome with interstitial emphysema and secondary subpleural bullae

DIAGNOSTIC CHECKLIST

- Pulmonary bullae are typically manifestations of paraseptal emphysema
- Bullae are recognized cause of secondary spontaneous pneumothorax
- Some authors use terms bulla/bleb interchangeably; indistinguishable on imaging





(Left) PA chest radiograph of a patient who presented with acute left chest pain and a spontaneous left pneumothorax shows a visible pleural line \implies and a large bulla \blacksquare in the left lung apex, likely responsible for the pneumothorax. (Right) Coronal CECT of the same patient shows the left pneumothorax 🛃 and a cluster of large left apical bullae 🖾. Paraseptal emphysema with giant bullous disease is one of the causes of secondary spontaneous pneumothorax.





(Left) Axial NECT of a patient with benign metastasizing leiomyoma and left upper lobe giant bullous disease shows a large left apical air-filled space with internal septations. (Right) Composite image with axial CECT of a patient with a left upper lobe bulla, which became secondarily infected, shows a thin-walled retrosternal bulla 乏 completely filled with air. Subsequent studies show an internal air-fluid level 🛃 within the bulla that progressed to a completely fluid-filled bulla 🖅 secondary to infection.

Cavity

KEY FACTS

TERMINOLOGY

- Cavity
 - Gas-containing space; lucency or air attenuation within nodule, mass, or consolidation
 - Implies lung necrosis and expulsion of necrotic material via tracheobronchial communication

IMAGING

- Radiography
 - Lucency within nodule, mass, or consolidation
 - May exhibit air-fluid level
 - Smooth or nodular cavity wall; thickness > 4 mm
- CT
 - Identification &/or assessment of extent of cavitation
 - Exclusion of pseudocavities: Cysts, bullae, blebs
 - Evaluation of cavity wall
 - Malignancy: Identification of other lesions, staging
 - Infection: Associated centrilobular nodules imply bronchogenic dissemination

TOP DIFFERENTIAL DIAGNOSES

- Infection
 - Necrotizing pneumonia, abscess, septic emboli
 - o Organisms: Bacteria, mycobacteria, fungi, protozoa, viruses
- Malignancy: Lung cancer, metastatic disease
- Autoimmune diseases
 - Vasculitis: Granulomatosis with polyangiitis o Rheumatoid arthritis
- Pulmonary infarct secondary to pulmonary thromboembolism

DIAGNOSTIC CHECKLIST

- Cavitation with associated centrilobular nodules should suggest active tuberculosis
- Multifocal cavitary nodules in setting of infection should suggest septic emboli
- Progression of consolidation to mass-like lesion with cavitation should suggest abscess formation

(Left) PA chest radiograph of a 58-year-old man who presented with cough and weight loss shows a left upper lobe mass-like consolidation with multiple intrinsic cavities \square of variable size secondary to primary squamous cell lung cancer. (Right) Axial NECT of a 64-year-old man with a right upper lobe squamous cell lung cancer shows a spiculated soft tissue mass with intrinsic cavitation manifesting with low-attenuation areas \blacksquare and intrinsic gas 🚬 Squamous cell carcinoma is the most common cell type of lung cancer to exhibit cavitation.

(Left) Coronal NECT of a 49year-old IV drug user who presented with fever and dyspnea shows multifocal bilateral peripheral nodules \blacksquare and consolidations \square ,

cavitation characteristic of septic emboli. (Right) Axial

night sweats shows a right

surrounding centrilobular nodules and tree-in-bud opacities typical of tuberculosis diagnosed on

sputum culture.









Centrilobular

KEY FACTS

TERMINOLOGY

• Abnormalities centered in bronchiolovascular core of secondary pulmonary lobules

IMAGING

- Radiography: May appear normal
- **CT**: Bronchiolitis and vascular nodules
 - Centrilobular micronodules
 - Solid or ground-glass
 - Tree-in-bud opacities
 - Subpleural sparing
 - Bronchiolitis ancillary findings: Mosaic attenuation, airtrapping, bronchial wall thickening, bronchiectasis
 - Vascular nodules ancillary findings: Dilated pulmonary trunk, right heart strain
 - Multiplanar reformatted images for optimal characterization of relationship of nodules to interlobar fissures
 - Absence of pleural or fissural involvement

PATHOLOGY

- Etiologies
 Bronchiolitis
 - Infectious bronchiolitis
 - Aspiration bronchiolitis
 - Respiratory bronchiolitis
 - Hypersensitivity pneumonitis
 - Follicular bronchiolitis
 - Vascular: Excipient lung disease, tumor emboli
 - Other: Cholesterol granulomas, pulmonary capillary hemangiomatosis
- Histology
 - Bronchiolitis: Luminal or submucosal cellular infiltration, bronchiolar narrowing
 - Excipient lung disease: Birefringent crystals in centrilobular arterioles
 - Cholesterol granulomas: Stellate lesions, cholesterol clefts, multinucleated giant cells, lymphocytes





(Left) Graphic shows the anatomic distribution of centrilobular nodules 🔁 at the center of the secondary pulmonary lobule that may involve the lobular bronchiole *⊡* or artery . There is no involvement of the periphery of the secondary pulmonary lobule, interlobar fissures, or interlobular septa. (Right) Axial NECT of a patient with aspiration bronchiolitis after laryngectomy shows basilar centrilobular micronodules 🔁, tree-in-bud opacities \square , and consolidations 🔁 with subpleural and fissural sparing.





(Left) Coronal HRCT of a patient with acute infectious bronchiolitis secondary to respiratory syncytial virus shows diffuse tree-in-bud nodules \square and upper lobe ground-glass opacities 🔁 (Right) Composite image with axial CECT (left) and MIP reformatted image (right) of a patient with respiratory bronchiolitis shows subtle centrilobular ground-glass nodules 🔁, more conspicuous on the MIP reformation. The nodules spare the subpleural lung, indicating their centrilobular location.

Consolidation

KEY FACTS

TERMINOLOGY

- Replacement of alveolar air by edema fluid, pus, blood, neoplastic cells, or other material (e.g., lipoprotein)
 Often implies infection (pneumonia)
- Synonyms: Airspace/alveolar consolidation
- Focal, patchy, multifocal, or diffuse
- Focal consolidation
 - o Nonsegmental, segmental, lobar
 - o Mass-like or tumor-like

IMAGING

- Radiography
 - Increased parenchymal density
 - Obscures underlying normal structures (e.g., bronchi, vessels)
 - Obscures adjacent structures
 - Sign of silhouette
 - May exhibit intrinsic air bronchograms
 - o May be spherical, sublobar, or lobar

- CT
 - Increased lung attenuation; obscures underlying lung architecture
 - May exhibit intrinsic air bronchograms &/or adjacent acinar or centrilobular nodules

PATHOLOGY

- Etiology
 - o Infection: Bacterial, mycobacterial, viral, fungal
 - Pulmonary alveolar edema or hemorrhage
 - o Neoplastic: Lung cancer, pulmonary lymphoma
 - Inflammatory: Organizing pneumonia, alveolar sarcoidosis, eosinophilic pneumonia, alveolar lipoproteinosis, lipoid pneumonia
 - Post treatment: Radiation or drug-induced pneumonitis

DIAGNOSTIC CHECKLIST

• Consolidations in adults should be followed to complete radiographic resolution to exclude underlying malignancy

(Left) PA chest radiograph of a patient with fever and leukocytosis shows a large right lung mass-like consolidation. (Right) Axial NECT of the same patient shows a dense right upper lobe consolidation with intrinsic air bronchograms 🗩 and adjacent ground-glass opacity on a background of interlobular septal thickening and intralobular lines \square (that produce the so-called crazypaving pattern). Community acquired pneumonia was diagnosed and resolved on follow-up imaging after treatment.











Cyst

KEY FACTS

TERMINOLOGY

- **Cyst**: Circumscribed spherical space lined by thin fibrous or epithelial wall, usually < 2 mm thick
- Lung cyst: Pulmonary thin-walled space that contains air but may contain fluid, air/fluid level, or solid material
 - Cystic lung disease: Series of conditions characterized by thin-walled air-filled spherical spaces
- Mediastinal cyst: Congenital anomaly of foregut budding, thymic, or pericardial origin; acquired cyst vs. cystic neoplasm
 - Unilocular or multilocular

IMAGING

- Radiography
 - Lung cysts: May not be visible or may manifest as linear opacities; larger cysts may manifest as thin-walled spherical lucencies
 - Mediastinal cyst: Mediastinal contour abnormality typically in middle mediastinum or cardiophrenic angle

• CT

- Optimal assessment of size, shape, number, wall characteristics, and distribution of lung cysts
- Contrast-enhanced CT for assessment of mediastinal cysts; assessment of cyst wall, cyst content, and presence or absence of soft tissue septa &/or mural nodules

PATHOLOGY

- Etiology
 - Cystic lung diseases: Lymphangioleiomyomatosis, Langerhans cell histiocytosis, lymphoid interstitial pneumonia, Birt-Hogg-Dubé, light chain deposition disease, Pneumocystis pneumonia, metastases
 - Congenital lung cysts: Intrapulmonary bronchogenic cyst, pulmonary airway malformation
 - Mediastinal congenital cysts: Bronchogenic cyst, enteric/neurenteric cyst, pericardial cyst, thymic cyst
 - Mediastinal cystic lesions: Mature teratoma, lymphangioma, cystic thymic neoplasms





(Left) Axial CECT shows lymphangioleiomyomatosis manifesting with multifocal pulmonary cysts of varying size with intervening normal lung parenchyma. The cysts are distributed diffusely throughout both lungs, the cyst walls are thin but perceptible, and there are no associated pulmonary nodules. (Right) Axial NECT of a smoker with pulmonary Langerhans cell histiocytosis shows upper *lobe predominant pulmonary* nodules \square and pulmonary cysts 🔁; the latter exhibit thick nodular walls and bizarre shapes.





(Left) Axial CECT of a patient with lymphoid interstitial pneumonia shows thin-walled pulmonary cysts in the left lung. The differential diagnosis for this case of cystic lung disease should also include Birt-Hogg-Dubé syndrome, light-chain deposition disease, and cystic metastases. (Right) Axial CECT of a 31-year-old man with chest pain shows a water attenuation mass \implies in the visceral mediastinum with a thin enhancing wall. The findings are characteristic of bronchogenic cyst. Note trace bilateral pleural effusions 😂.
Ground-Glass Opacity

KEY FACTS

TERMINOLOGY

- Ground-glass opacity: Increased lung density or attenuation that does not obscure underlying lung architecture (i.e., bronchi, vessels)
- Mechanisms
 - Alveolar filling &/or collapse
- Interstitial thickening
- o Increased blood volume
- Combination of above mechanisms

IMAGING

• Radiography

- Hazy increased lung density that does not obscure underlying structures
- Although term may be used to describe radiographic finding, it is typically reserved to describe CT findings
- CT
 - Increased lung attenuation that does not obscure underlying bronchovascular structures

PATHOLOGY

- Etiology
- o Acute
 - Pneumonia (including *Pneumocystis jirovecii*, viral, mycoplasma), hemorrhage, edema, acute interstitial pneumonia (AIP), acute respiratory distress syndrome (ARDS), eosinophilic lung disease, radiation pneumonitis, drug toxicity, E-cigarette or vaping product use-associated lung injury (EVALI)
- o Chronic
 - Interstitial pneumonias: Nonspecific interstitial pneumonia, desquamative interstitial pneumonia, respiratory bronchiolitis, respiratory bronchiolitisassociated interstitial lung disease
 - Hypersensitivity pneumonitis, drug toxicity, radiation pneumonitis, eosinophilic lung disease, vasculitis (with associated pulmonary hemorrhage or eosinophilic lung disease), lipoid pneumonia, adenocarcinoma (preinvasive, minimally invasive, invasive)

(Left) Axial NECT of a patient with acquired immune deficiency syndrome who presented with several days of dyspnea and fever shows patchy bilateral ground-glass opacities secondary to Pneumocystis jirovecii pneumonia. (Right) Coronal NECT of a patient with mitral valve disease who presented with acute dyspnea shows bilateral ground-glass opacities and acinar groundglass nodules \implies due to pulmonary edema. Infection, hemorrhage, and edema may all manifest with ground-glass opacity.





(Left) Axial NECT of a patient who presented with chronic dyspnea shows bilateral lower lobe ground-glass opacities. Biopsy demonstrated nonspecific interstitial pneumonia. (Right) Axial NECT of a smoker who presented with chronic dyspnea and cough shows patchy bilateral ground-glass opacities and cystic changes secondary to desquamative interstitial pneumonia. Chronic lung diseases that may manifest with ground-glass opacity include idiopathic interstitial pneumonias and chronic eosinophilic pneumonia.





TERMINOLOGY

- Definition: Destroyed lung with fibrosis and cysts with fibrous walls
- Term used to describe both CT and pathologic features

IMAGING

Radiography

- o Closely approximated ring shadows
 - Cysts 3-10 mm
 - Walls 1-3 mm thick
- Subpleural reticular opacities
- CT
 - Clustered lung cysts that share their walls
 - Cysts: Subpleural and multilayered/stacked
 - Comparable cyst diameter
 - Average size: 3-10 mm
 - May be as large as 25 mm
 - Finding specific for fibrosis; diagnostic criterion for usual interstitial pneumonia (UIP)

PATHOLOGY

- Etiologies
 - Fibrosing interstitial lung diseases: Basilar, subpleural
 UIP
 - Nonspecific interstitial pneumonia
 - Other: Sarcoidosis (peribronchovascular); chronic (fibrotic) hypersensitivity pneumonitis (upper lung); acute respiratory distress syndrome (anterior, subpleural)
- Histologic findings: Remodeled fibrotic lung with cystic airspaces and loss of normal lung architecture
 - Cysts: Few mm to several cm; variable cyst wall thickness; lined by metaplastic bronchiolar epithelium

DIAGNOSTIC CHECKLIST

- Subpleural honeycombing may mimic paraseptal emphysema on CT
 - Honeycombing: Stacked layers of subpleural cysts
 - o Paraseptal emphysema: Single layer of subpleural cysts





(Left) PA chest radiograph of a patient with usual interstitial pneumonia shows low lung volume and extensive coarse bilateral reticular opacities and the suggestion of round cystic spaces with visible walls. (Right) Axial prone HRCT of a patient with usual interstitial pneumonia shows stacked layers of cysts of similar sizes that share walls and exhibit a typical lower lobe and subpleural distribution. If not associated with other diseases, the pattern indicates idiopathic pulmonary fibrosis with such certainty that lung biopsy is not required.





(Left) Low-power photomicrograph (H&E stain) of a specimen of usual interstitial pneumonia shows dense fibrosis \supseteq and honeycomb cysts 🔁, which correlate with the layered cystic spaces seen on CT. (Right) Axial HRCT of a patient with end-stage sarcoidosis shows extensive honeycombing 🔁 with peribronchovascular distribution. This distribution may occur in both end-stage sarcoidosis and fibrotic hypersensitivity pneumonitis.

Interlobular Septal Thickening

KEY FACTS

TERMINOLOGY

- Thickening of interlobular septa, which outline secondary pulmonary lobule
- Normal interlobular septa are not visible on imaging

IMAGING

• Radiography

- o Thick interlobular septa manifest as Kerley lines
- Kerley B lines: Short horizontal lines perpendicular to pleura (1.5-2 cm long)
- Kerley A lines: Lines 2-6 cm long, upper lung zones, course obliquely from hilum toward lung periphery
- Kerley C lines: Net-like branching linear opacities at lung bases; Kerley B lines seen en face
- CT/HRCT
 - Thick interlobular septa
 - o Surround and delineate secondary pulmonary lobule
 - Smooth or nodular thickening
 - o Irregular septal thickening in pulmonary fibrosis

PATHOLOGY

- Etiology
 - Smooth interlobular septal thickening
 - Interstitial edema
 - Lymphangitic carcinomatosis
 - Alveolar lipoproteinosis
 - Other interstitial lung diseases
 - Nodular interlobular septal thickening
 - Lymphangitic carcinomatosis
 - Lymphoproliferative disorder
 - Sarcoidosis, silicosis, and coal workers pneumoconiosis
 - o Irregular interlobular septal thickening
 - Pulmonary fibrosis, end-stage sarcoidosis

DIAGNOSTIC CHECKLIST

- Interstitial edema is most common cause of interlobular septal thickening
- Nodular interlobular septal thickening should suggest malignancy

(Left) Coned-down AP chest radiograph shows asymmetric alveolar and interstitial edema, manifesting as illdefined airspace disease \supseteq and as Kerley B lines \supseteq , respectively. Perihilar haze, peribronchial thickening, and right pleural effusion are additional features of edema. (Right) PA chest radiograph of a 57-year-old man with advanced malignancy shows lymphangitic carcinomatosis that manifests as asymmetric bilateral interstitial opacities with interlobular septal thickening and Kerley A and C lines.





(Left) Axial NECT of a 43-yearold man with pulmonary alveolar lipoproteinosis shows diffuse smooth interlobular septal thickening and intralobular lines on a background of ground-glass opacity, producing the characteristic crazy-paving pattern. (Right) Axial NECT of a 52-year-old woman with chronic or fibrotic hypersensitivity pneumonitis shows subpleural reticulation, scattered thick interlobular septa \blacksquare , and mosaic $attenuation igodot \sum, consistent$ with fibrosing interstitial lung disease.





TERMINOLOGY

- Fine linear opacities identified within confines of secondary pulmonary lobule
- There are no intralobular septa: Term "intralobular septal thickening" is erroneous

IMAGING

- Radiography
 - o Intralobular lines not visible
- CT/HRCT
 - Fine irregular reticular opacities separated by few mm
 - o Located within secondary pulmonary lobule
 - When numerous: Fine reticular pattern

PATHOLOGY

- Etiology
 - Idiopathic pulmonary fibrosis
 - o Nonspecific interstitial pneumonia
 - End-stage sarcoidosis

- Connective tissue disease-associated interstitial lung disease
- o Chronic (fibrotic) hypersensitivity pneumonitis
- o Asbestosis
- Other diffuse fibrotic interstitial lung diseases
- Alveolar lipoproteinosis
- Parenchymal (intralobular) interstitium: Interstitial network of thin connective tissue fibers in alveolar walls; supports secondary pulmonary lobule
- Intralobular lines: Thick intralobular interstitium, typically due to fibrosis

DIAGNOSTIC CHECKLIST

- Intralobular lines should suggest interstitial fibrosis
- Combined interlobular septal thickening and intralobular lines: Reticular opacities
- Identification of intralobular lines on thin-section CT: Low interobserver agreement





(Left) Graphic shows the parenchymal and peripheral interstitium of the secondary pulmonary lobule. The peripheral interstitium extends along the interlobular septa 🔁 and subpleural regions while the parenchymal interstitium 🔁 forms a meshwork around alveoli and alveolar sacs within the secondary pulmonary lobule. (Right) Axial HRCT of a patient with scleroderma and fibrotic nonspecific interstitial pneumonia shows profuse interlobular septal thickening $\overline{\supseteq}$, intralobular lines $\overline{\supseteq}$, and traction bronchiectasis 🚬





(Left) Axial HRCT of a patient with idiopathic pulmonary fibrosis shows fine linear and ground-glass opacities within the confines of the secondary pulmonary lobule demarcated by thickened interlobular septa ⊇. Note bilateral subpleural honeycomb cysts. (Right) Axial NECT of a 43year-old man with alveolar proteinosis shows the characteristic crazy-paving CT pattern produced by diffuse bilateral patchy ground-glass attenuation on a background of interlobular septal thickening \supseteq and fine intralobular lines $\overline{\supseteq}$.

Mass

KEY FACTS

TERMINOLOGY

- Thoracic lesion > 3 cm in maximal diameter
 Typically solid, but may exhibit necrosis &/or cavitation
- May be located in any thoracic anatomic compartment
 - o Lung, pleura, mediastinum, chest wall, diaphragm

IMAGING

- Radiography
 - Lesion identification and localization to specific thoracic anatomic compartment
 - Lung mass: Surrounded by lung, well- or ill-defined, spiculated or lobular borders
 - Pleural mass: May exhibit obtuse angles with adjacent pleura and incomplete border sign
 - Mediastinal mass: Alteration of mediastinal contours; focal vs. diffuse; lateral radiography allows localization to specific mediastinal compartment
 - Chest wall mass: Incomplete border sign; may exhibit skeletal erosion/destruction &/or soft tissue involvement

- CT
 - Lung mass: Morphologic features and clinical staging (local invasion, lymphadenopathy, metastases)
 - Pleural mass: Focal vs. multifocal; evaluation of local invasion, lymphadenopathy, pleural effusion
 - Mediastinal mass: Assessment of lesion morphology and attenuation, identification of lymphadenopathy, evaluation of local invasion
 - Chest wall mass: Assessment and characterization of degree of skeletal &/or soft tissue involvement

PATHOLOGY

- Etiology
 - Lung: Lung cancer, lung abscess, metastasis
 - Pleura: Localized fibrous tumor of pleura, metastasis
 - Mediastinum: Thymic neoplasm, neurogenic neoplasm, lymphadenopathy, congenital cyst, vascular lesion
 - Chest wall: Metastasis, chondrosarcoma, myeloma

(Left) PA chest radiograph of a 65-year-old man who presented with cough and weight loss shows a large lobulated right upper lobe lung mass. (Right) Axial CECT of the same patient shows a large right upper lobe soft tissue mass that invades the adjacent mediastinum and produces mass effect on the right upper lobe bronchus with obliteration of the lumen of the posterior segmental bronchus 乏. Lung masses usually represent malignant neoplasms, most commonly primary lung cancer.





(Left) PA chest radiograph of a 24-year-old woman with facial swelling and malaise shows a large lobulated mediastinal mass that extends to both sides of the midline and was located in the anterior mediastinum on lateral radiography (not shown). (Right) Axial CECT of a 30year-old woman with a metastatic gynecologic malignancy shows a large left anterior chest wall mass 🔁 with rib destruction. Additional sternal 🔁 and vertebral 🔁 lesions with bone destruction are consistent with chest wall metastases.





TERMINOLOGY

• Miliary pattern

- o Pulmonary micronodules of uniform size; ≤ 3 mm
- o Discrete, round, well defined
- Profuse, bilateral
- Synonym
 - o Miliary nodules
- Term "miliary"
 - Derived from "millet" seeds
 - Lung nodules with size and appearance reminiscent of millet seeds

IMAGING

Radiography

- Bilateral, tiny, discrete, often profuse pulmonary micronodules
- Diffusely distributed
- May be subtle
- Lung mass may be visible in cases of lung cancer

• CT/HRCT

- Profuse, bilateral, discrete, well-defined pulmonary micronodules
- Random (diffuse, uniform) distribution; no specific relationship to secondary pulmonary lobule structures

TOP DIFFERENTIAL DIAGNOSES

- **Perilymphatic** nodules (e.g., sarcoidosis) occasionally difficult to differentiate from miliary micronodules
- **Centrilobular** nodules (e.g., cellular bronchiolitis) do not involve pleura/fissures

PATHOLOGY

- Etiology
 - Hematogenous metastases: Thyroid and renal cell cancers, melanoma, lung adenocarcinoma
 - o Hematogenous infection: Tuberculosis, fungal infection
 - Lung adenocarcinoma, with *EGFR* mutation/exon 19 deletions





(Left) Axial NECT of an immunocompromised patient with miliary tuberculosis shows profuse pulmonary micronodules that exhibit a miliary pattern and a random distribution. The miliary pattern is consistent with hematogenous dissemination of disease, in this case, infection. (Right) PA chest radiograph of an *immunocompromised patient* with disseminated coccidioidomycosis shows bilateral, profuse, miliary micronodules, consistent with hematogenous dissemination of fungal infection.





(Left) PA chest radiograph of a patient with advanced lung adenocarcinoma shows a dominant right upper lobe mass \blacksquare and multifocal bilateral pulmonary micronodules that exhibit a miliary pattern of metastatic disease. (Right) Axial CECT of the same patient shows a right upper lobe lobulated mass 🔁 (primary lung cancer) that encases the right upper lobe bronchus 🔁. Bilateral pulmonary miliary metastases are consistent with adenocarcinoma with EGFR mutation and exon 19 deletions.

Mosaic Attenuation

KEY FACTS

TERMINOLOGY

- Mosaic attenuation
 - Heterogeneous lung attenuation with alternating areas of low and high attenuation on CT
- Synonyms: Mosaic perfusion, mosaic oligemia
- Mosaic attenuation is more inclusive preferred term

IMAGING

- Radiography
 - Typically normal chest radiography
 - ± associated findings, such as bronchiectasis
- CT/HRCT
 - Heterogeneous patchwork-like lung attenuation
 - Alternating areas of low and higher attenuation
 - ± reduced vessel caliber in areas of lung hyperlucency
 - Bronchiectasis, bronchial wall thickening, and mucus plugs should suggest airways disease
 - Expiratory thin-section CT: Identification of air-trapping secondary to bronchiolar obstruction

PATHOLOGY

- Etiology
 - Patchy interstitial lung disease: Hypersensitivity pneumonitis, bronchiectasis
 - Constrictive bronchiolitis
 - Idiopathic
 - Complication of transplantation
 - Autoimmunity: Rheumatoid arthritis, Sjögren syndrome
 - Toxic inhalational injury
 - Other: Drug-induced lung disease, recurrent infection/aspiration, Swyer-James-MacLeod, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH), inflammatory bowel disease, paraneoplastic pemphigus
 - Occlusive vascular disease: Chronic pulmonary thromboembolism, pulmonary hypertension

(Left) Axial NECT of a patient with subacute (nonfibrotic) hypersensitivity pneumonitis shows mild diffuse mosaic attenuation of the lung parenchyma. This pattern of mosaic attenuation may be accentuated by expiratory imaging. (Right) Axial NECT of a patient with subacute (nonfibrotic) hypersensitivity pneumonitis shows heterogeneous lung attenuation with a patchwork of lower and higher attenuation areas. In this case, heterogeneity may be accentuated by patchy ground-glass opacity.





(Left) Axial NECT of a patient with cystic fibrosis shows bilateral mosaic attenuation/perfusion with areas of low attenuation \supseteq alternating with areas of higher attenuation \supseteq . Note bronchiectasis, bronchial wall thickening, and mucus plugs ■. (Right) Coronal CECT of a patient with chronic pulmonary thromboembolic disease shows mosaic attenuation/perfusion. Note enlarged blood vessel caliber \blacksquare in high-attenuation areas. Mosaic attenuation may occur with small airways or occlusive vascular diseases.





TERMINOLOGY

- Nodule
 - Rounded opacity with variable border characteristics
 - o Size: ≤ 3 cm
- Micronodule
 - Rounded opacity that measures < 3 mm

IMAGING

Radiography

- Rounded opacity (≤ 3 cm) surrounded by lung • May exhibit calcification or cavitation
- CT
 - Rounded opacity (\leq 3 cm) with variable borders • Nodules characterized as solid or subsolid
 - Solid nodules are of soft tissue attenuation
 - Subsolid nodules
 - □ Ground-glass (nonsolid) attenuation
 - □ Part-solid with both ground-glass and solid attenuation components

PATHOLOGY

- Etiology
 - Solitary pulmonary nodule – Granuloma
 - - Lung cancer, preinvasive lesion
 - Carcinoid
 - Hamartoma
 - Multiple diffuse micronodules
 - Characterized by distribution: Centrilobular, perilymphatic, or random

DIAGNOSTIC CHECKLIST

- Solitary nodules characterized as likely benign, possibly malignant, or indeterminate
 - Indeterminate nodules require further evaluation with follow-up imaging &/or tissue sampling
- Follow-up of solid and subsolid nodules based on Fleischner Society guidelines according to risk factors and size (including size of solid and nonsolid components)





(Left) PA chest radiograph of an asymptomatic 72-year-old woman demonstrates a subtle incidentally discovered spiculated left upper lobe solitary pulmonary nodule 🖂. There are no other radiographic abnormalities. (Right) Axial NECT of the same patient shows a left upper lobe spiculated solid nodule ightarrow with pleural tags and a small eccentric focus of cavitation anteriorly. These findings are highly suspicious for primary lung cancer. This nodule is amenable to imageguided percutaneous biopsy.





(Left) Axial CECT of an asymptomatic 80-year-old woman shows an incidentally discovered right upper lobe part-solid nodule \supseteq with spiculated borders, pleural tags, and a dominant solid component. Invasive adenocarcinoma was diagnosed at surgical excision. (Right) Axial NECT of a 40year-old asymptomatic woman shows an incidentally discovered left lower lobe subsolid ground-glass nodule *, which persisted on follow*up imaging. Atypical adenomatous hyperplasia was diagnosed at surgical excision.

Peribronchovascular

KEY FACTS

TERMINOLOGY

- Diseases that characteristically involve the peribronchovascular interstitium
- Peribronchovascular and perilymphatic distributions often coexist given anatomic continuum of lymphatic channels

IMAGING

- Radiography
 - Central pulmonary opacities
 - Peribronchial cuffing
- CT
 - o Bronchial wall thickening, nodularity
 - Perivascular thickening (optimally characterized with IV contrast)
 - Perivascular nodularity
 - Peribronchovascular consolidation
 - Peribronchial/perivascular lucency
 - Perilymphatic findings often coexist: Septal and fissural thickening &/or nodularity

PATHOLOGY

- Peribronchovascular infiltration
 - o Extravascular water, blood
 - Infection, granulation tissue
 - o Tumor
- o Air
- Etiologies
 - Hydrostatic pulmonary edema
 - Organizing pneumonia
 - Bronchopneumonia
 - o Kaposi sarcoma
 - Mucosa-associated lymphoid tissue lymphoma (MALToma)
 - o Pulmonary interstitial emphysema
 - o Interstitial pulmonary arterial hemorrhage

DIAGNOSTIC CHECKLIST

• Recognition of peribronchovascular pattern requires knowledge of anatomy of secondary pulmonary lobule

(Left) Axial NECT of a patient with cardiogenic pulmonary edema shows bilateral peribronchovascular consolidations with subpleural sparing. The process is typically peribronchovascular with later progression to involvement of the peripheral interstitium. (Right) Axial NECT of a patient with S. aureus bronchopneumonia shows patchy bilateral peribronchovascular These abnormalities may later progress to involve the bilateral lungs more extensively.





(Left) Axial HRCT of a patient with cryptogenic organizing pneumonia shows multifocal irregular peribronchovascular nodules ⇒ in the left lung. A frequent imaging pattern of organizing pneumonia is the presence of

peribronchovascular nodules, as shown in this case. (Right) Axial CECT of a patient with AIDS-related Kaposi sarcoma shows multifocal bilateral illdefined spiculated peribronchovascular nodules that exhibit a characteristic flame-shaped morphology

that exhibit a characteristic flame-shaped morphology and spare the subpleural lung parenchyma.





TERMINOLOGY

- Airspace disease distributed around 1 or more involved or normal secondary pulmonary lobules
 - Reversed halo sign likely represents manifestation of perilobular pattern/distribution
 - Processes that produce lung necrosis may exhibit similar morphologic appearance

IMAGING

- Radiography
 - Ill-defined pulmonary opacities; perilobular distribution not identifiable
- CT
 - Consolidation &/or ground-glass opacity distributed around 1 or more secondary pulmonary lobules
 - Patchy peribronchovascular opacities; often spare adjacent secondary pulmonary lobules
 - Reversed halo sign: Consolidation surrounding groundglass opacity or normal/relatively normal lung

PATHOLOGY

- Perilobular pattern thought to correlate with organizing pneumonia, poor histologic confirmation, as most cases are not biopsied
- Etiologies
 - Organizing pneumonia
 - Acute lung injury due to SARS-CoV-2 (COVID-19)
 - Infections including viral, bacterial, fungal (influenza, *Legionella*)
 - Idiopathic
 - E-cigarette or vaping use-associated lung injury
- Pulmonary infarction: Thromboembolic disease, vasculitis
- o Eosinophilic pneumonia

CLINICAL ISSUES

- Perilobular pattern is common in organizing pneumonia
- Whether identification of perilobular pattern is indication for steroid treatment remains to be determined





(Left) Axial CECT of a patient with acute lung injury related to COVID-19 shows peripheral predominant patchy groundglass opacities \supseteq that spare adjacent secondary pulmonary lobules \square , the so-called perilobular pattern. (Right) Axial CECT of a patient with cryptogenic organizing pneumonia shows a right lower lobe peripheral $consolidation \supseteq$ with intrinsic lucency that corresponds to a relatively spared secondary pulmonary lobule 🔁.





with acute lung injury due to Influenza type A infection shows extensive bilateral ground-glass opacities and consolidations that spare a few secondary pulmonary lobules 🔁 (Right) Coronal CECT of a patient with Rhinovirus infection shows extensive upper lobe predominant ground-glass opacities that spare subpleural secondary pulmonary lobules 🔁. While the perilobular pattern may be nonspecific, organizing pneumonia should be strongly considered in the differential diagnosis.

(Left) Axial CECT of a patient

Perilymphatic

KEY FACTS

TERMINOLOGY

• Abnormalities distributed along peripheral (i.e., subpleural and interlobular) and axial (i.e., peribronchovascular and centrilobular) interstitium

IMAGING

- Thick axial interstitium
 - Peribronchovascular interstitium
 - Peribronchial (bronchial wall) thickening
 - Perivascular thickening/nodularity: Pipe-cleaner sign (beaded bronchovascular bundles)
 - Perivascular thickening
 - o Centrilobular interstitium
 - Centrilobular nodules/micronodules
- Thick peripheral interstitium
 - Subpleural: Pleural and fissural
 - Nodularity
 - Pleural thickening
 - Pleural pseudoplaques (aggregated micronodules)

- o Interlobular
 - Nodular (beaded) &/or smooth septal lines (Kerley B lines on radiography)

PATHOLOGY

- Etiologies
 - Lymphangitic carcinomatosis
 - o Sarcoidosis
 - Pneumoconiosis (silicosis and coal worker's)
 - o Amyloidosis (alveoloseptal)
 - o Pulmonary edema (interstitial)
- Histologic features
 - Perilymphatic distribution correlates with anatomic distribution of pulmonary lymphatics
 - Pulmonary lymphatics course along axial and peripheral interstitium
 - Microscopic distribution of granulomas, cellular infiltrates, neoplastic processes, edema fluid (extravascular water)

(Left) Graphic shows the anatomic distribution of perilymphatic nodules located along pulmonary lymphatics about bronchovascular bundles 🔁 (i.e., axial interstitium), interlobular septa 🔁, and subpleural 🔁 regions (i.e., peripheral interstitium). (Right) Axial CECT of a patient with sarcoidosis shows bilateral perilymphatic micronodules manifesting with nodular 🔁 and smooth 🖂 septal lines, the pipe-cleaner sign 🔁 (i.e., peribronchovascular thickening and nodularity), and fissural nodularity 🔁.





(Left) Axial NECT of a patient with clear cell vaginal adenocarcinoma and lymphangitic carcinomatosis shows smooth and nodular septal lines *⊡*, polygonal arcades 🔁 as well as centrilobular 🔁, and fissural micronodules 🔁. (Right) Lowpower photomicrograph (H&E stain) of a transbronchial biopsy specimen from a patient with breast cancer and lymphangitic carcinomatosis shows nodular deposits of neoplastic cells 🔁 along perivascular 🔁 and interlobular septal lymphatics





TERMINOLOGY

• **Pneumatocele**: Thin-walled, gas-filled space surrounded by lung parenchyma: May be single or multiple

IMAGING

- Radiography
 - o Thin-walled, air-filled structure in lung parenchymao May not be visible on radiography
- CT
 - Focal or multifocal thin-walled air-filled
 - May be indistinguishable from cysts or bullae
 - Identification of subtle pneumatocele(s)
 - Assessment of associated abnormalities: Ground-glass opacity, consolidation, pneumothorax

PATHOLOGY

- Etiology
 - o Infection: Pneumocystis, Staphylococcus, COVID-19

- Trauma (children, young adults): Associated contusion, laceration, pneumothorax, pneumomediastinum
- Hydrocarbon inhalation/aspiration
- o Surgery, mechanical ventilation, endobronchial valveso Other: Burns, interstitial pulmonary emphysema
- Proposed mechanisms
 - Check-valve airway obstruction with peripheral overinflation
 - Extrusion of necrotic lung followed by check-valve airway obstruction and peripheral overinflation
 - Interstitial air that migrates into adjacent lung due to inflammation/necrosis of airway wall

CLINICAL ISSUES

- Complications
 - o Infection: Intrinsic air-fluid levelo Rupture into pleural space: Pneumothorax
- Natural history: Size may increase (days to weeks), complete resolution is typical (months to years)





(Left) PA chest radiograph of an asymptomatic patient evaluated for resolving pulmonary infection shows a well-defined, thin-walled, airfilled cystic structure 🔁 in the right lower lobe. Based on the evolution of the abnormality, the presumptive diagnosis of pneumatocele was made. (Right) Axial NECT of the same patient demonstrates the right lower lobe pneumatocele 🔁 that is characterized by intrinsic air and a thin wall. Note patchy middle lobe centrilobular ground-glass opacities , consistent withresolving pulmonary infection.





(Left) Axial NECT shows a left upper lobe pneumatocele manifesting as a large, thinwalled pulmonary cyst containing an air-fluid level. Pneumatoceles are indistinguishable from bullae on imaging, but typically resolve with time. (Right) Axial NECT of a patient with HIVrelated Pneumocystis pneumonia shows right upper lobe ground-glass opacities and several thin-walled, airfilled cystic structures \square , consistent with pneumatoceles. Affected patients are at risk for spontaneous pneumothorax.

Reticular Pattern

KEY FACTS

TERMINOLOGY

• Reticular pattern

- Multiple interlacing irregular linear opacities
- Fine, medium, coarse reticulation
- Indicative of interstitial fibrosis

IMAGING

• Radiography

- Multiple irregular linear opacities, resembling fisherman's net
- ± volume loss
- Cystic lung disease with summation of cyst walls may produce similar pattern
- CT/HRCT
 - o Intralobular lines
 - Irregular interlobular septal thickening
 - Traction bronchiectasis/bronchiolectasis
 - Architectural distortion
 - Honeycombing

• Reticulonodular pattern: Summation of reticular and micronodular patterns

PATHOLOGY

- Etiology
 - Idiopathic pulmonary fibrosis
 - o Nonspecific interstitial pneumonia
 - Connective tissue disease-associated interstitial lung disease
 - Chronic (fibrotic) hypersensitivity pneumonitis
 - End-stage sarcoidosis
 - o Asbestosis
- Reticular opacities correlate with interstitial fibrosis on histology
- Reticular pattern does not indicate honeycombing

DIAGNOSTIC CHECKLIST

• HRCT: Optimal modality for evaluating symptomatic patients with reticular pattern on radiography

(Left) PA chest radiograph of an older patient with idiopathic pulmonary fibrosis shows low right lung volume and a fine bibasilar reticular pattern. (Right) Coronal NECT of the same patient shows that the basilar reticular pattern seen on radiography corresponds to basilar subpleural reticulation, honeycomb cysts, and traction bronchiectasis. Although visualization of the reticular pattern does not necessarily correlate with honeycombing, in this case, some of the reticulations correspond to fibrosis and honeycombing.











TERMINOLOGY

- Secondary pulmonary lobule (SPL): Smallest discrete unit of lung structure marginated by connective tissue septa and supplied by lobular bronchiole and artery
- Components
 - o Lobular core: Lobular bronchiole, artery, and lymphatics
 - Typically contains ≤ 12 acini (range: 3-24)
- Size: 1-2.5 cm
- Morphology
 - Cuboidal or pyramidal in lung periphery
 - Hexagonal or polygonal in central lung
- Boundaries: Interlobular septa

IMAGING

- Radiography: SPL not visible in normal subjects
- CT/HRCT
 - Normal lobular artery may be visible centrally in SPL
 - Location of normal interlobular septa inferred by identification of peripheral pulmonary veins

- Imaging of Abnormal SPL
 - o Interlobular septal thickening
 - Smooth
 - Interstitial edema, lymphangitic carcinomatosis
 Nodular
 - Lymphangitic carcinomatosis, sarcoidosis, silicosis
 Irregular: Interstitial fibrosis
 - All may exhibit thickened centrilobular interstitium
 - Centrilobular abnormalities
 - Increased attenuation: Cellular bronchiolitis
 - Decreased attenuation: Centrilobular emphysema
 - Panlobular abnormalities
 - Increased attenuation: Lobular pneumonia
 - Decreased attenuation: Hypersensitivity pneumonitis, constrictive bronchiolitis, panlobular/paraseptal emphysema
 - Diffuse pulmonary micronodules: Characterized by distribution with respect to SPL as centrilobular, perilymphatic, or random





(Left) Graphic shows secondary pulmonary lobules bound by interlobular septa 🔁. A bronchiole 乏, a pulmonary artery $\overline{ \boldsymbol{ \boldsymbol{ 2 } } }$, and pulmonary lymphatics in the lobular core are surrounded by a connective tissue sheath \supseteq . (Right) Graphic depicts the secondary pulmonary lobule as seen on thin-section CT. The location of interlobular septa and the center of the lobule are inferred by identification of pulmonary veins \supseteq and the dot-like lobular artery 🔁 respectively. The lobular bronchiole \ge is not normally visible on CT.





(Left) Axial NECT shows normal secondary pulmonary lobules, including dot-like central lobular arteries \square and peripheral pulmonary veins 🖂 coursing within interlobular septa. (Right) Axial CECT of a 37-year-old woman with interstitial edema shows smooth interlobular septal thickening. Edema fluid manifests with thick interlobular septa 🔁 that outline basilar secondary pulmonary lobules and increased conspicuity of central lobular arteries \rightarrow due to thickened centrilobular interstitium.

Traction Bronchiectasis

KEY FACTS

TERMINOLOGY

- Traction bronchiectasis: Nonuniform bronchial dilatation caused by fibrosis
- Traction bronchiolectasis: Nonuniform bronchiolar dilatation secondary to fibrosis

IMAGING

- Radiography
 - Insensitive for identification of bronchiectasis
 - Clustered ring shadows &/or tram-line opacities with architectural distortion
- CT/HRCT
 - $\circ~$ Irregular bronchial dilatation \pm bronchial wall thickening
 - Traction bronchiolectasis: Dilated small subpleural airways located within 1-2 cm from pleural surface
 - May manifest as cysts or microcysts and may be difficult to differentiate from honeycombing
 - Assessment of associated architectural distortion, reticular opacities, honeycombing

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic pulmonary fibrosis
- Nonspecific interstitial pneumonia
- End-stage sarcoidosis
- Chronic (fibrotic) hypersensitivity pneumonitis
- Radiation fibrosis
 - Develops > 12 months post treatment
 - Abnormalities typically conform to radiation ports
- Late sequela of acute respiratory distress syndrome

PATHOLOGY

• Peribronchial/peribronchiolar retractile fibrosis versus bronchiolar proliferation

DIAGNOSTIC CHECKLIST

- Identification of traction bronchiectasis allows diagnosis of fibrosis in absence of honeycombing
- Poor prognosis in fibrotic interstitial lung disease
- Moderate interobserver agreement

(Left) Coronal NECT of a patient with idiopathic pulmonary fibrosis shows architectural distortion, honeycombing 🖂, right midlung zone traction bronchiectasis \blacksquare , and right basilar traction bronchiolectasis \supseteq . (Right) Axial NECT of a patient with scleroderma and nonspecific interstitial pneumonia shows mild diffuse bilateral groundglass attenuation, basilar traction bronchiectasis \rightarrow , and traction bronchiolectasis \bowtie , the latter characterized by dilated airways within 1-2 cm of the pleural surface.





(Left) Axial NECT of a patient with scleroderma and fibrotic nonspecific interstitial pneumonia shows bibasilar traction bronchiectasis \supseteq and bronchiolectasis 🔁 with adjacent reticular opacities, indicating fibrosis. (Right) Composite image with axial CECT of a patient who is 24 months post stereotactic body radiation therapy for lung cancer shows right lung paramediastinal cicatricial atelectasis with intrinsic irregular dilated bronchi 🖂 Findings of radiation fibrosis typically conform to the therapy port.





TERMINOLOGY

• CT pattern of centrilobular micronodules and branching opacities that resemble budding tree

IMAGING

- CT/HRCT
 - Centrilobular micronodules and branching opacities
 Y- or V-shaped
 - Characteristic subpleural lung sparing

TOP DIFFERENTIAL DIAGNOSES

- Perilymphatic nodules (e.g., sarcoidosis) involve fissures
- Miliary nodules (e.g., miliary infection): Random distribution

PATHOLOGY

- Etiology
 - o Small airways disease
 - Infectious bronchiolitis
 - □ Acute: Viral, bacterial (e.g., *Mycoplasma*), fungal

- □ Chronic: Tuberculosis, nontuberculous mycobacterial infection
- Aspiration bronchiolitis
 - Esophageal dysmotility, hiatus hernia, esophageal/gastric interventions, head and neck cancer
 - Lentil (leguminous vegetables) aspiration pneumonia
- Follicular bronchiolitis
 - Immunodeficiency, connective tissue disease (e.g., rheumatoid arthritis)
- Diffuse panbronchiolitis
 - Population of Asian descent
- Vascular diseases
 - Excipient lung disease: Intravenous injection of crushed oral tablets
- Tumor embolism or thrombotic microangiopathy
- Centrilobular distribution: Occur at center of secondary pulmonary lobule





(Left) Graphic shows the morphology and distribution of centrilobular micronodules and tree-in-bud branching opacities, which spare the subpleural lung , a characteristic feature of centrilobular processes, such as infectious or aspiration bronchiolitis. (Right) Axial NECT MIP reformatted image shows infectious bronchiolitis manifesting as centrilobular micronodules and branching tree-in-bud opacities ≥. Pulmonary veins \supseteq course within interlobular septa 🖂, which manifest as lowattenuation bands.





(Left) Coronal NECT MIP reformatted image of a patient with infectious bronchiolitis shows bilateral tree-in-bud opacities and multifocal left upper lobe lobular consolidations 🔁 that represent areas of associated bronchopneumonia. (Right) Axial NECT of a patient with aspiration bronchiolitis shows bilateral lower lobe predominant centrilobular micronodules and tree-in-bud opacities \supseteq that spare the subpleural and septal lung parenchyma. Note associated right lower lobe nodular consolidation 🖂

Introduction

The term "Aunt Minnie," coined by Dr. Ed Neuhauser and popularized by Dr. Benjamin Felson, refers to a constellation of radiologic findings that are considered virtually pathognomonic by gestalt (i.e., even my Aunt Minnie could make the diagnosis). In psychology, the gestalt theory refers to a holistic perception where the mental whole is greater than the sum of its components. For example, one recognizes an individual's face as a whole rather than as a sum of the eyes, nose, mouth, etc.. The recognition of radiographic and CT signs as characteristic of a given disease process is an excellent example of recognizing an "Aunt Minnie." The perception of such findings by gestalt facilitates a correct diagnosis. Radiologists should gain familiarity with the various imaging signs in order to expedite diagnosis and positively impact patient care.

CT Angiogram Sign

The CT angiogram sign is the visualization of enhancing vessels within a parenchymal opacity on CECT. This sign was originally thought to be specific for lepidic adenocarcinoma (formerly referred to as bronchioloalveolar carcinoma) but may be seen in a variety of processes (e.g., pneumonia, pulmonary edema, postobstructive pneumonitis, lymphoma, metastases). Absence of the angiogram sign implies derangement of the architecture of the underlying lung parenchyma.

Continuous Diaphragm Sign

The continuous diaphragm sign of pneumomediastinum consists of a continuous linear lucency extending across the midline above the diaphragm, a finding that results from mediastinal air tracking posterior to the heart. It is helpful in differentiating pneumomediastinum from pneumoperitoneum.

Crazy-Paving Sign

Crazy-paving refers to interlobular septal thickening and intralobular lines superimposed on ground-glass attenuation on thin-section CT and often exhibits a geographic distribution demarcated by normal lung. Initially described as characteristic of alveolar proteinosis, this sign can be present in a multitude of other processes, including pulmonary edema, alveolar hemorrhage, infection (e.g., pneumocystis pneumonia), and lipoid pneumonia.

Double Density Sign

The double density sign refers to increased right retrocardiac opacity with a convex lateral interface with the adjacent lung as seen through the right heart on frontal chest radiography and represents left atrial enlargement. A distance of > 7 cm between this interface and the left mainstem bronchus is considered confirmatory.

Doughnut Sign

Normally, the combined opacities of the aortic arch and the right and left pulmonary arteries manifests on the lateral chest radiograph as a horseshoe-shaped opacity. When there is subcarinal lymphadenopathy, the horseshoe-shaped opacity is completed inferiorly and resembles the morphology of a doughnut surrounding the central airways.

Feeding Vessel Sign

The feeding vessel sign refers to the finding of a pulmonary artery leading directly into a nodule or mass and often indicates hematogenous dissemination of disease (e.g., septic embolism, metastases, arteriovenous malformation, and, occasionally, lung cancer and granuloma).

Fleischner Sign

The Fleischner sign refers to proximal pulmonary artery enlargement on frontal chest radiography in the setting of often massive ipsilateral pulmonary embolism.

Hampton Hump

The Hampton hump refers to a lower lobe triangular or rounded subpleural opacity with its apex directed toward the ipsilateral hilum and represents the radiographic visualization of a peripheral pulmonary infarct.

Juxtaphrenic Peak Sign

The juxtaphrenic peak is a finding associated with upper lobe atelectasis and consists of a triangular opacity based on the ipsilateral hemidiaphragm at or near its highest point with the apex oriented superiorly. It is commonly seen in the presence of an inferior accessory fissure and is thought to represent superior retraction of that fissure with tethering of the diaphragmatic pleura and subpleural fat.

Split Pleura Sign

The nonfissural pleural surfaces are barely perceptible on CT. Separation of thickened enhancing visceral and parietal pleura by intervening fluid is known as the spilt pleura sign. Visualization of the "split pleura" is concerning for empyema but may be seen in other exudative pleural effusions (e.g., malignant effusion, hemothorax, postsurgical pleural effusion, and in other etiologies of chronic pleural fluid).

Subpleural Curvilinear Line Sign

The subpleural curvilinear line refers to a linear opacity that measures 1-3 mm in thickness and is located < 1 cm from and parallel to the pleura. This sign may be a manifestation of dependent atelectasis, pulmonary edema, pulmonary fibrosis, or asbestosis. When isolated, this abnormality should raise suspicion for asbestosis, and a careful search of other findings of asbestos exposure is recommended.

Tree-in-Bud Sign

The tree-in-bud sign refers to solid centrilobular nodules with contiguous short branching lines on thin-section CT. There is typically sparing of the subpleural and interlobar interstitium. This pattern is very common in bronchiolitis, particularly infectious bronchiolitis, but is rarely seen in the setting of arteriolar diseases (e.g., tumor emboli, talc or cellulose-induced granulomatosis, etc.).

Westermark Sign

The Westermark sign refers to unilateral lung hyperlucency on radiography or hypoattenuation on CT corresponding to oligemia distal to an occlusive pulmonary embolus.

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CT Angiogram Sign



CT Angiogram Sign



(Left) Oblique axial CECT of a patient with lung adenocarcinoma shows the CT angiogram sign that manifests with enhancing branching vessels that course within the lung mass and indicate preservation of the lung architecture within the infiltrative neoplasm. (Right) Oblique CECT of a patient with Klebsiella pneumonia shows the coexistence of the CT angiogram sign \blacksquare in the medial aspect of the consolidation and its absence in an area of decreased enhancement due to tissue

Continuous Diaphragm Sign



Continuous Diaphragm Sign



Continuous Diaphragm Sign

(Left) PA chest radiograph of a patient who presented with , chest pain and pneumomediastinum shows a horizontal linear lucency \supseteq extending across the midline and above the diaphragm, the so-called continuous diaphragm sign. Note bilateral supraclavicular subcutaneous gas. This should be differentiated from the cupola sign of pneumoperitoneum that manifests as an upper abdominal arcuate lucency. (Right) Sagittal CECT of the same patient shows extensive pneumomediastinum with retrocardiac involvement *⊡*.



Continuous Diaphragm Sign



(Left) AP chest radiograph of a patient involved in a motor . vehicle collision shows a pneumomediastinum that manifests with linear lucency surrounding the heart and the continuous diaphragm sign *⊡*. (Right) Axial CECT of the same patient shows a predominantly anterior pneumomediastinum that corresponds to the lucency surrounding the heart on radiography. Pneumomediastinum located posterior to the heart \square produces the continuous diaphragm sign on

radiography.

(Left) Axial HRCT of a patient with pulmonary alveolar proteinosis shows bilateral geographic areas of groundglass opacity on a background of interlobular septal thickening and intralobular lines, the so-called crazypaving sign. (Right) Axial HRCT of a patient with exogenous lipoid pneumonia shows multifocal bilateral geographic ground-glass opacities on a background of interlobular septal thickening and intralobular lines, the socalled crazy-paving sign, an atypical manifestation of lipoid pneumonia.

Crazy-Paving Sign



Crazy-Paving Sign



(Left) PA chest radiograph of a patient with severe mitral stenosis shows cardiomegaly and the double density sign, a laterally convex retrocardiac interface 🖻 medial to the right heart border \supseteq , due to left atrial enlargement. Note associated enlargement of the left atrial appendage 🛃 manifesting as a convexity along the upper left heart border. (Right) Axial CECT of the same patient shows marked dilatation of the left atrium with its right lateral border *⊡* located posterior and medial to the lateral wall of the right atrium \blacksquare .

Double Density Sign

Double Density Sign





Doughnut Sign



Doughnut Sign



(Left) PA chest radiograph of a patient with sarcoidosis shows bilateral hilar ➡, right paratracheal 🔼, and aortopulmonary window 🛃 lymphadenopathy. (Right) Lateral chest radiograph of the same patient shows subcarinal lymphadenopathy ∠ that manifests with infrahilar window opacity and produces the doughnut sign. The "doughnut" is formed by the aortic arch superiorly, the right and left hila anteriorly and posteriorly (respectively), and subcarinal

lymphadenopathy inferiorly.

Overview of Chest Imaging

Doughnut Sign





(Left) PA chest radiograph of a patient with metastatic renal cell carcinoma shows bilateral hilar 🔁 and right paratracheal 🔁 lymphadenopathy. (Right) Lateral chest radiograph of the same patient shows subcarinal lymphadenopathy \implies that manifests with opacity in the infrahilar window and produces the socalled doughnut sign. While nonspecific, symmetric mediastinal and hilar lymphadenopathy is a recognized manifestation of metastatic renal cell carcinoma.

Feeding Vessel Sign



Feeding Vessel Sign

(Left) Coronal CECT of a patient with septic embolism shows multifocal coexistent cavitary and solid pulmonary nodules. Several pulmonary artery branches course directly into some of the nodules, the so-called feeding vessel sign ► (Right) Composite image with axial (left) and MIP reformatted (right) CECT of a patient with an arteriovenous . malformation shows a right lower lobe nodule that exhibits the feeding vessel sign ■. MIP image demonstrates afferent and efferent pulmonary vessels, confirming the diagnosis.

Hampton Hump





Hampton Hump

(Left) PA chest radiograph of a patient with pulmonary thromboembolic disease shows a left lower lobe Hampton hump characterized by a peripheral subpleural $opacity \blacksquare$, corresponding to a pulmonary infarct. (Right) Composite image with axial CECT of the same patient shows a segmental left lower lobe pulmonary embolus 🛃 and a peripheral triangular subpleural opacity 🛃 with its apex oriented toward the left hilum and central lucencies, the latter indicative of necrosis and characteristic of a pulmonary infarct.

Overview of Chest Imaging

(Left) PA chest radiograph of a patient with complete right upper lobe atelectasis 🔁 secondary to primary lung cancer shows the juxtaphrenic peak sign 🛃, believed to result from upward retraction of the inferior accessory fissure, adjacent visceral and diaphragmatic pleura, and subpleural fat. (Right) Lateral chest radiograph of the same patient demonstrates anterosuperior shift of the major 🔁 fissure, also consistent with right upper lobe atelectasis. Note the juxtaphrenic peak 🛃.

Juxtaphrenic Peak Sign



Juxtaphrenic Peak Sign



(Left) PA chest radiograph of a patient with metastatic lung cancer and right upper lobe atelectasis shows the juxtaphrenic peak sign 🛃, which frequently occurs in right upper lobe atelectasis but may also be seen in left upper and middle lobe atelectasis. (Right) Coronal CECT of the same patient shows the morphologic features of the juxtaphrenic peak sign 🛃 formed by retraction of the inferior accessory fissure secondary to right upper lobe atelectasis 🛃. Note multifocal bilateral pulmonary metastases.

Juxtaphrenic Peak Sign

Juxtaphrenic Peak Sign





(Left) Axial NECT of a patient who presented with fever due to empyema shows a loculated left basilar pleural effusion. Note thickening and enhancement of the visceral \triangleright and parietal \triangleright pleura, forming the so-called split pleura sign. While this sign is always concerning for empyema, it may also be seen in chronic pleural effusions. (Right) Axial HRCT of a patient with asbestosis shows the subpleural curvilinear line sign that manifests as a thin parenchymal linear opacity that parallels the pleura igsquareand pleural plaques \supseteq .

Split Pleura Sign



Subpleural Curvilinear Line Sign



Overview of Chest Imaging

Tree-in-Bud Sign





Tree-in-Bud Sign

(Left) Axial HRCT of a patient with active tuberculosis shows clustered solid centrilobular micronodules and branching tree-in-bud opacities in the lower and right upper lobes, consistent with endobronchial dissemination of infection. Tree-in-bud opacities are a common CT feature of active tuberculosis. (Right) Axial HRCT of a patient with lentil aspiration bronchiolitis shows bilateral centrilobular and tree-in-bud opacities, more conspicuous in the right upper lobe.

Tree-in-Bud Sign



Tree-in-Bud Sign

(Left) Axial HRCT of an Asian patient with panbronchiolitis shows multifocal tree-in-bud opacities, right upper lobe bronchial wall thickening, and mosaic attenuation. Panbronchiolitis typically manifests with tree-in-bud opacities. (Right) Coronal CECT of a patient with cellulose granulomatosis shows extensive tree-in-bud opacities. Rarely, as in this case, the tree-in-bud sign may be secondary to arteriolar processes.

Westermark Sign







(Left) PA chest radiograph of a patient with pulmonary embolism who presented with chest pain and dyspnea shows relative hyperlucency of the right hemithorax as compared to the left due to right lung oligemia, the so-called Westermark sign. (Right) Coronal CECT MIP reformatted image of the same patient better demonstrates the right pulmonary oligemia and shows a large embolus 乏 in the right pulmonary artery. The Westermark sign may be subtle and difficult to detect on radiography.

Air Crescent Sign

KEY FACTS

TERMINOLOGY

- Definition: Crescent-shaped or circumferential radiolucency surrounding a nodule or mass
- Synonyms
 - o Meniscus sign
 - Monod sign: Typically used for fungus ball or mycetoma

IMAGING

- Mass or nodule surrounded by peripheral crescent-shaped radiolucency
- Mass or nodule within a lung cavity

TOP DIFFERENTIAL DIAGNOSES

- Abscess: Often completely air-filled or with air-fluid level
- Infarct: May cavitate and exhibit air or air-fluid level
- Infection: Tuberculosis, nocardiosis
- Malignancy: Cavitary necrotic neoplasm

PATHOLOGY

- Etiology: Angioinvasive aspergillosis, mycetoma within preexistent cavity (e.g., tuberculosis, sarcoidosis, bronchiectasis, lung cancer), hydatid disease
 - Angioinvasive aspergillosis: Arterial thrombosis and lung infarction
 - Preexistent cavity: Saprophytic fungus/fungus ball
 - Hydatid disease: Airway erosion by hydatid cyst

CLINICAL ISSUES

- Classically described in recovery phase of angioinvasive aspergillosis
- Also described in mycetoma within preexistent cavity

DIAGNOSTIC CHECKLIST

• Most cases of air crescent sign seen in clinical practice are secondary to mycetoma within preexistent cavity

(Left) Composite image with PA chest radiograph (left) and axial NECT (right) of a patient with sarcoidosis shows a right upper lobe mycetoma \supseteq that developed in a preexisting cavity and exhibits the air crescent sign 🔁. (Right) Composite image with axial NECT obtained in the supine (left) and prone (right) positions shows a patient with a right lower lobe mycetoma secondary to nontuberculous mycobacterial infection. Note the nondependent air crescent sign and migration of the fungus ball to the dependent portion of the cavity.





(Left) Composite image with PA chest radiograph (left) and axial NECT (right) of a patient with cavitary right upper lobe lung cancer shows a mycetoma within the cavity and the air crescent sign \square . (Right) Composite image with PA chest radiographs of 2 different patients shows a $mycetoma \ge in a cavity$ secondary to nontuberculous mycobacterial infection (left) and a complicated hydatid cyst with impending rupture \supseteq . Both lesions exhibit the air crescent sign. (Courtesy P. Boiselle, MD.)





TERMINOLOGY

- Obscuration of abnormal mediastinal or paramediastinal contours as they extend above the clavicles into neck on frontal chest radiography
- Implies lesion location in both thorax and neck
- Corollary 1: Any mediastinal mass that extends into neck typically exhibits cervicothoracic sign
- Corollary 2: Upper posterior mediastinal or paravertebral masses are located completely within chest and do not exhibit cervicothoracic sign

IMAGING

- PA/AP chest radiography
 - Obscuration of lesion's contours as it extends cephalad to clavicles
- CT
 - o Mediastinal or paramediastinal lesion location
 - Documentation of affected mediastinal compartment
 - Confirmation of extension of mass into neck

TOP DIFFERENTIAL DIAGNOSES

- Completely intrathoracic upper paravertebral masses (that do not exhibit cervicothoracic sign)
 - PA/AP chest radiography demonstrates well-defined lesion contours above clavicles
 - Classically seen in neurogenic neoplasms

DIAGNOSTIC CHECKLIST

- Caudal portion of mass outlined by aerated lung
- Cephalad portion of mass obscured by surrounding neck soft tissues
- Etiology
 - Intrathoracic thyroid masses (common)
 - Tortuous head/neck vessels (common)
 - o Lymphoma
 - o Lymphangioma
 - o Mediastinal hematoma
 - Head/neck vessel aneurysm
 - Superior sulcus (Pancoast) tumor





(Left) Coned-down PA chest radiograph of a patient with a large thyroid goiter with intrathoracic extension shows widening of the upper mediastinum. Note the bilateral well-defined borders of the lesion $\overline{\square}$, which "disappear" 🔁 above the level of the clavicles as the mass loses its interface with the lung and courses into the neck, the so-called cervicothoracic sign. (Right) Coronal oblique CECT reformation of the same patient shows a large intrathoracic goiter \supseteq and its relationship with the lung.





(Left) Coned-down PA chest radiograph of a patient with a tortuous brachiocephalic trunk shows an abnormal convexity along the right upper mediastinum \supseteq that fades away \square above the ipsilateral clavicle. (Right) Coronal oblique NECT of the same patient shows a tortuous right brachiocephalic trunk 🔁 outlined by aerated lung, which produces a well-defined border of the vessel on PA chest radiography. The abnormal radiographic convexity fades as the vessel courses into the neck and is no longer outlined by lung.

Comet Tail Sign

KEY FACTS

TERMINOLOGY

- Definition: CT sign characterized by curvilinear opacities that course toward the hilum from a peripheral subpleural lung mass
 - Classically described in **rounded atelectasis**

IMAGING

Radiography

- Peripheral subpleural lung mass
- Adjacent pleural abnormality (e.g., effusion, thickening)
- May exhibit dense ipsilateral hilum on PA radiography
- CT
 - Criteria for rounded atelectasis
 - Well-marginated 2- to 7-cm subpleural mass
 - Forms acute angles with adjacent pleura
 - Sharp peripheral margin; ill-defined/irregular hilar margin
 - Comet tail sign
 - Lower lobe predominance; posterior > > anterior

- Intrinsic punctate calcifications (1/3)
- **Comet tail sign**: Swirling or curving vessels and bronchi that course from a subpleural lung mass toward the ipsilateral hilum
- PET/CT
 - o Typically no FDG-avidity
 - PET/CT may be helpful for documentation of lack of metabolic activity in the absence of prior studies
 - FDG-avidity: Consider biopsy or resection

PATHOLOGY

- Chronic pleural reaction
- Etiology: Asbestos-related pleural disease, postsurgical (e.g., CABG), chronic heart failure, hepatic hydrothorax, pulmonary infarct, interstitial lung disease, postinfectious pleuritis, pleural tuberculosis, end-stage renal disease

DIAGNOSTIC CHECKLIST

• Consider rounded atelectasis in peripheral subpleural mass with adjacent pleural thickening and comet tail sign on CT

(Left) PA chest radiograph of an asymptomatic patient shows a dense right infrahilar mass \supseteq with irregular borders that simulates primary lung cancer. (Right) Axial CECT of the same patient shows a right lower lobe subpleural mass 🔁 located posterior to the right infrahilar region. Note adjacent curvilinear bronchovascular structures 🔁 that exhibit the characteristic morphologic features of the comet tail sign, consistent with rounded atelectasis. Note bilateral pleural plaques 🖂, consistent with asbestosrelated pleural disease.





(Left) Composite image with axial NECT (left) and FDG PET/CT (right) of a patient status post coronary artery bypass graft shows rounded atelectasis manifesting as a *left lower subpleural mass* with no FDG uptake \supseteq , the latter helps exclude malignancy. Note adjacent left pleural thickening and effusion 🔁. (Right) Axial NECT MIP reformatted image of a patient with rounded atelectasis shows a right lower lobe mass with punctate calcifications, which may be present in nearly 1/3 of all cases.





TERMINOLOGY

• Definition: Zone of ground-glass attenuation surrounding pulmonary soft tissue nodule, mass, or consolidation

IMAGING

- CT
 - Soft tissue nodule, mass, or consolidation with varying amounts of surrounding ground-glass opacity
 - Ground-glass opacity: Opacity that does not obscure pulmonary vessels
 - Ground-glass opacity optimally characterized on thinsection CT

TOP DIFFERENTIAL DIAGNOSES

- Reversed halo sign
 - Central ground-glass opacity with surrounding crescentic or ring-like consolidation
 - Differential diagnosis
 - Organizing pneumonia

- Infection
- Granulomatosis with polyangiitis, infarct, sarcoidosis, radiofrequency ablation, COVID-19

PATHOLOGY

- Ground-glass opacity classically represents hemorrhage, but may also represent inflammation or neoplasm
- Etiology
 - Infectious: Angioinvasive fungus (classically *Aspergillus*, also *Candida*, *Mucor*, etc.), mycobacteria, rickettsia, viruses, septic embolism
 - Inflammatory: Granulomatosis with polyangiitis, eosinophilic pneumonia, cryptogenic organizing pneumonia, endometriosis
 - Neoplastic: Kaposi sarcoma, lung adenocarcinoma, metastasis (e.g., angiosarcoma, choriocarcinoma, osteosarcoma, pancreatic cancer)
 - Trauma: Laceration/contusion, post biopsy, catheterinduced pulmonary pseudoaneurysm





(Left) Axial NECT of a patient with angioinvasive aspergillosis shows a left upper lobe soft tissue nodule with surrounding groundglass opacities \supseteq , the socalled CT halo sign. While nonspecific, this sign is frequently seen in angioinvasive fungal infections, especially in immunosuppressed patients. (Right) Axial CECT of a patient with acute histoplasmosis shows a right upper lobe soft tissue nodule 🔁 with surrounding ground-glass opacities \square , the so-called CT halo sign.





with metastatic pancreatic carcinoma shows a right lower lobe subpleural soft tissue $nodule \supseteq$ with surrounding ground-glass opacities 🔁. Part-solid pulmonary metastases are commonly seen in patients with metastatic pancreatic carcinoma and may simulate primary lung adenocarcinoma. (Right) Axial NECT of a patient with blunt chest trauma shows a right upper lobe cavitary nodule (pulmonary laceration) with surrounding groundglass opacities (pulmonary contusion) 🔁

(Left) Axial CECT of a patient

Deep Sulcus Sign

KEY FACTS

TERMINOLOGY

• Definition: Basilar lucency and deepening of lateral costophrenic angle/sulcus secondary to pneumothorax

IMAGING

- Radiography
 - Lucency extending from lateral costophrenic angle toward hypochondrium
 - Depression of ipsilateral hemidiaphragm compared to contralateral side
 - Ancillary findings: Visible pleural line confirms pneumothorax, ↑ sharpness of cardiomediastinal silhouette, ↑ sharpness of mediastinal fat, ↑ sharpness of diaphragm, double diaphragm sign (air outlining central and anterior hemidiaphragm)
- CT
 - Confirmation of pneumothorax in doubtful cases
 - o Helps establish etiology if unclear on radiography

TOP DIFFERENTIAL DIAGNOSES

- Pneumoperitoneum
 - Left upper quadrant loculated pneumoperitoneum; confirmation with erect or lateral decubitus abdominal radiography
- COPD
 - Hyperaeration may deepen lateral costophrenic angle; CT may be required for exclusion of pneumothorax
 - Vanishing lung syndrome (large/extensive bullae) may mimic pneumothorax

CLINICAL ISSUES

- 30% of all pneumothoraces are undetected on supine chest radiography
- Useful in bedridden patients and when pleural adhesions preclude typical findings of pneumothorax

DIAGNOSTIC CHECKLIST

• Deep sulcus sign should suggest large pneumothorax

(Left) Supine AP chest radiograph of a patient with a left pneumothorax after central line insertion shows the deep sulcus sign \square , characterized by deepening of the left costophrenic angle associated with left basilar hyperlucency and paucity of vascular markings. Note the subtle left apical pleural line Image: Description: Descrip radiograph of the same patient immediately after insertion of left thoracostomy tube 🔁 shows marked improvement of the deep sulcus sign, secondary to improved left pneumothorax.

(Left) AP chest radiograph of an intubated patient with left pneumothorax after blunt trauma shows a left deep sulcus sign and no visible pleural line. Note that the abnormality is obscured by pulmonary opacities and subcutaneous gas. A deep sulcus sign may the only finding of pneumothorax on chest radiography. (Right) AP chest radiograph of a patient with cardiac arrhythmia who required cardiopulmonary resuscitation shows a moderate to large left pneumothorax manifesting with the deep sulcus sign \square .









TERMINOLOGY

- Definition: Water density band (> 2 mm) that represents pericardial effusion and separates mediastinal and subepicardial fat stripes on radiography
- Synonyms: Sandwich sign, Oreo cookie sign, bun sign

IMAGING

• Radiography

- Retrosternal water attenuation band between 2 fat density stripes on lateral chest radiography
- Often more conspicuous if narrow window (more contrast) used to view images
- May be visible on PA chest radiography, as lucent band subjacent to cardiac border
- Interim enlargement of heart and cardiomediastinal silhouette may be identified using comparison prior studies
- CT
 - Fluid between mediastinal and subepicardial fat

TOP DIFFERENTIAL DIAGNOSES

- Pneumomediastinum
 - Linear air collections in retrosternal region without conspicuous water density component
- Morgagni hernia
 - Retrosternal opacity; may exhibit intrinsic lucency and occasionally air-filled bowel loops
- Mediastinal fat
 Retrosternal opacity, may exhibit intrinsic fat density

DIAGNOSTIC CHECKLIST

- High index of suspicion and window manipulation (i.e., narrow window) important for identification of this finding
- Prior radiographs helpful for identification of interim increase in size of cardiac silhouette
- Rapid changes almost always associated with pericardial effusion
- Consider further evaluation with echocardiography for confirmation or if radiography inconclusive





(Left) PA chest radiograph of a patient with a moderate pericardial effusion shows diffuse enlargement of the cardiomediastinal silhouette with a globular morphology concerning for the water bottle sign of pericardial effusion. (Right) Lateral chest radiograph of the same patient shows a water density band outlined by anterior 🖂 and posterior 🔁 fat density stripes, the so-called fat pad or Oreo cookie sign. While not always visible, when present, this sign is very specific for the diagnosis of pericardial effusion.





(Left) Axial CECT of the same patient confirms a moderate circumferential pericardial effusion outlined anteriorly by mediastinal fat \supseteq and posteriorly by subepicardial fat 🔁. Note small bilateral pleural effusions. (Right) PA chest radiograph of a patient with a moderate pericardial effusion shows an enlarged cardiac silhouette and a subtle arcuate lateral lucency \supseteq that represents subepicardial fat adjacent to pericardial fluid. While not as frequently visualized, the fat pad sign may be seen on frontal chest radiography.

Finger-in-Glove Sign

KEY FACTS

TERMINOLOGY

- Finger-in-glove sign
 - Also referred to as gloved finger sign
 - Impaction or inspissation of mucus within dilated bronchi
 - Imaging findings resemble fingers within a glove
 - Applicable to findings on radiography &/or crosssectional imaging

IMAGING

- Radiography
 - Branching tubular soft tissue opacities
 Converge toward ipsilateral hilum
 - May manifest as nodules or masses
 - May be rounded, ovoid, or lobulated
- CT
 - Endobronchial soft tissue or water density secretions
 - Hyperdense mucus common in allergic bronchopulmonary aspergillosis
 - May be indistinguishable from endoluminal neoplasm

TOP DIFFERENTIAL DIAGNOSES

- Allergic bronchopulmonary aspergillosis
 - Single most common cause of finger-in-glove sign
 - History of asthma or cystic fibrosis
 - Blood eosinophilia, ↑ total serum IgE, precipitins to *Aspergillus*
 - o Mucus may be hyperdense from deposited calcium salts
- Bronchial atresia
 - Asymptomatic (most)
 - Surrounding hyperinflation and oligemia on CT
 - Recurrent infection (~ 20%); enlarging nodule/mass
- Malignancy
 - Uncommon manifestation of central cell lung cancer; lung cancer must be excluded when finger-in-glove sign present
 - Endobronchial metastases: Breast, kidney, colon, rectum, uterus, and skin primary malignancies
- Less common: Carcinoid, lipoma, hamartoma, foreign body

(Left) PA chest radiograph of a 42-year-old woman with allergic bronchopulmonary aspergillosis shows right lower lobe tubular branching $opacities \longrightarrow$ that exhibit the finger-in-glove sign. (Right) Composite image with coronal NECT MIP reformatted image (left) and sagittal NECT (right) of the same patient shows the finger-in-glove sign in the right lower lobe. Hyperdense mucus \square is characteristic of allergic bronchopulmonary aspergillosis. The finger-inglove sign may be used to describe both radiographic and CT abnormalities.

(Left) Axial CECT MIP reformatted image of a patient with carcinoid tumor shows a bronchocentric tumor with an endoluminal component 🔁 and distal branching inspissated mucus within dilated bronchi 🔁 (Right) Axial CECT MIP reformatted image of a patient with an endobronchial metastasis from clear cell renal carcinoma shows left upper lobe bronchial obstruction and peripheral branching opacities secondary to endobronchial obstructing tumor with distal mucus inspissation 🖂









TERMINOLOGY

• Definition: Hilar "mass" toward which pulmonary artery branches "converge" represents enlarged pulmonary artery

IMAGING

- PA chest radiography
 - Right &/or left pulmonary artery branches converge to hilar "mass"
 - **Pulmonary hypertension**: Dilated pulmonary trunk, dilated right and left pulmonary arteries
 - **Pulmonic stenosis**: Dilated pulmonary trunk, dilated left pulmonary artery
- Lateral chest radiography
 - Enlarged pulmonary trunk
 - No anterior or posterior mediastinal mass
- CT
 - Dilated pulmonary trunk (> 3 cm)
 - Pulmonary hypertension
 - Dilated pulmonary trunk

- Dilated right and left pulmonary arteries
- Pulmonic stenosis
 - Dilated pulmonary trunk
 - Dilated left pulmonary artery

TOP DIFFERENTIAL DIAGNOSES

- Hilum overlay sign
 - Pulmonary artery visible through > 1 cm from lateral margin of convexity appearing to represent cardiomediastinal silhouette
- Left atrial appendage enlargement
- Hilar abnormality below mainstem bronchusCardiomegaly and pericardial effusion
 - Pulmonary artery remains lateral to hilar/cardiomediastinal convexity

PATHOLOGY

• Etiologies: Pulmonary hypertension, pulmonic stenosis





(Left) PA chest radiograph of a 76-year-old woman with longstanding pulmonary hypertension shows bilateral hilar enlargement and large pulmonary artery branches 🔁 that "converge" toward the enlarged hila 🛃, the so-called hilum convergence sign. Note markedly enlarged pulmonary trunk 🖾. (Right) Lateral chest radiograph of the same patient shows large pulmonary artery branches 🔁 that "converge" toward the bilateral enlarged hila 🛃 secondary to pulmonary artery enlargement from pulmonary hypertension.

(Left) PA chest radiograph of a patient with pulmonic stenosis shows a left hilar mass 🔁 and pulmonary artery branches 🔁 that "converge" toward it. The left hilar mass represents an enlarged left pulmonary artery. Unlike the hilum overlay sign, the enlarged left hilum corresponds to the enlarged left pulmonary artery rather than being visible through it. (Right) 3D MR of the same patient shows dilatation of the pulmonary $trunk \blacksquare$ thought to be due to a systolic jet generated as blood flows through the stenotic pulmonic valve.

Hilum Overlay Sign

KEY FACTS

TERMINOLOGY

• Convexity/mass that projects over hilum through which ipsilateral pulmonary arteries are still visible

IMAGING

• PA chest radiography

- Pulmonary artery interface > 1 cm medial to interface of abnormal convexity
- Peripheral calcifications common in vascular masses
- Pitfall: Rotated PA chest radiograph may simulate abnormal convexity projecting over hilum

• Lateral chest radiography

- Lesion localization anterior or posterior to hilum, typically in mediastinum
- CT
 - Mass anterior or posterior to hilum
 - IV contrast useful for establishing vascular etiology
 - Vascular lesions often enhance with contrast but may manifest as soft tissue masses when thrombosed

TOP DIFFERENTIAL DIAGNOSES

• Hilum convergence sign

- Pulmonary artery branches arise from lateral aspect of hilar convexity
- o Indicates pulmonary artery enlargement
- Left atrial appendage enlargement
 Abnormal convexity below left mainstem bronchus
- Cardiomegaly and pericardial effusion
 - Pulmonary artery remains lateral to abnormal convexity

PATHOLOGY

- Classically described for anterior mediastinal masses; also seen in middle and posterior mediastinal masses
- Etiology
 - Neoplasm: Thymic neoplasm, lymphoma, germ cell neoplasm, mediastinal lymphadenopathy
 - o Vascular lesion: Pseudoaneurysm, aneurysm
 - Mimics: Loculated pleural effusion, parenchymal airspace disease

(Left) PA chest radiograph of a patient with thymoma shows an abnormal left hilar $convexity/mass \implies through$ which the left hilar vessels are still identified, the so-called hilum overlay sign indicative of a mass residing anterior or posterior to the hilum, in this case, the anterior mediastinum. (Right) Axial CECT of the same patient shows a left prevascular mediastinal soft tissue mass *⊡*. Anterior/prevascular mediastinal masses are the most common cause of the hilum overlay sign.





(Left) PA chest radiograph of a patient with mediastinal lymphoma shows a right hilar mass \supseteq through which the right pulmonary artery Ξ is identified, the so-called hilum overlay sign. (Right) PA chest radiograph of a patient status post CABG complicated by aneurysm formation shows a left hilar convexity/mass 🔁 through which the hilar vessels remain visible, consistent with the hilum overlay sign. Awareness that vascular lesions may produce this sign is critical for the formulation of an appropriate differential diagnosis.





TERMINOLOGY

- Radiographic sign based on lesion border characteristics
 - Combination of well-defined (outlined by pulmonary or ambient air) and ill-defined (in continuity with adjacent pleura, mediastinum, chest wall) lesion borders
 - May manifest on single or orthogonal projections
 - o Implies extrapulmonary lesion location

IMAGING

- Radiography
 - Opacity with coexistent well- and ill-defined ("incomplete") borders
 - Extrapulmonary lesion location
 - Cannot discern chest wall from cutaneous lesions
 - Obtuse angles with adjacent pleura/chest wall
- CT
 - Confirms lesion location
 - Pleura
 - Chest wall, skin

PATHOLOGY

- Etiology
 - Pleural lesions: Loculated effusion, pleural plaque, metastasis, localized fibrous tumor, mesothelioma, calcifying fibrous tumor
 - o Chest wall lesions: Lipoma, metastasis, plasmacytoma, primary osseous malignancy
 o Nipple and skin nodules/tags
- Sharp border correlates with tangential imaging of lesion border in contact with air (i.e., lungs, ambient)
- Ill-defined border correlates with silhouette sign produced by lesion in continuity with pleura &/or chest wall and absence of surrounding air
- Obtuse angle at pleura/chest wall interface loses tangential relationship to x-ray beam

DIAGNOSTIC CHECKLIST

• Consider extrapulmonary lesion if incomplete border sign is present on radiography





(Left) PA chest radiograph of a patient with a calcifying fibrous tumor of the pleura shows a calcified oblong mass in the left lower hemithorax with a well-defined medial border *→* and ill-defined (incomplete) lateral border 🖂 The incomplete border sign is characteristic of extrapulmonary lesions, which may be located in the pleura, chest wall, or skin. Rarely, pulmonary lesions may exhibit this radiographic sign. (Right) Axial NECT of the same patient shows an oblong densely calcified left basilar pleural mass 🔁.





(Left) PA chest radiograph of a patient with loculated pleural fluid in the right major fissure shows both well- 🔁 and illdefined 🖾 lesion borders as the fluid collection approaches the chest wall &/or its margin becomes more obtuse. (Right) Composite image with PA chest radiograph (left) and axial NECT (right) shows a chest wall lipoma that exhibits the incomplete border sign on radiography \blacksquare and diffuse fat attenuation 🛃 on CT. The distinct inferomedial border results from tangential imaging of the lesion border surrounded by lung.

Luftsichel Sign

KEY FACTS

TERMINOLOGY

- Luftsichel sign: Crescentic lucency outlining aortic arch on frontal radiography secondary to left upper lobe atelectasis
- "Luftsichel" from German, air sickle or air crescent

IMAGING

- PA chest radiography
 - Left paraaortic crescentic lucency that extends from left apex to left superior pulmonary vein; represents aerated left lower lobe superior segment adjacent to aortic arch (outlined by hyperexpanded left lower lobe)
 - Hazy perihilar opacity that fades superiorly, laterally, and inferiorly and represents atelectatic left upper lobe

• Lateral chest radiography

- Anterior displacement of left major fissure
- CT
 - Atelectatic lobe extends toward anterior chest wall and exhibits V-shaped posterior margin toward hilum
 - Visualization of obstructing endobronchial lesion

• **PET/CT**: Identification of FDG-avid central neoplasm within atelectatic lobe

TOP DIFFERENTIAL DIAGNOSES

- Anterior herniation of hyperinflated right lung across midline with leftward displacement of anterior junction line
- Medial pneumothorax: Not necessarily associated with other signs of volume loss
- Bullous disease adjacent to aortic arch: No other signs of volume loss

PATHOLOGY

- Hyperexpanded and displaced left lower lobe superior segment interposed between aortic arch and atelectatic left upper lobe
- Etiology
 - Endobronchial obstructing lesion: Typically lung cancer, endobronchial metastasis, pulmonary lymphoma (rare)
 - Non-neoplastic bronchial stenosis: Complication of pulmonary vein ablation, endobronchial valves

(Left) PA chest radiograph of a patient with a centrally obstructing left upper lobe squamous cell lung cancer shows complete left upper lobe atelectasis and the Luftsichel sign. The former manifests as a vague left mid and upper lung zone opacity and the latter as a sickleshaped lucency

(hyperexpanded left lower lobe) that outlines the aortic arch (Right) Lateral chest radiograph of the same patient shows complete left upper lobe atelectasis outlined posteriorly by the anteriorly displaced left major fissure ().





(Left) Axial NECT of the same patient shows complete atelectasis of the left upper lobe 🔁 secondary to a central mass that obstructs the proximal left upper lobe bronchus 🔁. The Luftsichel sign is typically associated with centrally obstructing primary lung cancers. (Right) Axial fused FDG PET/CT of the same patient shows a large central FDG-avid mass within the completely atelectatic left upper lobe. Note diffuse centrilobular emphysema in the aerated lung in this patient with primary lung cancer.





Reversed Halo Sign

KEY FACTS

TERMINOLOGY

- Definition: Central ground-glass opacity surrounded by concentric or crescentic consolidation on CT
- Synonym: Atoll sign
 - o Atoll: Coral island with central volcano crater

IMAGING

- Radiography
 - Nodule, mass, or consolidation
- CT
 - Nodule or mass; rounded, ovoid, slightly lobulated
 - Ring-shaped or crescentic consolidation with groundglass opacity center

TOP DIFFERENTIAL DIAGNOSES

- Organizing pneumonia (idiopathic or from any etiology)
- Fungal infection: Angioinvasive aspergillosis, zygomycosis
- Other infections: Bacterial pneumonia, paracoccidioidomycosis, tuberculosis

- Acute lung injury secondary to COVID-19
- Sarcoidosis, lymphomatoid granulomatosis, granulomatosis with polyangiitis
- Neoplasm, infarct
- Radiofrequency ablation
- Differentiation from CT **halo sign**: Consolidation with surrounding ground-glass opacity

PATHOLOGY

- Organizing pneumonia
 - Ring-shaped or crescentic peripheral consolidation corresponds to organizing pneumonia
 - Central ground-glass opacity corresponds to alveolar septal inflammation and intraalveolar cellular debris

DIAGNOSTIC CHECKLIST

- Visualization of reversed halo sign should suggest diagnosis of organizing pneumonia
- Other entities in differential diagnosis should also be considered





(Left) Axial CECT of a patient status post bilateral lung transplantation complicated by mucormycosis shows a left upper lobe ground-glass opacity mass with a peripheral crescentic consolidation rim \blacktriangleright the so-called reversed halo or atoll sign. (Right) Axial NECT of a 25-year-old woman with systemic lupus erythematosus and organizing pneumonia shows subpleural , consolidations that exhibit the reversed halo sign 🔁. When the peripheral consolidation is crescentic, as opposed to concentric, it is often referred to as the atoll sign.





(Left) Axial CECT of a patient with pulmonary involvement related to COVID-19 infection shows peribronchovascular ground-glass opacities. The right lower lobe nodule exhibits the reversed halo sign \square . (Right) Axial CECT of a 51year-old man with acute pulmonary thromboembolism shows subpleural nodular consolidations \implies that exhibit the reversed halo sign. The reversed halo sign should be differentiated from the CT halo sign. The latter is characterized by central soft tissue attenuation surrounded by ground-glass opacity.

Rigler and Cupola Signs

KEY FACTS

TERMINOLOGY

- **Rigler sign**: Pneumoperitoneum that allows visualization of both sides of the bowel wall
- **Cupola sign**: Pneumoperitoneum accumulated under central tendon of diaphragm

IMAGING

• Chest radiography

- Normally, only luminal surface of bowel wall is outlined by gas
- **Rigler sign**: Discernible bowel wall, outlined by luminal gas (inner wall) and free peritoneal gas (outer wall)
- **Cupola sign**: Arcuate lucency over lower thoracic spine, caudal to heart; well-defined superior margin, ill-defined inferior border; often superiorly concave
- Useful in supine patients, as infradiaphragmatic gas may not be evident
- When in doubt, upright or left lateral decubitus radiography may help confirm pneumoperitoneum

TOP DIFFERENTIAL DIAGNOSES

- Pneumomediastinum
 - Continuous diaphragm sign (tends to be linear) may mimic cupola sign (tends to be curved)
- Normal bowel loops
 - Adjacent bowel loops may mimic Rigler sign
 - Gas in transverse colon, lesser sac, or pericardium may mimic cupola sign
- Oral contrast
 - Residual contrast from recent CT may increase apparent bowel wall density and may simulate Rigler sign
- Mach bands: Optical illusion that exaggerates contrast between adjacent structures of differing density

DIAGNOSTIC CHECKLIST

- Identification of pneumoperitoneum may be challenging in supine patients
- Consider upright or left lateral decubitus radiography for confirmation

(Left) AP supine chest radiograph of a patient with a large pneumoperitoneum due to hollow viscus perforation shows visualization of both sides of the bowel walls in the right upper quadrant \supseteq (i.e., Rigler sign) and a curvilinear lucency from gas collected along the central tendon of the diaphragm (i.e., cupola sign) 🔁. (Right) Coned-down PA chest radiograph shows a large right upper quadrant pneumoperitoneum. Note that aas outlines both sides of the bowel wall \supseteq due to the presence of both intra- and extraluminal gas.





(Left) AP chest and abdomen radiograph of a neonate with complicated acute necrotizing enterocolitis shows a large pneumoperitoneum that manifests as a subtle lucency over the abdomen (sometimes referred to as the football sign *→* due to its morphology). Note the subtle Rigler sign \square . (Right) Left lateral decubitus radiograph of the same patient shows free peritoneal gas 🔁 outlining the liver surface and visualization of the bowel wall (i.e., Rigler sign) 🔁 in the right mid abdomen.





S-Sign of Golden

KEY FACTS

TERMINOLOGY

• Definition: Coexistence of superomedial displacement of the minor fissure and a hilar mass in setting of right upper lobe atelectasis

IMAGING

PA chest radiography

- Superomedial displacement of minor fissure
- Central or medial convexity of minor fissure
- Right hilar mass
- Lateral chest radiography
 - Anterosuperior displacement of major fissure
- CT
 - Identification and characterization of endobronchial obstructing lesion
 - Staging of malignancy
 - Intravenous contrast rarely necessary, but may help demonstrate central obstructing lesion

TOP DIFFERENTIAL DIAGNOSES

Right upper lobe atelectasis without central mass
 May exhibit superomedial displacement of minor fissure
 Absence of medial convexity (from central mass)

PATHOLOGY

- S-sign of Golden
 - Named after Golden, who described characteristic reverse S configuration
 - Reverse S formed by superomedially displaced minor fissure and hilar convexity from central mass
- Etiology
 - Lung cancer (most common)
 - o Lymphadenopathy
 - Mediastinal tumor (with associated bronchial obstruction)
 - Endobronchial metastasis
 - o Infection, e.g., bronchoinvasive aspergillosis (rare)





(Left) PA chest radiograph of a patient with a central right upper lobe lung cancer shows right upper lobe atelectasis with superior displacement of the minor fissure \supseteq and a medial convexity produced by the central mass $\overline{\square}$, the socalled S-sign of Golden. The same principle may be applied to any centrally obstructing mass associated with atelectasis. (Right) Coronal CECT of the same patient shows superior displacement of the minor fissure \supseteq due to complete obstruction of the right upper lobe bronchus 🔁 and resultant atelectasis.





(Left) Axial FDG PET/CT of the same patient shows FDG-avid mediastinal lymphadenopathy *⊡* and no significant FDG avidity within the atelectatic right upper lobe \square , which is not involved by tumor. In this case, PET/CT helps identify optimal biopsy sites. (Right) Axial FDG PET/CT of the same patient shows FDG-avid mediastinal and right hilar $lymphadenopathy \longrightarrow$ as well as a central right upper lobe mass 🔁. Note marked superomedial displacement of the minor fissure 🔁.
Signet Ring Sign

KEY FACTS

TERMINOLOGY

- Signet ring sign: Characteristic CT morphology of dilated airway and adjacent pulmonary artery (in cross section)
 Dilated airway represents "ring"
 - Adjacent pulmonary artery represents "stone"
- Bronchial dilatation with bronchoarterial ratio > 1
 Bronchoarterial ratio = 1.5 may be normal in older asymptomatic individuals and at high altitude
- Bronchial dilatation is commonly irreversible

IMAGING

• Radiography

- Bronchiectasis may be subtle or not visible
- o Tram-track sign: Visible parallel thick bronchial walls
- Air-fluid levels indicate superimposed infection
- CT
 - Dilated bronchus (in cross section) > adjacent artery
 - Absence of bronchial tapering
 - Mosaic attenuation and expiratory air-trapping

PATHOLOGY

- Etiology
 - Congenital (primary ciliary dyskinesia, cystic fibrosis, Williams-Campbell syndrome)
 - Immunodeficiency (common variable immunodeficiency)
 - Infection (pneumonia, nontuberculous mycobacterial infection)
 - o Inflammation (allergic bronchopulmonary aspergillosis)
 - Proximal airway obstruction (lung cancer)
 - Interstitial lung disease (traction bronchiectasis)
- Inflamed bronchial wall
- Luminal mucopurulent exudate: Neutrophils, macrophages
- Bronchial wall destruction, loss of fibromuscular tissue, erosion/loss of bronchial wall cartilage
- Decreased submucosal glands
- Squamous metaplasia of bronchial epithelium
- Thin bronchial wall appears thick due to peribronchial fibrosis that involves adjacent lung parenchyma

(Left) Graphic shows the signet ring sign \supseteq defined as a bronchial diameter larger than that of the adjacent pulmonary artery (bronchoarterial ratio > 1) on cross section. (Right) Axial CECT of a patient with chronic obstructive pulmonary disease and recurrent infection shows left upper lobe bronchiectasis that exhibits the so-called signet ring sign: A dilated bronchus \supseteq and its adjacent pulmonary artery 🔁. The dilated airway represents the "ring" and the adjacent vessel the "stone."





(Left) Composite image with axial (left) and sagittal (right) CECT of a patient with postinfectious bronchiectasis shows varicose bronchiectasis \square , which exhibits the signet ring sign \supseteq when viewed in cross section. (Right) Axial NECT of a 34-year-old man with ulcerative colitis and bronchiectasis shows diffuse cylindrical bronchiectasis and bronchial wall thickening. The abnormal bronchoarterial pairs exhibit the so-called signet ring sign 🔁 when viewed in cross section.





Silhouette Sign

KEY FACTS

TERMINOLOGY

- Definition
 - Obscuration of cardiomediastinal silhouette or diaphragm interface previously outlined by aerated lung
 - Produced by loss of contrast from adjacent aerated alveoli replaced by water density material (e.g., pus, atelectasis, tumor, fluid, blood)

IMAGING

- Radiography
 - Middle lobe or right upper lobe anterior segment abnormality obscures right heart border
 - Lingular or left upper lobe anterior segment abnormality obscures left heart border
 - Left upper lobe apicoposterior segment abnormality obscures aortic arch
 - Lower lobe basilar segment abnormality obscures adjacent hemidiaphragm
 - Pleural effusion obscures ipsilateral hemidiaphragm

- Margin of mediastinal mass extending into neck obscured above clavicle due to absence of adjacent aerated lung (i.e., **cervicothoracic sign**)
- Margin of mediastinal mass extending into abdomen obscured below diaphragm due to absence of adjacent aerated lung (i.e., **thoracoabdominal sign**)

• CT

 Allows further characterization of indeterminate lesions that produce sign of silhouette (e.g., while consolidation requires radiographic follow-up to resolution, persistent consolidation requires CT for exclusion of underlying malignancy or other lesion)

PATHOLOGY

- Etiology
 - o Consolidation (e.g., pneumonia)
 - o Atelectasis
 - Neoplasm (e.g., cancer)
 - o Pleural effusion



(Left) PA chest radiograph of a child with lingular pneumonia shows obscuration of the left cardiac border \supseteq by the adjacent airspace disease. A left lower lobe consolidation may manifest as an abnormality in a similar location but will not obscure the left heart border. (Right) PA chest radiograph of a patient with nontuberculous mycobacterial infection and involvement of the middle lobe and lingula shows subtle obscuration of the right and left cardiac borders \supseteq by adjacent airspace disease &/or atelectasis.

(Left) PA chest radiograph of a patient with acquired immunodeficiency syndrome and Staphylococcus aureus pneumonia shows a left apical consolidation that obscures the adjacent aortic arch and is therefore located in the left upper lobe apicoposterior segment. (Right) PA chest radiograph of a patient with systemic lupus erythematosus shows a moderate left pleural effusion that exhibits a meniscus sign \square and obscures the left hemidiaphragm and left heart border due to displacement of adjacent aerated lung by pleural fluid.





Overview of Chest Imaging

Introduction

Lung Volume

Total lung capacity (TLC) is defined as the total volume of pulmonary air at the end of maximal inspiration. The average lung capacity of healthy adults is approximately 6 L, but varies with age, sex, and body composition. Chest radiographs are obtained at the end of maximal inspiration and provide a visual estimate of a subject's TLC. Radiographic estimates of lung volume may be affected by imaging technique and by the patient's position, general condition, and body habitus.

Volume Loss

The term atelectasis is derived from the Greek words *ateles* and *ektasis*, which mean imperfect and expansion, respectively. The term collapse is used synonymously with atelectasis to signify complete or partial (typically reversible) defective lung expansion, lung collapse, and associated volume loss. The volume of lung involved in atelectasis ranges from complete atelectasis involving an entire lung to lobar, segmental, &/or subsegmental lung collapse.

Imaging Assessment

Atelectasis demonstrates protean imaging manifestations based on the extent of collapse, the mechanism of volume loss, and the type of atelectasis. Atelectasis and volume loss are frequently encountered imaging abnormalities and are frequent among critically ill hospitalized patients, particularly those undergoing surgical procedures. Atelectasis in the inpatient population is often identified on portable radiography and may be secondary to a malpositioned endotracheal tube or a central obstructing mucus plug, and often responds to treatment with respiratory therapy &/or bronchoscopy. Atelectasis results in impaired gas exchange of CO₂ and O₂ and produces various degrees of intrapulmonary shunting. Affected patients may complain of dyspnea, tachypnea, cough, and sputum production. Physical examination and auscultation may reveal pulmonary crackles, decreased or absent breath sounds, &/or diminished thoracic expansion. Radiographic identification of atelectasis in the outpatient setting is a more ominous finding, as in many cases, it is produced by a central obstructing lesion, often a malignant neoplasm. Affected patients should be evaluated with chest computed tomography (CT) for direct visualization and assessment of the obstructing lesion, identification of associated abnormalities (such as locally invasive behavior, metastatic disease, and lymphadenopathy), and clinical staging. Bronchoscopy can provide tissue sampling of these central lesions and yield a definitive diagnosis.

Principal Types and Mechanisms of Atelectasis

Two major types of atelectasis are *obstructive* and *nonobstructive*, although combinations of these two may occur. Nonobstructive atelectasis includes the following subtypes: *Compression, relaxation, adhesive, cicatrization*, and *replacement* atelectasis. Additional types of atelectasis include the middle lobe syndrome, dependent, and osteophyte-induced, and rounded. *Postoperative* atelectasis is of particular importance given its frequency and impact on patient recovery.

Obstructive atelectasis, also referred to as **resorptive atelectasis**, occurs when there is a luminal airway obstruction somewhere between the trachea and the alveoli, which allows distal gas to be absorbed. Because pulmonary perfusion is unimpared, gas uptake into the blood continues while no additional gas enters the affected airspaces. When all the gas is absorbed, complete atelectasis ensues. Entities that produce obstructive atelectasis include tumors and neoplasms (which may produce endoluminal or extrinsic airway obstruction), mucus plugs, malpositioned endotracheal tubes, broncholiths, and aspirated foreign bodies, all of which may coexist with varying degrees of underlying airway stenosis. Administration of high inspiratory oxygen concentrations exacerbates the process as oxygen is rapidly absorbed. Room air contains a high percentage of nitrogen, which is slowly absorbed into the blood and thus contributes to airway patency in spite of proximal obstruction. Therefore, affected patients on room air with complete airway obstruction develop collapse within 18-24 hours, whereas a similar obstruction in patients on 100% O₂ may produce complete collapse in less than 1 hour and often within 5 minutes.

Compression atelectasis results from increased pressure on the lung which causes alveolar collapse. During normal respiration diaphragmatic excursions produce decreased intrapleural and alveolar pressures, which facilitate passive transit of air into the lung. Supine inpatients and patients undergoing general anesthesia experience cephalad migration of the diaphragm, which decreases pressure gradient differences and predisposes to atelectasis.

Relaxation (passive) atelectasis occurs secondary to space occupying pleural processes that result in loss of contact between the normally apposed parietal and visceral pleurae. Examples include pneumothorax and pleural effusion, both of which may result in passive loss of volume of the adjacent lung.

Adhesive atelectasis is related to surfactant deficiency, whether through an abnormality of surfactant itself, its local availability and distribution, or through insufficient surfactant production. Alterations of surfactant manifest as increased alveolar surface tension which predisposes to alveolar collapse. Etiologies of adhesive atelectasis include respiratory distress syndrome (RDS) of premature infants and acute respiratory distress syndrome (ARDS) of adults. Other etiologies include pneumonia, smoke inhalation, prolonged shallow breathing, pulmonary thromboembolism, and acute radiation pneumonitis.

Cicatrization (cicatricial) atelectasis is secondary to fibrosis, which produces lung retraction and volume loss. Retractile forces may act upon airways to produce associated traction bronchiectasis &/or bronchiolectasis. Cicatrization atelectasis may be localized or multifocal and is characterized by associated architectural distortion. Etiologies include processes that lead to pulmonary fibrosis and lung destruction, including chronic infections, chronic inflammatory processes, and radiation.

Replacement atelectasis is an unusual entity in which a large number of alveoli are replaced by tumor. The prototypical malignancy that may produce replacement atelectasis is primary pulmonary invasive mucinous adenocarcinoma.

Other Important Types of Atelectasis

Subsegmental atelectasis is also referred to as linear, discoid, or plate-like and was formerly referred to as "Fleischner lines" and attributed to small mucus plugs obstructing peripheral airways. Subsegmental atelectasis may be horizontal, oblique, or near vertical and is most frequently encountered in the mid to lower lung zones. Perihilar subsegmental or linear

atelectasis has been described as an early sign of centrally located primary lung cancer.

Gravity-dependent or dependent atelectasis is common and is frequently identified on conventional chest CT. It affects the posterior dependent aspects of the lungs on supine imaging due to a combination of decreased alveolar volume and increased perfusion. Dependent atelectasis may obscure early findings of basilar subpleural fibrosing interstitial lung disease but typically resolves on prone CT imaging.

Osteophyte-induced atelectasis and fibrosis is frequently identified on chest CT of asymptomatic older subjects and typically affects the paravertebral right lower lobe. It manifests as focal interstitial abnormalities and increased attenuation in the subpleural lung parenchyma adjacent to exuberant osteophytes, and is considered one of several well recognized age-related pulmonary changes.

Postoperative atelectasis deserves special mention, as it is a well-known surgical complication with significant morbidity and mortality when untreated. Postoperative atelectasis affects nearly 90% of patients subjected to general anesthesia and occurs within 72 hours. It is thought to result from a combination of resorptive and compression atelectasis and is most common in abdominal and thoracic surgeries, particularly cardiac surgeries and surgeries that require cardiopulmonary bypass. Additional contributory factors include obesity, advanced age, retained secretions, and concurrent pulmonary edema. Factors that decrease the risk for postoperative atelectasis include nonabdominal surgeries, normal weight, day-case surgery, short-acting anesthetics, adequate pain control, and avoidance of long-lasting opioids and neuromuscular blocking agents. Special ventilatory maneuvers may be used in postoperative patients as well as upright position, early ambulation, incentive spirometry, and respiratory therapy to prevent or alleviate atelectasis.

Rounded atelectasis is characteristically associated with adjacent pleural thickening that may result from asbestosrelated pleural disease or previous thoracic surgery, notably involving the left hemithorax in patients with previous coronary artery bypass graft surgery. It manifests as a subpleural lung mass of varying size and may mimic lung cancer. Imaging identification of typical morphologic features, such as stable size, subpleural location, adjacent pleural thickening, and the comet tail sign, allow a confident prospective imaging diagnosis.

Middle lobe syndrome refers to chronic or recurrent middle lobe atelectasis, although a similar process may affect the lingula. As in other types of atelectasis, obstructive (endoluminal and extraluminal) and nonobstructive etiologies have been described. Obstructive middle lobe syndrome is often caused by adjacent lymphadenopathy, whereas nonobstructive etiologies include inflammatory processes and anatomic abnormalities. The chronically atelectatic lung may develop intrinsic bronchiectasis.

Imaging Signs of Atelectasis

Direct and indirect signs of atelectasis were originally described for and applied to chest radiographic interpretation. Increased utilization of chest CT allows correlation of these radiographic abnormalities and signs with cross-sectional imaging findings and provides a better understanding of the imaging features of atelectasis and volume loss.

Direct Signs of Atelectasis

Direct signs of atelectasis include **fissural displacement** and bronchovascular crowding. As the lung loses volume, ipsilateral interlobar fissures may migrate in the direction of the collapsing lobe. Identification of changes in fissural morphology and position is important in the early diagnosis of atelectasis. The direction and appearance of fissural displacement depend on the affected portion of the lung and frequently produce characteristic and recognizable imaging findings. Likewise, loss of alveolar volume may bring together adjacent bronchovascular structures and produce so-called bronchovascular crowding. Direct signs of atelectasis may be subtle, and comparison to prior imaging enhances identification of these abnormalities and facilitates early diagnosis.

Indirect Signs of Atelectasis

Pulmonary opacification results from absence of intraalveolar air which results in pulmonary opacity of water density on radiography and of soft tissue attenuation on CT. The **shifting granuloma sign** refers to a change in the imaging location of a visible pulmonary landmark such as a calcified granuloma, nodule, or surgical clip due to adjacent or surrounding volume loss. Compensatory expansion or lung hyperinflation occurs as a response to adjacent or contralateral atelectasis. Anatomic **displacement** of normal structures, such as the mediastinum, heart, trachea, hemidiaphragm, &/or hilum, may occur in response to adjacent or contralateral atelectasis. These normal structures will characteristically shift toward the side of volume loss. **Rib approximation** is another indirect sign that occurs ipsilateral to the volume loss.

Classic Signs of Atelectasis

The reverse S-sign of Golden or S-sign of Golden is typical of right upper lobe atelectasis and is characterized by upward and medial displacement of the lateral aspect of the minor fissure and a medially located convexity produced by a central obstructing mass. This finding is highly concerning for primary lung cancer, and affected patients should be promptly evaluated with contrast-enhanced chest CT. The Luftsichel **sign** is typical of left upper lobe atelectasis and is caused by compensatory expansion of the left lower lobe, which migrates upward, abuts the aortic arch, and produces a characteristic adjacent sickle-shaped lucency. It may occur in benign or malignant bronchial obstruction. The **juxtaphrenic peak sign** is often associated with upper lobe volume loss and manifests as upward "tenting" of the ipsilateral hemidiaphragm associated with an inferior accessory fissure.

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(Left) Graphic shows radiographic findings of progressive right upper lobe atelectasis with elevation and medial displacement of the minor fissure on the PA view and upward displacement of the minor and upper portion of the major fissures on the lateral view. There is increasing opacity of the atelectatic lobe with progressive loss of volume. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows right upper lobe atelectasis secondary to an obstructing right upper lobe cancer.

(Left) Graphic shows radiographic findings of progressive middle lobe atelectasis with inferior displacement of the minor fissure and anterior displacement of the inferior major fissure, forming a triangular opacity on the lateral view that tapers to the right hilum. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows obscuration of the right heart border on the PA view and the triangular-shaped opacity of the atelectatic middle lobe on the lateral view.

(Left) Graphic shows findings of progressive right lower lobe atelectasis with medial displacement of the major fissure on the PA view forming a triangular opacity and inferior displacement of the minor fissure. Increasing opacity of the lower lobe projects over the lower thoracic spine. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows right lower lobe atelectasis with displacement of major 🔁 and minor fissures \blacksquare , and obscuration of the posterior right hemidiaphragm.

Right Upper Lobe Atelectasis



Middle Lobe Atelectasis



Right Lower Lobe Atelectasis



Right Upper Lobe Atelectasis



Middle Lobe Atelectasis



Right Lower Lobe Atelectasis



Combined Middle and Right Lower Lobe Atelectasis



Combined Middle and Right Lower Lobe Atelectasis



(Left) Graphic shows findings of progressive combined middle and right lower lobe atelectasis, typically caused by obstruction of the bronchus intermedius. A band of increased opacity extends across the entire lung base on both PA and lateral views. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows a band-like opacity across the right lung base on both views and inferior displacement of the right hilum caused by a carcinoid tumor in the bronchus intermedius.

Left Upper Lobe Atelectasis



Left Upper Lobe Atelectasis



(Left) Graphic shows findings of progressive left upper lobe atelectasis with increasing opacity in the perihilar and retrosternal regions, hyperinflation of the lower lobe, and anterior displacement of the major fissure on the lateral view. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows left upper lobe atelectasis. The displaced major fissure forms a sharp interface \blacksquare along the posterior edge of the opaque atelectatic left upper lobe. Bronchoscopy revealed primary lung cancer.

Left Lower Lobe Atelectasis





Left Lower Lobe Atelectasis

(Left) Graphic shows findings of progressive left lower lobe atelectasis with medial displacement of the major fissure on the PA view, forming a triangular opacity. On the lateral view, increasing opacity of the lower lobe projects over the lower thoracic spine. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows left lower lobe atelectasis, manifesting with subtle increased opacity over the lower thoracic spine that obscures the adjacent elevated left hemidiaphragm.

DIFFERENTIAL DIAGNOSIS

Common

- Lung Cancer
- Endobronchial Secretions
- Malpositioned Endotracheal Tube
- Pleural Effusion/Pneumothorax/Pleural Thickening

Less Common

- Foreign Body
- Radiation Therapy

Rare but Important

• Endobronchial Neoplasm

ESSENTIAL INFORMATION

Key Differential Diagnosis Issues

- Atelectasis
 - Incomplete expansion of all or part of the lung with corresponding decrease in lung volume
 - Collapse often reserved for complete atelectasis
- Mechanism
 - o Obstructive (resorptive)
 - Mucus plug, malpositioned endotracheal tube, foreign body, tumor, airway rupture, bronchial stenosis
 - Resorption of air
 - Complete within 24 hours; no air bronchogram
 - Obstructive pneumonitis: Consolidation limits volume loss
 - Relaxation/passive
 - Volume loss secondary to space-occupying process
 - Pleural effusion, pneumothorax, pleural mass
 - o Adhesive
 - Surfactant deficiency
 - Reduces alveolar surface tension
 - Radiation pneumonitis
 - $\hfill\square$ Limited to irradiated lung
 - 1-6 months after completion of radiation
 - Ischemia distal to thromboembolism
 - 🗆 Subsegmental, segmental
 - Cicatrization (scar)
 - Volume loss associated with retraction of fibrotic lung (irreversible) and traction bronchiectasis
 - Tuberculosis, idiopathic pulmonary fibrosis, radiation fibrosis
- Radiographic signs of atelectasis
 - Direct signs
 - Displacement of interlobar fissures
 - Crowding of vessels and bronchi
 - Indirect signs
 - Localized increased opacity
 - Mediastinal shift, hilar displacement, hemidiaphragm elevation
 - Shifting granuloma sign
 - Compensatory expansion of unaffected lung
 - Rib approximation
- Patterns
 - Lobar atelectasis
 - Right upper lobe
 - □ Superior and medial collapse

- Obscures right superior mediastinal contours
- Elevation of horizontal fissure
- Complete collapse: Lobe marginated against mediastinum
- Juxtaphrenic peak: Triangular opacity extending cephalad from diaphragm
- S sign of Golden: Central obstructing mass, downward concavity of lateral minor fissure, downward convexity of medial minor fissure, reverse S configuration on frontal radiography
- Left upper lobe
 - Anterior and superior displacement toward anterior chest wall, hyperexpanded left lower lobe superior segment migrates upward and behind upper lobe
 - Luftsichel sign: Left upper lobe collapse, upward and medial migration of hyperexpanded left lower lobe superior segment between aortic arch and collapsed lobe
- Middle lobe
 - Medial collapse toward heart, downward displacement of minor fissure, superior displacement of major fissure
 - CT: Triangular or trapezoidal opacity with apex directed toward hilum
 - Middle lobe syndrome: Recurrent or chronic atelectasis (neoplasm, inflammation, infection)
- Lower lobes
 - □ Similar on right and left because of symmetric anatomy
 - □ Left lower lobe: Obscured left hemidiaphragm, retrocardiac opacity
 - CT: Triangular or rounded opacity in costovertebral angle
- o Linear (plate-like) atelectasis
 - Subsegmental atelectasis with linear shape, almost always abuts pleura
 - Oriented in any plane
 - □ Variable thickness: Few mm to cm
- Rounded atelectasis
 - Pleural thickening or fluid tethers adjacent lung with invagination or pleural groove along atelectatic lung
 - Chronic peripheral subpleural volume loss
 - Adjacent pleural abnormality: Thickening (88%), fluid (60%), calcification (40%)
 - □ Asbestos-related pleural disease
 - May mimic lung cancer
- Complete atelectasis
 - Opaque hemithorax, ipsilateral mediastinal shift
 - Hilar mass + lobar atelectasis: Highly suggestive of primary lung cancer
- Cicatricial atelectasis
 - Volume loss associated with retraction of fibrotic lung parenchyma
 - Increased elastic recoil: Traction bronchiectasis and bronchiolectasis
 - Associations
 - □ Granulomatous infection
 - Noninfectious granulomatous disease
 - Radiation fibrosis

Helpful Clues for Common Diagnoses

• Lung Cancer

- Squamous cell carcinoma: Most important neoplastic cause of large airway obstruction
 - 2/3 of squamous cell carcinomas manifest as endobronchial masses
- Central obstructing endobronchial mass
- Lobar or segmental atelectasis ± consolidation
 - CECT: Typically delineates low-attenuation central neoplasm against enhancing atelectatic lung
- Identification of lobar collapse in outpatient population
 - Should prompt exclusion of centrally obstructing lung cancer
 - Contrast-enhanced chest CT for further evaluation

• Endobronchial Secretions

- Common etiology of atelectasis in hospitalized patients
 - Sudden onset of lobar or total lung collapse; typically identified on radiography
 - Usually relieved with respiratory therapy &/or bronchoscopy

• Malpositioned Endotracheal Tube

- Common cause of volume loss and atelectasis in critically ill patients
- Diagnosis confirmed on portable radiography
- Usually relieved by endotracheal tube reposition or replacement

Pleural Effusion/Pneumothorax/Pleural Thickening

- Massive pleural effusion should raise concern for malignancy
 - Opaque hemithorax; variable mediastinal shift
 - CECT: Pleural thickening, nodules, or masses in malignant effusion; assessment of atelectatic lung
- Large pneumothorax may produce passive atelectasis of adjacent lung
- Rounded atelectasis
 - Peripheral subpleural mass-like lesion
 - Comet-tail sign: Curvilinear orientation of bronchovascular structures toward mass
 - High specificity: 92%

Helpful Clues for Less Common Diagnoses

• Foreign Body

- Most common cause of endobronchial abnormality in childhood
 - Food, tooth fragment
 - □ Radiopaque foreign body in only 5-15% of cases
 - Early diagnosis in childhood; may be delayed in adults
- Imaging: Chronic volume loss, recurrent pneumonia, bronchiectasis
 - Chronic inflammatory reaction about foreign body; endobronchial lesion with lobar or segmental collapse
 - Must be differentiated from lung cancer

Radiation Therapy

- History of treated thoracic malignancy
- Consolidation ± volume loss, well-defined curvilinear margins that conform to therapy port, band-like opacity
 - 12 months after therapy completion: Evolution to cicatricial atelectasis
 - Architectural distortion with traction bronchiectasis

Helpful Clues for Rare Diagnoses

Endobronchial Neoplasms

- o Malignant
 - Carcinoid: Completely or partially endobronchial, may exhibit enhancement ± Ca++
 - Mucoepidermoid carcinoma
 - Metastasis
 - □ 2% of autopsies of patients with solid tumors
 - Most commonly associated with renal and colorectal carcinomas
 - Sessile or polypoid endobronchial lesion, narrowing or irregularity of airway lumen, lobar/segmental/subsegmental atelectasis, and postobstructive pneumonia
- Benign: Hamartoma, lipoma, neurofibroma, fibroepithelial polyp

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Lung Cancer

Lung Cancer



(Left) Coned-down PA chest radiograph of a 50-year-old man shows right upper lobe collapse due to a central obstructing squamous cell carcinoma that produces the radiographic S sign of Golden with superior migration of the minor fissure \supseteq and a central $convexity \ge corresponding to$ the mass. (Right) Axial CECT of the same patient shows a heterogeneously enhancing right hilar mass 🔁 that obstructs the right upper lobe bronchus. The minor fissure is concave *⇒* adjacent to the atelectatic lung and convex 🖂 adjacent to the mass.

Atelectasis

Overview of Chest Imaging

(Left) PA chest radiograph of a 73-year-old man with small cell lung cancer shows left upper lobe atelectasis due to a central mass \supseteq that produces a convex interface at the hilum. The hyperinflated left lower lobe superior segment forms a crescent-shaped lucency \square that outlines the aortic arch and manifests as the Luftsichel sign. (Right) Coronal CECT of the same patient shows left upper lobe atelectasis 🔁, the obstructing central mass 🖂, and the hyperinflated left lower lobe \square located between the aortic arch and the collapsed lung.

Lung Cancer



Lung Cancer

Malpositioned Endotracheal Tube

(Left) PA chest radiograph of a patient with obstructing endobronchial secretions shows middle and right lower lobe atelectasis with intrinsic bronchiectasis \supseteq , obscuration of the right heart border and medial right hemidiaphragm, and inferior displacement of the minor and major fissures → (Right) AP chest radiograph shows a malpositioned endotracheal tube \supseteq with the tip in the right mainstem bronchus distal to the carina with resultant atelectatic changes \bowtie in the left lung.



Pleural Effusion/Pneumothorax/Pleural Thickening



Pleural Effusion/Pneumothorax/Pleural Thickening

(Left) AP chest radiograph shows an opaque right hemithorax secondary to complete right lung atelectasis adjacent to a massive malignant right pleural effusion. Note contralateral mediastinal shift \square due to mass effect. (Right) Coned-down AP chest radiograph of a patient with acute chest pain and dyspnea shows a large left tension pneumothorax, marked left lung atelectasis \supseteq , and mass effect on the mediastinum. Although suggested on imaging, tension physiology is a clinical diagnosis.





Endobronchial Secretions

Atelectasis

Pleural Effusion/Pneumothorax/Pleural Thickening



Foreign Body



(Left) Axial CECT of a patient with asbestos-related pleural disease shows bilateral lower lobe rounded atelectasis 🖂 that exhibits the comet tail sign, characterized by the curvilinear morphology of the bronchovascular bundles. Note adjacent calcified pleural plaques 🖂. (Right) Axial CECT (bone window) of an 80-yearold man who aspirated a dental filling and presented with a new left upper lobe opacity shows the metallic foreign body 🔁 in the lumen of the superior lingular segmental bronchus and surrounding atelectasis \blacksquare .

Foreign Body





(Left) Coned-down PA chest radiograph of a 61-year-old woman who underwent volume reduction therapy with bronchial valves (inset shows the bronchial valves \implies shows resultant left upper lobe atelectasis. The bronchial valves act as an obstructing foreign body to achieve volume reduction. (Right) Axial CECT of a 58-year-old man status post radiation therapy for primary lung cancer shows cicatricial atelectasis affecting the superior segment of the right lower lobe \supseteq and the medial segment of the middle lobe 🔁.

Endobronchial Neoplasm





Endobronchial Neoplasm

(Left) Composite image with coronal CECT (left) and virtual bronchoscopy (right) shows a central obstructing left lower lobe carcinoid tumor \supseteq and resultant peripheral lower lobe atelectasis 🔁. Carcinoid tumor may be entirely endobronchial, as in this case. (Right) Axial NECT of a 63year-old woman with renal cell carcinoma shows right upper lobe consolidation and volume loss 🖾 secondary to a central endobronchial metastasis \supseteq that completely obstructs the right mainstem bronchus.

Overview of Chest Imaging

Cicatricial Atelectasis

KEY FACTS

TERMINOLOGY

- Synonym: Cicatrization atelectasis
- Reduction in alveolar air volume in setting of pulmonary fibrosis

IMAGING

- Radiography
 - Focal or multifocal involvement
 - Increased opacity of affected lung
 - Variable volume reduction of affected lung; ± increased volume of unaffected lung, mediastinal shift
 - o Mass-like, nodular, consolidative, or band-like opacities ± architectural distortion
 - Intrinsic bronchiectasis
- CT
 - Assessment of extent of involvement
 - Characterization of mass-like opacity; identification of associated architectural distortion, intrinsic traction bronchiectasis &/or bronchiolectasis

PATHOLOGY

- Pulmonary fibrosis; typically localized
- Etiologies
 - Radiation-induced fibrosis
 - End-stage sarcoidosis
 - Sequela of infection (e.g., tuberculosis, histoplasmosis, necrotizing pneumonia)
 - o Pneumoconiosis (e.g., progressive massive fibrosis)

CLINICAL ISSUES

- Most common symptoms
 - o Asymptomatic
 - Shortness of breath, dyspnea
 - o Cough

DIAGNOSTIC CHECKLIST

• CT assessment of nodular or mass-like radiation-induced cicatricial atelectasis for signs of tumor recurrence (e.g., obliteration of previously visualized bronchiectatic airways)

(Left) Axial CECT shows right upper lobe atelectasis with dense fibrosis and traction bronchiectasis 🔁, consistent with cicatricial atelectasis. Note mild superior mediastinal displacement toward the right due to adjacent volume loss. (Right) PA chest radiograph of a patient with healed tuberculosis demonstrates a heterogeneous right upper lobe opacity with associated volume loss and hilar retraction, intrinsic architectural distortion, and traction bronchiectasis \square , typical of cicatricial atelectasis.











KEY FACTS

TERMINOLOGY

• Localized typically subpleural lung volume loss

IMAGING

- Radiography
 - o Subpleural mass-like opacity
 - Bronchovascular structures converge to lesion
 - Pleural thickening &/or calcification
 - ± blunt costophrenic angles
- CT
 - Wedge-shaped or rounded peripheral subpleural opacity; lower lobe predominant; may be multifocal
 - Adjacent pleural thickening ± calcification
 - **Comet tail sign**: Convergence of bronchovascular structures to lesion
 - Volume loss in affected lobe; hyperlucency of nonatelectatic lobe
 - Air bronchogram in hilar aspect of peripheral opacity
- FDG PET/CT: No FDG avidity

TOP DIFFERENTIAL DIAGNOSES

- Lung cancer
- Pulmonary infarct
- Localized fibrous tumor of pleura

PATHOLOGY

- Pleural plaques, pleural fibrosis; asbestos-related pleural disease
- Pleural effusions

CLINICAL ISSUES

- Typically asymptomatic: Incidental finding on imaging
- M > F
- Age range 59-65 years

DIAGNOSTIC CHECKLIST

• Consider rounded atelectasis in asymptomatic patient with lower lobe peripheral mass-like opacity with the comet tail sign adjacent to pleural thickening ± calcification





(Left) Graphic shows the morphologic features of rounded atelectasis characterized by focal subpleural mass-like volume loss \square that exhibits the comet tail sign \blacksquare and occurs adjacent to pleural thickening E. (Right) Fused axial FDG PET/CT of a patient with a longstanding right pleural effusion demonstrates a masslike opacity \blacksquare in the right lower lobe that is not FDGavid and represents rounded atelectasis. Note adjacent right pleural effusion and pleural thickening 🛃.





(Left) Axial CECT (lung window) shows a rounded peripheral mass-like lesion 🔁 in the posterior subpleural left lower lobe that exhibits the comet tail sign 🔁. Rounded atelectasis is often incidentally discovered on chest CT. (Right) Axial CECT (soft tissue window) of the same patient demonstrates thickening and high attenuation of the adjacent pleura ➡, the latter secondary to prior talc pleurodesis. Common causes of rounded atelectasis include asbestos-related pleural disease and pleural effusion.



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Introduction

Thoracic developmental abnormalities often manifest in neonates, infants, and children, may be diagnosed antenatally on obstetrical ultrasound, or may be identified in symptomatic or asymptomatic adults. Recognition of typical cross-sectional imaging features allows distinction of developmental lesions from other thoracic pathologies.

Spectrum of Developmental Abnormalities

Thoracic developmental lesions may affect any anatomic region, including the airways, lung, mediastinum, heart, systemic and pulmonary vessels, diaphragm, &/or chest wall.

Tracheobronchial Tree

The trachea and bronchi originate from the primitive lung bud, which undergoes sequential branching to form the developing airways. These come in contact with the primitive mesenchyme to induce lung parenchymal development. Tracheobronchial anomalies may include variant tracheobronchial branching, congenital lobar overinflation (CLO), congenital pulmonary airway malformation (CPAM), and congenital bronchial atresia (CBA). The latter is characterized by focal interruption of a segmental airway lumen, a distal mucocele, and surrounding hyperlucency. A confident prospective diagnosis of CBA is of utmost importance, as surgical management is rarely indicated. Anomalous bronchial branching is a frequent incidental finding on chest CT and usually has no clinical significance. However, recognition of variant tracheobronchial branching allows the radiologist to impact the planning of bronchoscopic procedures in selected cases.

Lung

Lung development occurs in synchrony with tracheobronchial development, and it is difficult to separate airway anomalies, such as CPAM from pulmonary anomalies. CPAM involves the lung with findings that range from microscopic to small or large cysts. One of the most debated and poorly understood developmental anomalies is pulmonary sequestration. Sequestered lung lacks a normal communication with the tracheobronchial tree and has a systemic blood supply. Extralobar sequestration (ELS) is thought to result from an anomalous primitive foregut bud that induces parenchymal development to form extrapulmonary lung tissue. Intralobar sequestration (ILS), as the name implies, occurs within the confines of an otherwise normal pulmonary lobe. ILS affects males and females equally, does not have a strong association with other congenital anomalies, and is often diagnosed in adulthood. Because affected patients often present with signs and symptoms of infection and because the affected lung often exhibits chronic inflammation, it has been postulated that ILS may be an acquired lesion. Whatever its etiology, the diagnosis of ILS requires a high index of suspicion and identification of a systemic blood supply to the affected lung.

Pulmonary Circulation

Partial anomalous pulmonary venous return (PAPVR) is often diagnosed incidentally on contrast-enhanced chest CT. Affected patients may be symptomatic due to the resultant left-to-right shunt or because of a sinus venosus atrial septal defect, which is associated with right-sided PAPVR. Arteriovenous malformations (AVM) produce a direct communication between a pulmonary artery and a pulmonary vein without an intervening capillary bed, affected patients are at risk for systemic embolic events and may present with stroke or peripheral infarcts and abscesses, and management typically involves selective catheter angiography and embolization to obliterate the shunt.

Systemic Circulation

Developmental abnormalities of the systemic circulation are common, and cross-sectional imaging features are diagnostic. Arterial abnormalities include aberrant subclavian arteries, anomalous origin of the left vertebral artery, and anomalies of the aortic arch (right aortic arch, double aortic arch, aortic coarctation). Anomalies of the systemic veins include accessory azygos fissure, persistent left superior vena cava (PLSVC), and meandering pulmonary vein. PLSVC is rarely diagnosed prospectively on radiography, but may be identified following placement of central vascular catheters or pacemakers, which follow a characteristic vertical left paramediastinal course into the coronary sinus and right atrium.

Heart and Valves

Significant congenital heart lesions typically manifest in neonates, but some may escape early detection and manifest in adulthood. Atrial septal defect is the most common shunt lesion to be initially diagnosed in an adult, as affected patients may become increasingly symptomatic due to the presence of a chronic left-to-right shunt and resultant pulmonary hypertension.

Pulmonic stenosis may be diagnosed incidentally because of a mediastinal contour abnormality produced by pulmonary trunk enlargement associated with left pulmonary artery enlargement. Bicuspid aortic valve may manifest with valvular calcifications indicative of aortic stenosis and may exhibit associated ventricular hypertrophy and dilatation of the ascending aorta.

Diaphragm

Congenital diaphragmatic hernia (CDH) is the most severe congenital anomaly of the diaphragm and results from partial agenesis of one or both hemidiaphragms with herniation of abdominal viscera, stomach, &/or bowel into the thorax. CDH may be diagnosed antenatally and typically affects neonates and infants. Prognosis is related to the presence or absence of associated congenital anomalies, the size of the diaphragmatic defect, and the extent of herniation. Bochdalek hernia refers to herniation of abdominal contents (typically fat) through the Bochdalek foramen, which is the normal remnant of the pleuroperitoneal canal. It affects asymptomatic adults, may mimic an intrathoracic mass, and is readily diagnosed on cross-sectional imaging. Morgagni hernia also affects asymptomatic adults and manifests as a cardiophrenic angle lesion that may contain variable amounts of peritoneal fat and bowel.

Chest Wall

Congenital chest wall anomalies include scoliosis, Poland syndrome, and pectus deformities (pectus excavatum, pectus carinatum). Affected patients may be symptomatic or may be referred for cosmetic surgery. Pectus excavatum deformity is a depression of the lower sternum that produces mass effect on the heart and cardiac rotation with resultant obscuration of the right cardiac border on frontal chest radiography, which may be confused with middle lobe atelectasis or pneumonia.

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Tracheobronchial Tree Anomaly



Anomaly of Systemic Circulation

(Left) Coronal CECT (lung window) of a 43-year-old man imaged because of a radiographic abnormality shows large areas of left upper and left lower lobe hyperlucency and a left lower lobe nonenhancing tubular $opacity \blacksquare$, which represented a mucocele secondary to congenital bronchial atresia. (Right) Composite image with CECT in lung (left) and soft tissue (right) window shows heterogeneous left lower lobe attenuation with systemic vascular supply \square , diagnostic of intralobar sequestration.

Anomaly of Pulmonary Circulation

Anomaly of Systemic Circulation



(Left) Composite image with axial CECT in lung (left) and soft tissue (right) window shows a lobulated right upper lobe nodule that exhibits a feeding artery 🛃 and intense contrast enhancement, consistent with arteriovenous malformation. Embolotherapy is indicated to prevent systemic embolization. (Right) Coronal oblique CTA (MIP image) shows partial anomalous pulmonary venous return ➡ of the left upper lobe pulmonary vein, often an incidental finding. However, the resultant left-to-right shunt may produce symptoms.



Aortic Arch Anomaly



(Left) AP chest radiograph of a patient with chest pain shows a left pectoral dual chamber pacer/ICD with leads coursing into the right heart 🛃 via a persistent left superior vena cava 🛃, which drains into the coronary sinus. (Right) Composite image with PA chest radiograph (left) and CECT (right) shows an abnormal upper mediastinal $contour \ge secondary to a$ right aortic arch. Note characteristic finding of associated aberrant retroesophageal left subclavian artery 🔁.

KEY FACTS

TERMINOLOGY

• Variations in number and position of bronchi

IMAGING

- Anomalous bronchi originating from trachea • Tracheal bronchus: Right, left, bilateral
- Anomalous bronchi arising from bronchial tree
 - Right preeparterial bronchus
 - Right posteparterial bronchus
 - Left preeparterial bronchus
 - Left prehyparterial bronchus
 - Accessory cardiac bronchus
- Situs inversus: Right hyparterial bronchus, left eparterial bronchus
- Heterotaxy syndrome
 - Bronchial isomerism
 - Bilateral hyparterial bronchi (bilateral left-sidedness)
 - Bilateral eparterial bronchus (bilateral right-sidedness)

TOP DIFFERENTIAL DIAGNOSES

- Paratracheal air cyst
- Situs inversus
- Heterotaxy

CLINICAL ISSUES

- Usually asymptomatic
- Tracheal bronchus, accessory cardiac bronchus
 Infection, hemoptysis, atelectasis, bronchiectasis

DIAGNOSTIC CHECKLIST

- Consider anomalous bronchial abnormalities in childhood recurrent pneumonia &/or atelectasis
- Anomalous bronchial branching is common incidental finding on adult chest CT
- Identification and characterization of anomalous bronchial branching is valuable to clinicians prior to bronchoscopy, endobronchial treatment, intubation, and surgeries requiring single-lung ventilation

(Left) Graphic illustrates variable tracheobronchial branching. The most commonly encountered bronchial branching variants are right preeparterial bronchus, right tracheal bronchus, and accessory cardiac bronchus. (Right) Axial NECT minIP reformatted image shows an anomalous right tracheal bronchus 🔁 arising from the right lateral tracheal wall. In this case, note the presence of adjacent small air bubbles \blacksquare distal to the bronchus. Tracheal bronchus almost exclusively arises on the right side.





(Left) Composite image with axial (left) and coronal (right) NECT shows a displaced right apical segmental tracheal bronchus 🔁 arising from the right lateral tracheal wall. The right upper lobe bronchus 🔁 lacked an apical segmental branch. (Right) Composite image with coronal CECT shows a supernumerary right upper lobe apical segmental tracheal bronchus 🔁 arising from the right lateral tracheal wall and coursing under the azygos arch \bowtie and cephalad toward the right apex. Note the normal right upper lobe apical segmental bronchus ₽.





Synonyms

- Congenital bronchial anomalies
- Tracheobronchial branching anomalies
- Variant tracheobronchial branching
- Tracheal diverticulum: Tracheocele, paratracheal air cyst
- Tracheal bronchus: Pig bronchus, bronchus suis
 - Displaced right upper lobe (RUL) tracheal bronchus; normal anatomic bronchial branching pattern in swine

Definitions

- Tracheal diverticulum: Paratracheal blind-ending air-filled structure
- Tracheal bronchus: Bronchus arising from trachea
- **Supernumerary bronchus**: Coexists with normal branching bronchi
- **Displaced bronchus**: Displacement of lobar or segmental bronchus to anomalous location

IMAGING

General Features

- Best diagnostic clue
 - Variations in bronchial number and position; typically incidental findings on CT
- Location
 - o Anomalous bronchi originating from trachea
 - Tracheal bronchus: Right, left, bilateral
 - Anomalous bronchi originating from bronchial tree
 - Preeparterial, posteparterial, prehyparterial, posthyparterial
 - Gross upward displacement of middle lobe bronchus
 - Suprasuperior bronchus
 - Subsuperior bronchus
 - Accessory cardiac bronchus
 - Bridging bronchus

Radiographic Findings

- Identification of typical normal lobar bronchial branching
 RUL bronchus: Eparterial
 - Origin from right mainstem bronchus above (proximal to) right pulmonary artery
 - o Left upper lobe (LUL) bronchus: Hyparterial
 - Origin from left mainstem bronchus below (distal to) left pulmonary artery
- Variant bronchial anatomy rarely identified on radiography

CT Findings

- Optimal evaluation of tracheobronchial tree and bronchial branching patterns
- **Tracheal bronchus**: Tracheal origin; directed toward upper lobe
 - Most located on right; rarely on left or bilateral
 - Distal trachea; < 2 cm above carina
 - o Types
 - Displaced: Lobar or segmental bronchus displaced to trachea from normal position
 - True tracheal (pig) bronchus: Tracheal origin of RUL bronchus
 - Supernumerary: Lobar or segmental bronchus coexists with normal upper lobe counterpart

– Blind-ending

Right preeparterial bronchus

- Origin from right mainstem bronchus proximal to RUL bronchus; directed to RUL
- o Most (82%) are displaced segmental bronchi
- Displaced pre-eparterial apical segmental bronchus is most common variant
- Right posteparterial bronchus
 - Origin distal to RUL bronchus; directed toward RUL
 - Segmental or subsegmental
- Left preeparterial bronchus
 - o Most common left-sided anomaly
 - Origin from left mainstem bronchus proximal to left pulmonary artery
 - Most are displaced bronchi

• Left prehyparterial bronchus

• Origin from left mainstem bronchus below (distal to) left pulmonary artery, proximal to LUL bronchus; directed to LUL

• Left posthyparterial bronchus

- Origin below LUL bronchus; directed to LUL
- No reported cases in English literature
- Not included in some classifications
- Gross upward displacement of middle lobe bronchus
 - Middle lobe bronchus origin at level of RUL bronchus; may originate from RUL bronchus

• Suprasuperior bronchus

- Displaced subsegmental bronchus of right lower lobe (RLL) superior segment
- Origin from mainstem or intermediate bronchus
- Subsuperior bronchus
 - Supernumerary bronchus directed to superior segment
 - o Origin below superior segmental bronchus

Accessory cardiac bronchus

- Supernumerary bronchus
- Origin from medial right mainstem or intermediate bronchus
- Courses caudally and medially toward heart
- Blind ending or associated with lung parenchyma ± accessory fissure
- Origin cephalad to middle lobe bronchus origin
- o Types
 - Short diverticular
 - Intermediate; long diverticulum, no arborization
 - Long; supplies small undeveloped lobule

Bridging bronchus

- Ectopic bronchus
- Origin from left mainstem bronchus; supplies right lung
- Type 1: Right mainstem bronchus ends in RUL bronchus; intermediate bronchus origin from left mainstem bronchus
- Type 2: Blind-ending right mainstem bronchus; right lung supplied by displaced right mainstem bronchus that originates from left mainstem bronchus

Imaging Recommendations

- Best imaging tool
 - MDCT: Multiplanar reformatted images
 - MDCT: Increased understanding and identification of mild and complex tracheobronchial anomalies

- Protocol advice
 - Shaded surface display
 - Virtual bronchoscopy
 - Minimum intensity projection (minIP) for display of lowest attenuation value within dataset: Ideal for airway visualization

DIFFERENTIAL DIAGNOSIS

Paratracheal Air Cyst

- Tracheal diverticulum; tracheocele
- Small rounded air-filled thin-walled cyst
- Right posterolateral tracheal wall near thoracic inlet
- Tracheal communication often inapparent

Situs Inversus

- Right hyparterial bronchus
- Left eparterial bronchus
- Dextrocardia, right aortic arch, right gastric bubble

Heterotaxy Syndrome

- Left bronchial isomerism (polysplenia)
 - Asymptomatic adult; ± congenital heart disease
 - Bilateral hyparterial bronchi; bilateral left-sidedness
 - ± azygos continuation of inferior vena cava, persistent left superior vena cava
- Right bronchial isomerism (asplenia)
 o Infant with severe cyanotic congenital heart disease
 - o Bilateral eparterial bronchi; bilateral right-sidedness

Bronchial Atresia

- Bronchial branching pattern may be normal
- Tubular, rounded, branching mucocele; surrounding hyperlucent lung

PATHOLOGY

General Features

- Etiology
 - Congenital; anatomic variant
 - o Pathogenesis
 - Poorly understood
 - Various developmental theories
 - Reduction: Involution and suppression of original bronchial distribution
 - Migration (extension): Basic bilateral hyparterial morphology with subsequent movement or migration of bronchi to new locations
 - □ Selection: Disturbances of local morphogenesis
 - Tracheal bronchus: Occurs 29-30 days after onset of differentiation of lobar bronchi
 - Accessory cardiac bronchus: Always supernumerary bronchus
- Associated abnormalities
 - Other tracheobronchial branching anomalies
 - o Congenital tracheal stenosis, pulmonary artery sling
 - Congenital heart disease: Ventricular septal defect, conotruncal heart defects, aortic coarctation, atrioventricular canal defects
 - Down syndrome
 - Situs inversus: Congenital heart disease, primary ciliary dyskinesia

• Isomerism: Congenital heart disease; spectrum of heterotaxy-related abnormalities

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Usually asymptomatic; incidental finding on imaging
 - o Tracheal bronchus, accessory cardiac bronchus
 - Infection, hemoptysis
 - Atelectasis, bronchiectasis
- Other signs/symptoms
 - Intubated patients with tracheal bronchus may have recurrent or chronic partial upper lobe atelectasis

Demographics

- Age
- o Anyage
- Epidemiology
 - Proximal or distal segmental or subsegmental bronchial displacement in 10% of individuals
 - Right tracheal bronchus
 - 0.1-1.3% (adults); 1.5-2% (children)
 - Accessory cardiac bronchus
 - 0.07-0.5% of general population

Natural History & Prognosis

• Good prognosis

Treatment

- Usually no treatment
- Treatment of complications

DIAGNOSTIC CHECKLIST

Consider

- Anomalous bronchial abnormalities in childhood recurrent pneumonia &/or atelectasis
- Anomalous bronchial branching is common incidental finding on adult chest CT

Image Interpretation Pearls

• MDCT is modality of choice for identification of anomalous bronchi, particularly those affecting central airways

Reporting Tips

• Identification and characterization of anomalous bronchial branching is valuable information for clinicians prior to fiberoptic bronchoscopy, endobronchial treatment, endotracheal intubation, surgeries requiring single-lung ventilation (video-assisted thoracoscopic surgery)

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(Left) Axial CECT of an 84year-old man shows an incidentally identified displaced right apical segmental tracheal bronchus The right upper lobe bronchus (not shown) exhibited only anterior and posterior segmental branches. (Right) Coronal CECT shows a displaced right upper lobe apical segmental preeparterial bronchus 🔁 arising from the right mainstem bronchus. The right upper lobe bronchus 🔁 lacked a right apical segmental branch. This is one of the most frequently seen bronchial branching variants.





(Left) Axial NECT shows an accessory cardiac bronchus 🔁 arising from the medial wall of the bronchus intermedius. Accessory cardiac bronchus may be associated with aspiration pneumonitis or hemoptysis. (Right) Composite image with axial (left and center) and coronal (right) CECT of a 67-year-old man shows an incidentally identified accessory cardiac bronchus \supseteq that originates from the medial aspect of the bronchus intermedius and supplies a small lung lobe, bound by an accessory fissure $\overline{\mathbf{A}}$





(Left) Composite image with coronal CECT shows an supernumerary left upper lobe apicoposterior segmental prehyparterial bronchus 🖂 arising proximal to the left upper lobe bronchus anddistal to the left pulmonary artery. Both bronchi course cephalad to supply the left upper lobe. (Right) Volumetric 3D reformatted image shows a bridging bronchus. The right mainstem bronchus 🔁 supplies the right upper lobe bronchus. The bronchus intermedius arises from the distal left mainstem bronchus ➡. (Courtesy J. Kim, MD.)

KEY FACTS

TERMINOLOGY

- Mucosal herniation through tracheal wall
- Synonyms
 - Tracheal diverticulum
 - o Tracheocele
 - Lymphoepithelial cyst

IMAGING

- Radiography
 - Rarely visible; right paratracheal lucency
- CT
 - Small rounded thin-walled air-filled cyst
 - No calcification, air-fluid level or lung markings
 - Right posterior paratracheal region at thoracic inlet
 Location in > 95% of cases
 - Right posterolateral tracheal wall at thoracic inlet
 - Visible tracheal communication in only 35%

TOP DIFFERENTIAL DIAGNOSES

- Pneumomediastinum
- Paraseptal emphysema
- Apical lung hernia
- Zenker diverticulum
- Laryngocele

PATHOLOGY

 Cyst lined with normal ciliated columnar epithelium; communicates with trachea

CLINICAL ISSUES

- Usually asymptomatic
- Rarely chronic cough and dyspnea
- Common incidental finding on CT

DIAGNOSTIC CHECKLIST

• Consider paratracheal air cyst in well-circumscribed right paratracheal lucency at thoracic inlet

(Left) Axial NECT shows a 56year-old man with mild apical paraseptal emphysema 🖂 and an incidental right paratracheal air cyst 🔁 separated by intervening pleura. Paratracheal air cysts can sometimes be confused with paraseptal emphysema. Multiplanar reformatted images may assist in this distinction. (Right) Graphic shows a right paratracheal air $cyst \square with a narrow tracheal$ communication. Paratracheal air cysts are most common on the right at the thoracic inlet, but can occur anywhere along the trachea.





(Left) Axial CECT shows a right paratracheal air cyst containing wispy internal secretions 🔁. Often void of intrinsic material, luminal communication may allow accumulation of secretions and debris. (Right) Coronal CECT minIP reformatted image of a patient status post chest trauma shows a right paratracheal air cyst partly filled with secretions. The characteristic location and absence of mediastinal fluid/gas allows confident distinction of paratracheal air cyst from traumatic injury.





- Synonyms
- Tracheal diverticulum
- Tracheocele
- Lymphoepithelial cyst

Definitions

• Mucosal herniation through tracheal wall

IMAGING

General Features

- Best diagnostic clue
 - Small rounded air-filled thin-walled cyst posterior to trachea
- Location
 - Right posterolateral tracheal wall at the thoracic inlet
 > 95%
 - Junction of cartilaginous ring and membranous trachea
 - Esophagus reinforces this junction on the left
- Size
 - Usually < 2 cm in diameter; often largest in craniocaudal dimension
 - Dynamic variability
 - ↑ on expiration; \downarrow on inspiration
- Morphology
 - No calcification, air-fluid level or lung markings
 - May contain secretions/debris
 Wall thickening uncommon (33%)
 - Typically single; rarely multiple

Imaging Recommendations

- Best imaging tool
 - CT is modality of choice for assessment of airways
- Protocol advice
 - Multiplanar reconstructions to find tracheal communication; differentiation from other diagnostic considerations

Radiographic Findings

- Radiography
 - Rarely visible; right paratracheal lucency

CT Findings

- NECT
 - Air-filled cyst adjacent to right posterolateral trachea
 - Tracheal communication visible in only 35%

Ultrasonographic Findings

- Grayscale ultrasound
 - May be mistaken for calcified parathyroid mass due to location and echogenicity of air

DIFFERENTIAL DIAGNOSIS

Pneumomediastinum

• Typically multifocal; gas insinuating among mediastinal structures

Paraseptal Emphysema

• Multiple pulmonary subpleural cysts aligned in rows

Zenker Diverticulum

• Usually located more cephalad; often contains fluid

Laryngocele

• Located more cephalad; paraglottic gas or fluid collection

Apical (Sibson) Lung Hernia

• Typically larger; contains lung parenchyma

PATHOLOGY

General Features

- Etiology
 - Congenital
 - Defect in endodermal differentiation of membranous posterior trachea or tracheal cartilage
 - Acquired
 - Prolonged ↑ intrathoracic pressure: Chronic cough, chronic obstructive pulmonary disease
 - Recurrent respiratory infections → weak tracheal musculature
 - Typically larger than congenital types

Gross Pathologic & Surgical Features

- Cyst communicates with trachea, channel measures 1.5-2 mm in length, 1 mm in diameter
- Location at transition point between intrathoracic and extrathoracic trachea

Microscopic Features

• Cyst lined with normal ciliated columnar epithelium

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- o Usually asymptomatic
- Chronic cough and dyspnea
- Other signs/symptoms
 - Dysphonia due to mass effect on adjacent recurrent laryngeal nerve

Demographics

- All ages
- Common incidental finding on CT; up to 3.7% of cases

Treatment

- No treatment if asymptomatic
- Surgical resection if symptomatic

DIAGNOSTIC CHECKLIST

Consider

 Paratracheal air cyst when well-circumscribed right paratracheal lucency is encountered at thoracic inlet

Image Interpretation Pearls

- Vast majority of paratracheal cysts are incidental findings
- Should **not be mistaken** for pneumomediastinum or pneumothorax

SELECTED REFERENCES

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Bronchial Atresia

KEY FACTS

TERMINOLOGY

- Bronchial atresia (BA)
- Congenital focal atresia of subsegmental, segmental, or lobar bronchus

IMAGING

- Radiography
 - Well-defined rounded, ovoid, tubular, or branching mucocele
 - Surrounded by hyperlucent lung parenchyma
 - Expiratory air-trapping in affected lung
- CT
 - Rounded, tubular, or branching mucocele
 - Nonenhancing, low-attenuation mucocele
 - Surrounding wedge-shaped hyperlucent lung
 - Intrinsic air or air-fluid level suggests infection
 - Exclusion of central obstructing neoplasm
- **V/Q scintigraphy**: Hypoperfusion and absent or delayed ventilation of affected pulmonary segment

TOP DIFFERENTIAL DIAGNOSES

- Causes of mucoid impaction: Allergic bronchopulmonary aspergillosis, endobronchial neoplasm, bronchiectasis
- Arteriovenous malformation
- Intralobar sequestration
- Intrapulmonary bronchogenic cyst
- Congenital lobar overinflation

CLINICAL ISSUES

- Symptoms/signs
 - Asymptomatic adult (60%)
 - Cough, recurrent infection, dyspnea, chest pain

DIAGNOSTIC CHECKLIST

- Consider BA in asymptomatic patient with central nodular, tubular, or branching opacity surrounded by hyperlucent lung
- Prospective imaging diagnosis allows conservative management of asymptomatic patients

(Left) PA chest radiograph of an asymptomatic 41-year-old woman with bronchial atresia shows left upper lung zone hyperlucency and hyperexpansion surrounding a tubular branching opacity 🔁 that represented a mucocele located distal to the point of atresia. (Right) Composite *image with ventilation (top)* and perfusion (bottom) scintigraphy of the same patient shows matching left upper lobe ventilation \blacksquare and perfusion 🗈 defects. Delayed imaging may demonstrate delayed ventilation of the affected lung.

(Left) PA chest radiograph coned-down to the right lung base of a patient with bronchial atresia shows a right lower lobe branching opacity \blacksquare consistent with mucoid impaction. (Right) Composite image with axial CECT of the same patient in lung (left) and soft tissue (right) window shows a low-attenuation right lower lobe branching $mucocele \Longrightarrow$ surrounded by hyperlucent lung parenchyma \blacksquare . After exclusion of a central obstructing neoplasm, the imaging findings are diagnostic of bronchial atresia.









- AbbreviationsBronchial atresia (BA)
- Synonyms
- Congenital bronchial atresia (CBA)

Definitions

• Congenital focal atresia of subsegmental, segmental, or lobar bronchus

• Normal distal bronchial tree

• Mucocele: Mucoid impaction distal to BA • Synonym: Bronchocele

IMAGING

General Features

- Best diagnostic clue
 - Rounded, tubular, or branching opacity with surrounding pulmonary hyperlucency
- Location
 - In decreasing order
 - Left upper lobe
 - Apicoposterior segment most commonly affected
 - Right upper lobe
 - Left lower lobe
 - Middle lobe
 - Right lower lobe
 - o Typically segmental: Rarely lobar or subsegmental
- Size
 - o Variable
- Morphology
 - o Mucocele
 - Rounded, ovoid
 - Tubular
 - May exhibit branching morphology

Radiographic Findings

- Radiography
 - $\circ~$ Mucocele surrounded by hyperlucent lung
 - o Visualization and characterization of **mucocele**
 - Well-defined round, ovoid, tubular, or branching morphology
 - Central location
 - Longitudinal axis of mucocele oriented toward ipsilateral hilum
 - Air-fluid levels within mucocele consistent with superimposed infection

• Hyperlucent lung parenchyma

- Surrounds mucocele
- Decreased markings and vascularity

$\circ~$ Expiratory air-trapping of hyperlucent lung

CT Findings

- NECT
 - Identification and characterization of **mucocele**
 - Well-defined spherical, ovoid, tubular, or branching
 - Longitudinal axis oriented toward ipsilateral hilum
 - Low attenuation: -5 to 25 HU; may rarely exhibit high attenuation or calcification

- Interval enlargement, intrinsic air or air-fluid levels suggest infection
 - □ *Aspergillus* spp. may cause indolent infection with interval growth
- Evaluation of bronchial tree to determine relationship of normal bronchi to mucocele
- Assessment of hyperlucent lung parenchyma
 - Wedge-shaped hyperlucent lung; surrounds mucocele
 - Hyperlucency related to collateral ventilation, airtrapping, and hypoperfusion
- Finding of mucocele and peripheral lung hyperinflation in up to 83% of cases of BA
- CECT

• Mucocele

- Low attenuation
- Absence of contrast enhancement; distinction from vascular lesion, such as arteriovenous malformation
- Rare reports of mucocele calcification
- Exclusion of central obstructing neoplasm
- Dynamic xenon-enhanced dual-energy CT
 - Depicts regional collateral ventilation in atretic segment
 - o Low level wash-in, delayed wash-out

Nuclear Medicine Findings

- V/Q scan
 - Hypoperfusion of affected pulmonary segment
 - Absent or delayed ventilation of affected segment
 Affected segment may exhibit delayed washout secondary to air-trapping

MR Findings

- Identification and assessment of mucocele
 High signal intensity mucocele on T1WI and T2WI
- Fetal MR imaging
 - Hyperexpanded lung; high signal intensity on T2WI
 - Inconsistent visualization of mucocele, unless central

Ultrasonographic Findings

 Prenatal diagnosis: Echogenic fluid-filled lung distal to atresia

Imaging Recommendations

- Best imaging tool
 - Diagnosis may be suspected on radiography
 - CT is imaging modality of choice to assess suspected BA
 - Identification of mucocele and surrounding hyperlucent lung
 - Exclusion of centrally obstructing neoplasm
- Protocol advice
 - Multiplanar reformatted images for evaluation of bronchial anatomy and extent of involvement
 - Expiratory radiography or CT for documentation of airtrapping distal to mucocele

DIFFERENTIAL DIAGNOSIS

Other Causes of Mucoid Impaction

- Allergic bronchopulmonary aspergillosis
 - History of asthma
 - Upper lobe bronchiectasis

- Finger-in-glove branching opacities corresponding to endoluminal mucus plugs; may exhibit high attenuation on NECT
- Endobronchial neoplasm
 - May exhibit peripheral mucus plugs
 - o May exhibit peripheral hyperlucent lung
 - CECT for differentiation of central neoplasm from peripheral mucus plug
- Bronchiectasis
 - May exhibit mucus plugs and superimposed infection
 - Typically multifocal

Arteriovenous Malformation

- Direct communication between feeding pulmonary artery and draining pulmonary vein
- Contrast enhancement
- No bronchial obstruction, hyperlucency, or hyperinflation

Intralobar Sequestration

- Heterogeneous attenuation
- May exhibit areas of hyperlucency
- Anomalous feeding artery typically arises from descending thoracic aorta
- Characteristic lower lobe location

Intrapulmonary Bronchogenic Cyst

- Lower lobe location; medial 1/3 of lung
- May be fluid-filled, air-filled, or both (air-fluid level)

Congenital Lobar Overinflation

- Neonates and infants with respiratory distress
- Typically lobar, not segmental
- Left upper lobe most commonly affected
- Progressive lobar hyperinflation with mass effect due to check-valve bronchial obstruction

PATHOLOGY

General Features

- Etiology
 - 2 theories of pathogenesis
 - Disconnection of bronchial cells from bronchial bud
 - Postulated to occur in 4th to 6th weeks of gestation
 - Disconnected cells undergo normal division with resultant normal distal bronchial branching
 - In utero vascular insult
 - □ Focal ischemia after 16th week of gestation
 - Focal bronchial injury results in atresia with normal development of distal bronchi
 - Obstruction to proximal drainage with mucocele formation
- Associated abnormalities
 - Pediatric patients
 - Bronchogenic cyst
 - Congenital pulmonary airway malformation
 - Sequestration
 - Reports of systemic arterial supply

Gross Pathologic & Surgical Features

• Focal short-segment BA; no connection between bronchus distal to atresia and proximal feeding bronchus

- Mucocele distal to atresia
- Overexpanded lung distal to atresia; likely from collateral ventilation
 - Pores of Kohn, canals of Lambert
- Reported bacterial, mycobacterial, viral, and fungal infections

Microscopic Features

- Alveolar overexpansion
- Signs of infection/inflammation in complicated BA
- Airways plugged with mucus
- No evidence of lung destruction

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Asymptomatic adult (60%); incidental imaging finding
 - Cough, recurrent infection, dyspnea
- Other signs/symptoms
- Wheezing, hemoptysis
 - Decreased breath sounds over affected lung

Demographics

- Age
 - Wide age range
 - Mean age at diagnosis: 17 years
- Sex
 - o M:F = 16:9

Natural History & Prognosis

• Excellent

Diagnosis

- Imaging diagnosis after exclusion of central obstructing lesion
- Bronchoscopy may be normal or may reveal blind-ending bronchus

Treatment

- None for asymptomatic patients
- Surgical resection for intractable or recurrent infection
- Reported endobronchial treatment with transbronchial aspiration and creation of patent communication with central bronchi

DIAGNOSTIC CHECKLIST

Consider

• BA in asymptomatic patient with central nodular, tubular, or branching opacity surrounded by hyperlucent lung

Image Interpretation Pearls

 Prospective imaging diagnosis allows conservative management of asymptomatic patients

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- Masroujeh R et al: Endobronchial treatment of bronchial atresia. Am J Respir Crit Care Med. 200(3):e25-6, 2019

Bronchial Atresia





(Left) Axial CECT minimumintensity projection (minIP) image of a patient with bronchial atresia shows a lingular branching mucocele \square with surrounding pulmonary hyperlucency 🔁 and allows identification of the adjacent affected bronchus 2. (Right) Composite image with axial CECT of a patient with persistent fever shows a right lower lobe branching opacity with an intrinsic air-fluid level \blacktriangleright and surrounding lung hyperlucency 🔁, consistent with bronchial atresia with infected mucocele.





(Left) Axial CECT shows extensive right lower lobe hyperlucency and 1 of several extensions of a branching mucocele ➡. The patient was prospectively diagnosed with bronchial atresia. (Right) Axial CECT of the same patient obtained at a later date because of acute symptoms of cough and fever shows a new irregular consolidation 🔁 in the affected right lower lobe, consistent with pneumonia. Patients who fail to respond to antibiotic treatment may require surgical excision of the affected lung.





(Left) Coronal CECT of an asymptomatic 66-year-old woman shows a nonenhancing branching mucocele 🛃 surrounded by hyperlucent left upper lobe, characteristic of bronchial atresia. No further imaging or management is required. (Right) Axial NECT (soft tissue window) of a patient with left lower lobe bronchial atresia shows a branching mucocele, which exhibits internal layering milk of calcium \blacksquare . Although this is an atypical manifestation of bronchial atresia, the other morphologic features were diagnostic.

KEY FACTS

TERMINOLOGY

- Extralobar sequestration (ELS)
- Sequestered lung • No communication with tracheobronchial tree
 - Systemic blood supply

IMAGING

- Radiography
 - Basilar homogeneous mass, well-defined borders
 - Adjacent to posteromedial hemidiaphragm
 - Large lesions may produce opaque hemithorax
- CT
 - Homogeneous or heterogeneous soft tissue mass
 - May exhibit cystic changes from intrinsic pulmonary airway malformation
 - Visualization of systemic vascular supply
- **MR**: Homogeneous or heterogeneous soft tissue mass± cystic spaces with systemic blood supply
- Prenatal diagnosis with ultrasound &/or MR

TOP DIFFERENTIAL DIAGNOSES

- Congenital pulmonary airway malformation
- Neuroblastoma

PATHOLOGY

- Well-defined supernumerary lung tissue with systemic blood supply
- Associated congenital anomalies (> 50%): Congenital diaphragmatic hernia, type II pulmonary airway malformation

CLINICAL ISSUES

- Neonates, infants; M:F = 4:1; rarely diagnosed in asymptomatic adults
- Symptoms/signs: Respiratory distress, feeding difficulties
- Surgical excision

DIAGNOSTIC CHECKLIST

• Consider ELS in neonates with intrathoracic soft tissue mass with systemic blood supply

(Left) AP chest radiograph of a newborn with a left basilar cystic lesion diagnosed on prenatal ultrasound shows a homogeneous spherical lobular mass \implies in the left inferior hemithorax. (Right) Composite image with axial (top) and coronal (bottom) T2WI FS MR of the same patient shows a multilocular T2-bright cystic lesion with thin low signal intensity tissue septa. A systemic feeding vessel was not visualized, but extralobar sequestration with intrinsic pulmonary airway malformation type 2 was diagnosed at surgery.





(Left) Coronal CECT of an infant with extralobar sequestration shows a welldefined triangular mass 🔁 in the left inferior hemithorax supplied by an anomalous vessel 🛃 that arises from the descending thoracic aorta. (Courtesy D. Frush, MD.) (Right) Graphic illustrates the morphologic features of extralobar sequestration characterized by supernumerary lung tissue invested in pleura \blacksquare , located in the left inferior hemithorax, and supplied by the systemic circulation \square .





Abbreviations

• Extralobar sequestration (ELS)

Definitions

- Sequestered lung
 - No normal communication to tracheobronchial treeSystemic blood supply
- ELS
 - Supernumerary lung tissue often covered by pleura, separate from adjacent lung

IMAGING

General Features

- Best diagnostic clue
 - Left lower thoracic soft tissue mass with systemic blood supply in neonate
- Location
- Basilar thorax adjacent to hemidiaphragm
- Size
 - Wide range; may occupy entire hemithorax
- Morphology
- Ovoid, spherical, pyramidal

Radiographic Findings

- Basilar triangular opacity, well-defined borders
- Adjacent to posteromedial hemidiaphragm
- No intrinsic air, air-fluid levels, air bronchograms
- Large lesions may produce opaque hemithorax

CT Findings

- CECT
 - Homogeneous or heterogeneous soft tissue mass with well-defined borders
 - May exhibit intrinsic fluid-filled cysts; no intralesional gas
 - Visualization of systemic vascular supply
 - Single or multiple feeding vessels

MR Findings

- Homogeneous or heterogeneous soft tissue mass
- Identification of intrinsic cystic spaces
- Identification of systemic blood supply

Angiographic Findings

- Rarely performed
- Identification of arterial blood supply
 - Thoracic or abdominal aorta (80%)
 - Other (15%): Splenic, gastric, subclavian, intercostals
 - o Multiple arteries (20%)

Prenatal Ultrasound

- Homogeneous, echogenic mass with well-defined borders
 Mass effect on mediastinum in large lesions
- Identification of intralesional cysts
- Identification of systemic blood supply

Imaging Recommendations

- Best imaging tool
 - Prenatal ultrasound for early diagnosis

• Multidetector CT angiography for surgical planning and identification of vascular supply

DIFFERENTIAL DIAGNOSIS

Congenital Pulmonary Airway Malformation (CPAM)

- Congenital lung lesion of neonates and infants
- Microcystic CPAM (solid-appearing) may mimic ELS
 Normal blood supply and venous drainage

Neuroblastoma

- Malignant neoplasm of sympathetic ganglia
- May be congenital
- Elongate paravertebral soft tissue mass

PATHOLOGY

General Features

- Associated abnormalities
 - Associated congenital anomalies (> 50%)
 - Congenital diaphragmatic hernia (most common)
 - Type II CPAM

Gross Pathologic & Surgical Features

- Ovoid, spherical, or pyramidal soft tissue mass
- Pleural investment in thoracic lesions
- Characteristic systemic blood supply and systemic venous drainage
- May exhibit internal cystic changes

Microscopic Features

- Resembles normal lung with bronchial, bronchiolar, alveolar dilatation
- Intrinsic pulmonary airway malformation type II (50%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Respiratory distress, feeding difficulties
 - May be asymptomatic

Demographics

- Age
 - Neonates, infants; majority diagnosed by 6 months
 Rarely diagnosed in asymptomatic adult
- Sex
- o M:F = 4:1

Natural History & Prognosis

 Excellent prognosis in absence of congenital anomalies or pulmonary hypoplasia

Treatment

• Surgical excision

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- Fukui T et al: Extralobar pulmonary sequestration in the middle mediastinum. Gen Thorac Cardiovasc Surg. 65(8):481-3, 2017

Intralobar Sequestration

KEY FACTS

TERMINOLOGY

- Intralobar sequestration (ILS)
- Sequestration: No normal communication with tracheobronchial tree + systemic blood supply
- ILS: Shares visceral pleura of affected lobe

IMAGING

- Radiography
 - Lower lobe lung mass or consolidation
 - o Well-defined, lobular, irregular, or ill-defined margins
 - Homogeneous or heterogeneous
- CT
 - Lesion identification and characterization
 - Basilar consolidation or mass
 - Solid &/or cystic components
 - May contain fluid, air, air-fluid levels
 - Identification of systemic blood supply
- MRA: Identification of systemic feeding vessel(s)

TOP DIFFERENTIAL DIAGNOSES

- Pneumonia
- Lung abscess
- Lung cancer
- Extralobar sequestration

PATHOLOGY

- Systemic arterial supply, pulmonary venous drainage
- Chronic inflammation, cysts, extensive fibrosis

CLINICAL ISSUES

- Signs and symptoms: Fever, productive cough, chest pain
- Treatment: Lobectomy

DIAGNOSTIC CHECKLIST

- Consider ILS in patient with persistent lower lobe abnormality and history of recurrent infection
- CTA is imaging modality of choice for characterization of ILS and identification of systemic blood supply

(Left) PA chest radiograph of a 42-year-old woman with intralobar sequestration who presented with recurrent pulmonary infection shows a left lower lobe retrocardiac opacity 🔁 with irregular borders. The lesion did not resolve with antibiotic treatment. (Right) Axial CECT of the same patient shows a triangular left lower lobe soft tissue mass \blacksquare with adjacent architectural distortion. The lesion exhibited heterogeneous attenuation at this level on soft tissue window images (not shown).





(Left) Axial CECT of the same patient shows the systemic aortic branch \blacksquare that supplied the intralobar sequestration. Such vessels characteristically course within the pulmonary ligament. (Right) Graphic shows the morphologic features of intralobar sequestration, which is typically a heterogeneous lower lobe lesion with irregular borders often with intrinsic solid and cystic components. The latter may contain air, fluid, &/or air-fluid levels. An anomalous systemic aortic branch \blacksquare supplies the lesion.





- Abbreviations
- Intralobar sequestration (ILS)

Definitions

- From Latin "sequestrare" (to be separated)
- ILS (~ 75%)
- Shares visceral pleura of affected lobe
- Pulmonary sequestration
 - No normal communication with tracheobronchial treeSystemic blood supply
- Extralobar sequestration (~ 25%)
 Supernumerary lung tissue
 - Separate pleural investment when intrathoracic
- Bronchopulmonary foregut malformation
 - Pulmonary sequestration (extralobar sequestration or ILS) with patent foregut communication (esophagus, stomach) (rare)

IMAGING

General Features

- Best diagnostic clue
 - Chronic basilar mass, consolidation, or cystic lesion in patient with recurrent infection
- Location
 - Lower lobes, slightly more common on left (55-64%)
 - Posterior basilar segments > medial basilar segments
- Size
- o Variable
- Morphology
 - Irregular borders
 - o Often heterogeneous with solid &/or cystic components

Radiographic Findings

- Lower lobe lung mass or consolidation (persistent on serial imaging)
- Well-defined, lobular, irregular, or ill-defined margins
- Homogeneous lesion
 - May mimic mass or consolidation
- Heterogeneous lesion
 - May exhibit cystic spaces with intrinsic air/air-fluid levelsPredominantly cystic lesions may occur
- Large lesions may produce mass effect on adjacent lung and mediastinum

CT Findings

- Lesion identification and characterization
- Basilar consolidation or mass
- Irregular borders with adjacent nonsequestered lung
 May exhibit well-defined lobular borders
 - May mimic neoplasm
- Surrounding lung may appear hyperlucent or emphysematous; may mimic air-trapping
- CECT
 - Heterogeneous attenuation accentuated by contrast enhancement of solid areas of lesion
 - Intrinsic air, fluid, and soft tissue components
 - Single or multiple intralesional cystic changes: May contain air, fluid, &/or air-fluid levels

- Solid lesions may mimic consolidation
 May exhibit intralesional branching vessels
- Identification of systemic blood supply
 - ~ 80% of cases on CECT or CT angiography
 - Systemic artery arising from distal descending thoracic or upper abdominal aorta
 - Anomalous artery typically large (6-7 mm in diameter in congenital cases); smaller irregular arteries in acquired cases
 - Multiple systemic arteries in up to 20% of cases
 - Feeding artery often courses within pulmonary ligament
 - Nonvisualization of systemic artery does not exclude diagnosis

MR Findings

- MR not routinely performed
- Lesion characterization
 - Variable signal intensity of cystic components
 - Typically high signal intensity on T2WI
- MRA
- Identification of systemic feeding vessel(s)

Ultrasonographic Findings

- Prenatal ultrasound
 - Solid homogeneous well-circumscribed echogenic mass
 - Cyst components possible with hybrid lesions
 - Doppler imaging for identification of systemic arterial supply

Angiographic Findings

- Catheter angiography rarely performed
- Identification of feeding vessel(s)
 - o Thoracic aorta (75%)
 - o Abdominal aorta (20%)
 - Intercostal artery (5%)
 - o Multiple arteries (16%)
- May allow identification of venous drainage
 - o 95% have pulmonary venous drainage
 - 5% have systemic venous drainage, usually via azygos, hemiazygos, superior vena cava, or intercostal routes

Imaging Recommendations

- Best imaging tool
 - CTA is imaging modality of choice for characterization of ILS and identification of systemic blood supply
- Protocol advice
 - Multiplanar reformatted images and maximum-intensity projection (MIP) images for optimal identification and characterization of vascular supply and venous drainage

DIFFERENTIAL DIAGNOSIS

Pneumonia

- Consolidation, mass-like consolidation
- No systemic blood supply
- Resolution with antibiotic treatment

Lung Abscess

- Mass/mass-like consolidation
 - Intrinsic cavitation
 - No systemic blood supply

- Slow response to antibiotic treatment
- May rarely require external drainage

Lung Cancer

- Preferential upper lobe involvement
- Mass/mass-like consolidation
- May exhibit cavitation
- Locally invasive
- No systemic blood supply

Postobstructive Pneumonia

- Endoluminal tumor/obstructing lesion • Volume loss
 - Peripheral consolidation
- No systemic blood supply

Extralobar Sequestration

- Supernumerary lung tissue
- Well-defined pyramidal basilar soft tissue mass
 May exhibit intrinsic fluid-filled cysts
- 90% in left inferior hemithorax
 - Other locations
 - Diaphragm
 - Abdomen
 - Mediastinum
- Systemic arterial supply
- Typically systemic venous drainage

PATHOLOGY

General Features

- Etiology
 - Controversy regarding etiology
 - Postulated congenital etiology
 - Increasing reports of ILS in neonates and infants with increased utilization of prenatal ultrasound
 - Reports of coexistent intralobar and extralobar sequestrations in same infant
 - Postulated acquired etiology
 - Most lesions originally described in adults
 - Rare association with other congenital anomalies
 - Normal pulmonary venous drainage
 - Postulated chronic lower lobe pneumonia with loss of pulmonary artery supply/airway communication and subsequent acquisition of systemic blood supply from parasitized pulmonary ligament arteries

Gross Pathologic & Surgical Features

- 98% of cases in lower lobes
 - Left slightly more common than right
- Intralobar location
 No normal communication with tracheobronchial tree
- Thick, fibrous visceral pleura over lesion
- Cut section
 - o Solid &/or cystic components
 - Dense fibrotic consolidated lung
 - Cysts contain blood, pus, or gelatinous material
 - Cystic spaces resemble ectatic bronchi
- ILS surrounded by nonsequestered lung
- Systemic arterial supply
- Pulmonary venous drainage

Microscopic Features

- Chronic inflammation, vascular sclerosis, cystic changes, extensive fibrosis
- Atherosclerosis of anomalous feeding arteries

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Signs and symptoms of pulmonary infection
 - o Fever
 - Productive cough
 - Chest pain, may be pleuritic
- Other signs/symptoms
 - o Hemoptysis
 - 15-20% asymptomatic: Incidental imaging abnormality

Demographics

- Age
 - o Anyage
 - Infancy
 - Late childhood
 - Young adulthood
 - Adulthood
 - o 50% > 20 years of age
- Sex
 - \circ M = F

Natural History & Prognosis

• Excellent prognosis following surgical excision

Treatment

- Lobectomy
 - Symptomatic lesions, recurrent infection
 - Preoperative imaging for identification of systemic feeding vessels
 - Endovascular occlusion of arterial supply prior to surgery can be utilized to reduce intraoperative bleeding

DIAGNOSTIC CHECKLIST

Consider

• ILS in patient with recurrent or persistent lower lobe pulmonary abnormality and history of recurrent infection

Image Interpretation Pearls

• CTA is imaging modality of choice for characterization of ILS and identification of systemic blood supply

Reporting Tips

• Multiplanar reformatted images and MIP images for optimal identification and characterization of vascular supply and venous drainage

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Intralobar Sequestration





(Left) Composite image with coronal CECT of a 65-year-old woman shows a right lower lobe intralobar sequestration that manifests as a multicystic lung lesion 🔁 with systemic blood supply \blacksquare from the descending thoracic aorta. (Right) Composite image with axial CECT of a 41-year-old man shows a left lower lobe cavitary nodule 🔁 with nodular cavity walls and systemic blood supply ➡ from the descending thoracic aorta, consistent with an intralobar seauestration. Intralobar sequestration may mimic primary lung cancer.





(Left) PA chest radiograph of a patient with recurrent pulmonary infection demonstrates a complex right lower lobe mass-like consolidation with cystic/cavitary components and intrinsic air-fluid levels \supseteq . (Right) Composite image with axial NECT in lung (top) and soft tissue (bottom) window demonstrates a lobulated right lower lobe lesion with intrinsic fluid, soft tissue, and air-fluid levels. The lesion is supplied by an anomalous systemic artery \blacksquare arising from the descending aorta.





(Left) Axial NECT of a 28-yearold woman with intralobar sequestration shows a hyperlucent right lower lobe posterior basilar segment with intrinsic dilated vascular structures. A large anomalous vessel was identified in the adjacent mediastinum. (Right) Coronal oblique CECT of the same patient shows the large systemic artery \supseteq that supplied the sequestration and originated from the celiac axis. Intralobar sequestration may exhibit soft tissue attenuation, cystic changes, &/or hyperlucent lung.

KEY FACTS

TERMINOLOGY

- Diffuse pulmonary lymphangiomatosis (DPL)
- Congenital disorder: Increased number and complexity of lymphatic channels
- Involves lymphatics in interlobular septa, pleura, and peribronchovascular regions

IMAGING

• Radiography

- Diffuse bilateral reticular opacities
- Unilateral or bilateral pleural effusion
- Cardiomegaly from pericardial effusion
- CT
 - Smooth interlobular septal thickening
 - Patchy ground-glass opacities
 - Pleural effusion; pleural thickening
 - o Mediastinal soft tissue infiltration/lymphadenopathyo Pericardial effusion
- CT following direct lymphangiography may aid in diagnosis

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary lymphangiectasis
- Pulmonary edema
- Lymphangitic carcinomatosis
- Erdheim-Chester disease

CLINICAL ISSUES

- Symptoms/signs
 - Dyspnea, wheezing
 - o Pleural effusion, chylothorax
 - Restrictive and obstructive pulmonary function abnormalities
- Children and young adults
- Treatment: Diet, surgery, radiation
- Progressive, often fatal disease

DIAGNOSTIC CHECKLIST

• Consider DPL in children or adults with unexplained diffuse interlobular septal thickening and chylous pleural effusions

(Left) Axial CECT of a patient with diffuse pulmonary lymphangiomatosis shows typical CT features, including smooth thickening of interlobular septa 🔁 and centrilobular micronodules ₽ E A Constant State thick peribronchovascular lymphatics. (Right) Axial CECT of the same patient shows soft tissue infiltration \blacksquare of the mediastinum due to proliferation of abnormal lymphatic tissue. Mediastinal soft tissue infiltration is a common finding in diffuse pulmonary lymphangiomatosis.











Abbreviations

• Diffuse pulmonary lymphangiomatosis (DPL)

Definitions

- Congenital disorder: Increased number and complexity of anastomosing lymphatic channels
- Lymphatics in interlobular septa, pleura, peribronchovascular regions

IMAGING

General Features

 Best diagnostic clue
 Diffuse thickening of interlobular septa and bronchovascular structures, mediastinal fat infiltration

Radiographic Findings

- Diffuse bilateral reticular opacities
- Unilateral/bilateral pleural effusion(s); chylothorax
- Cardiomegaly from pericardial effusion

CT Findings

- Smooth interlobular septal thickening; thick peribronchovascular interstitium
- Patchy ground-glass opacities
- Pleural effusion; pleural thickening
- Mediastinal soft tissue infiltration
- Pericardial effusion
- Lymphadenopathy uncommon
- CT findings after direct lymphangiography: Abnormal contrast distribution in pulmonary interstitium, chest wall, mediastinum, pericardium; dilated lymphatic channels

MR Findings

- Pleural/pericardial effusions
- Heterogeneous hyperintense signal in mediastinum and paraspinal regions on T2WI: Abnormal lymphatic tissue

Imaging Recommendations

- Best imaging tool
 - CT and HRCT optimally demonstrate peribronchovascular/septal thickening and mediastinal fat infiltration
 - o CT after direct lymphangiography may aid in diagnosis

DIFFERENTIAL DIAGNOSIS

Pulmonary Lymphangiectasis

- Dilated pulmonary lymphatics, no increase in number
- Neonates with respiratory distress
- Interlobular septal thickening, chylous pleural effusion

Pulmonary Edema

- Cardiogenic and noncardiogenic
- Smooth septal and peribronchovascular thickening
- Patchy ground-glass opacities, pleural effusion

Lymphangitic Carcinomatosis

- Advanced malignancy; typically adenocarcinoma
- Smooth or nodular asymmetric septal thickening
- Pleural effusion, lymphadenopathy

Erdheim-Chester Disease

- Perilymphatic cellular infiltration
- Smooth interlobular septal and pleural thickening
- Symmetric osteosclerosis

PATHOLOGY

General Features

- Etiology
 Onknown
- Associated abnormalities
- o Chylothorax
- o Chylopericardium
- Chylous ascites
- Reports of protein-wasting enteropathy and lymphopenia

Gross Pathologic & Surgical Features

• Thick interlobular septa, peribronchovascular interstitium, pleura

Microscopic Features

- Increased diameter, number, and complexity of interstitial lymphatic channels
- Reports of involvement of other organs (any tissue in which lymphatics are found)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea, wheezing, hemoptysis, chyloptysis, bronchial casts
- Other signs/symptoms
 - Restrictive and obstructive pulmonary function abnormalities
 - Pleural effusion, chylothorax

Demographics

- Age
 - Children and young adults
- Sex
 No predilection

Natural History & Prognosis

• Progressive, often fatal disease

Treatment

- Dietary treatment
- Surgical treatment of pleural effusions
- Thoracic duct ligation
- Radiation therapy with variable success

DIAGNOSTIC CHECKLIST

Consider

• DPL in children or adults with unexplained diffuse interlobular septal thickening and chylous pleural effusions

SELECTED REFERENCES

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Apical Lung Hernia

KEY FACTS

TERMINOLOGY

• Protrusion of upper lobe apical segment into neck through Sibson fascia (covers lung apex) defect

IMAGING

- Radiography
 - Apical lucency extending into base of neck
 - o Lateral tracheal deviation
 - Easily missed if examination is not made in inspiration or during Valsalva maneuver
- CT
 - o Continuity of apical lucency with adjacent lung
 - Lung constriction at hernia aperture

TOP DIFFERENTIAL DIAGNOSES

- Paratracheal air cyst
- Esophageal diverticula
- Laryngocele

PATHOLOGY

- Weakening or tearing of Sibson fascia anteromedially, between anterior scalene and sternocleidomastoid muscles
- Etiology
 - O Usually congenital in infants and childrenO Usually acquired in adults
- Repeated, prolonged Valsalva maneuver

CLINICAL ISSUES

- Signs/symptoms
 - Soft, bulging mass in supraclavicular region
 - Cough, hoarseness, dysphagia
- Male > female
- Treatment
- None required
- Usually reduces easily
- Surgery if incarcerated, symptomatic, or for cosmetic reasons

(Left) Graphic shows the anatomy of apical lung hernia. The herniation of the lung apex To ccurs through adefect in Sibson fascia \blacksquare , which allows protrusion of the lung apex into the adjacent neck. (Right) PA chest radiograph shows protrusion of the right lung apex ➡ into the right neck soft tissues, consistent with an apical lung hernia. Apical lung hernias are usually congenital abnormalities in children that tend to resolve spontaneously. Most apical lung hernias are asymptomatic, intermittent, and reducible.





(Left) PA chest radiograph shows lucency in the right neck with mild tracheal deviation to the left, consistent with an apical lung hernia 🔁. (Right) Coned-down PA chest radiograph of the same patient obtained during a Valsalva maneuver shows ballooning of the apical lung hernia. Apical lung hernias in adults are usually acquired, result from previous surgery or trauma, and are also reported in wind instrumentalists, weight lifters, and patients with chronic cough and emphysema.





Synonyms

• Cervical lung hernia

Definitions

- Protrusion of upper lobe apical segment into neck through Sibson fascia (covers lung apex) defect
- Sibson fascia = deep cervical fascia, suprapleural fascia

IMAGING

General Features

- Location
 - o Typically unilateral, may be bilateral
 - o Right > left
- Size
- o Variable size

Imaging Recommendations

- Best imaging tool
 - Fluoroscopy
 - Hernia manifests or worsens with Valsalva maneuver, cough, maximal inspiration
 - Reducibility of hernia may be assessed dynamically
- Protocol advice
 - Coronal and sagittal CT reformatted images improve anatomic delineation of apical hernia

Radiographic Findings

- Apical lucency that extends into base of neck
- Lateral tracheal deviation
- Best seen with maximal inspiration or Valsalva

CT Findings

- Continuity of apical lucency with adjacent lung
- Lung constriction at hernia aperture
- Lung parenchyma between anterior scalene and sternocleidomastoid muscles
- Tracheal deviation
- False-negative CT due to intermittent nature of some apical hernias
 - Obtain images at maximal inspiration to improve detection

DIFFERENTIAL DIAGNOSIS

Paratracheal Air Cyst

• Mucosal herniation through tracheal wall

Esophageal Diverticula

- Do not usually cause lateral tracheal deviation
- Unlike apical hernia, may exhibit air-fluid level
- Contrast esophagram helpful

Laryngocele

• Dilated appendix of laryngeal ventricle

Lateral Pharyngeal Diverticulum

• Mucosal herniation through thyrohyoid membrane

Apical Bulla

- Associated paraseptal emphysema
- No mass effect

PATHOLOGY

General Features

Etiology

- o Usually congenital in infants and children
 - 60% of congenital lung hernias are apical
 - Associated with hernias in other locations (umbilical, inguinal)
- Usually acquired in adults
 - Penetrating trauma
 - Surgery
 - Chest wall neoplasm, infection
 Increased intrathoracic pressure
 - Wind instrumentalists
 - Emphysema, chronic cough
 - Weight lifters
 - Repeated, prolonged Valsalva maneuver

Gross Pathologic & Surgical Features

- Weakening or tearing of Sibson fascia, which covers lung apex
 - Usually anteromedially, between anterior scalene and sternocleidomastoid muscles
 - o Defect usually large, hernia easily reducible

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic
- Other signs/symptoms
 - Soft, bulging mass in supraclavicular region
 - Cervical pain
 - o Cough, hoarseness, dysphagia
 - Neuropathic pain from nerve root compression

Demographics

- Age
 - Patients may present in childhood or adulthood
- Sex
 - o Male > female
- Epidemiology
 - Very rare condition
 - Apical lung hernias account for ~ 33% of lung hernias
 - ~ 65% lung hernias are "thoracic"; around lateral
 - margin of thorax, through ribs
 - Diaphragmatic lung hernia rarest

Natural History & Prognosis

- Congenital apical hernias tend to resolve spontaneously
- Incarceration rare
- ↑ risk of pneumothorax with placement of central venous catheter or tracheostomy

Treatment

- None; usually reduces easily
- Surgery for incarcerated or symptomatic hernias or cosmetic reasons

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 Chaturvedi A et al: Imaging of thoracic hernias: types and complications. Insights Imaging. 9(6):989-1005, 2018
TERMINOLOGY

- Proximal interruption of pulmonary artery (PIPA): Failed development of proximal pulmonary artery
 - "Interruption" preferred over "absence": Intact pulmonary trunk and contralateral pulmonary artery

IMAGING

- Radiography
 - o Small ipsilateral lung and hilum
 - o Aortic arch contralateral to interrupted pulmonary artery
- CT
 - Unilateral absence of pulmonary artery
 - Contralateral aortic arch
 - Normal bronchial branching pattern
 - Bronchiectasis from recurrent infections
 - o Mosaic attenuation from variable perfusion
 - Parenchymal and subpleural cysts, honeycombing
 - Visualization of ipsilateral collateral systemic arteries

TOP DIFFERENTIAL DIAGNOSES

- Swyer-James-MacLeod syndrome
- Mediastinal fibrosis
- Scimitar syndrome

PATHOLOGY

• Left PIPA: Higher incidence of congenital cardiovascular anomalies

CLINICAL ISSUES

- Symptoms/signs
 - May be incidental finding in asymptomatic patient
 - Recurrent pulmonary infection, dyspnea, hemoptysis
 - Pulmonary hypertension
- Prognosis: Determined by associated cardiac anomalies and pulmonary artery hypertension
- Many can be conservatively managed, although embolization &/or pneumonectomy may be necessary

(Left) PA chest radiograph of a patient with proximal interruption of the right pulmonary artery shows a small right hilum \supseteq , a small right lung, and compensatory left lung hyperinflation. As in this case, the aortic arch \blacksquare is typically contralateral to the interrupted pulmonary artery. (Right) Axial CECT of the same patient shows interruption of the right pulmonary artery at its expected origin 🛃. The serrated contour of the right pleural surface \square is produced by the systemic collateral vessels that supply the right lung.





(Left) Axial CECT of the same patient shows a small hypoplastic right lung with cystic changes \bowtie and subtle peripheral reticular opacities \supseteq related to the systemic collateral vessels that supply the affected lung. Bronchiectasis 🔁 is a frequent finding related to chronic pulmonary infection. (Right) Axial CECT of the same patient shows bilateral areas of mosaic attenuation. Ipsilateral low attenuation 😂 is likely due to hypoperfusion. Contralateral areas of low attenuation \blacksquare may be due to surrounding overperfusion.





Abbreviations

• Proximal interruption of pulmonary artery (PIPA)

Synonyms

- Unilateral absence of pulmonary artery (UAPA)
 - "Interruption" preferred over "absence": Intact pulmonary trunk and contralateral pulmonary artery

Definitions

• Failed development of proximal pulmonary artery

IMAGING

General Features

- Best diagnostic clue
 - Small hilum, small ipsilateral lungContralateral aortic arch
- Location
 - Right > left

Radiographic Findings

- Radiography
 - Affected hemithorax
 - Volume loss, ipsilateral mediastinal shift, ipsilateral hemidiaphragm elevation
 - Small or indistinct hilum
 - Fine linear peripheral opacities: Systemic collateral vessels that supply hypoplastic lung
 - Rib notching (intercostal collaterals)
 - Unaffected hemithorax
 - Compensatory lung hyperinflation
 - Enlarged hilum from increased blood flow
 - Aortic arch typically contralateral to interrupted pulmonary artery
 - Cardiomegaly: Associated cardiac anomalies, pulmonary hypertension

CT Findings

- CTA
 - Proximal pulmonary artery: Completely absent or ends within 1 cm of origin
 - Contralateral aortic arch
 - Normal bronchial branching pattern; bronchiectasis from recurrent infections
 - o Mosaic attenuation
 - Affected lung: Hypoxic vasoconstriction
 - Unaffected lung: Overperfusion
 - No expiratory air-trapping
 - Parenchymal and subpleural cysts, honeycombing
 - Collateral circulation
 - Enlarged vessels: Bronchial, internal mammary, and intercostal arteries
 - Fine peripheral reticulation
 - Pleural thickening and rib notching

MR Findings

• Evaluation of associated congenital cardiac abnormalities

Angiographic Findings

• Documentation of absence of pulmonary artery and systemic collateral vessels

Nuclear Medicine Findings

• V/Q scan

No perfusion of affected side
Normal ventilation of affected side

Imaging Recommendations

Best imaging tool

• CTA is optimal modality

DIFFERENTIAL DIAGNOSIS

Swyer-James-MacLeod Syndrome

- Obliterative bronchiolitis in infant or child
- Unilateral hyperlucent lung with small ipsilateral pulmonary artery
- Expiratory air-trapping

Mediastinal Fibrosis

- Hilar or mediastinal (often calcified) soft tissue with stenosis of adjacent airways and vessels
- Focal and diffuse types

Scimitar Syndrome

- Right lung hypoplasia
- Anomalous venous return of right lung; anomalous vein resembles scimitar (Turkish sword)

PATHOLOGY

General Features

- Etiology
 - Involution of proximal 6th primitive aortic arch
 Intrapulmonary vessels remain intact
- Associated abnormalities
 - Left interruption has higher incidence of congenital cardiovascular anomalies
 - Most commonly tetralogy of Fallot

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - May be incidental finding in asymptomatic patient
 - Recurrent pulmonary infection, dyspnea, hemoptysis
- Other signs/symptoms
 Pulmonary hypertension
- Rare; 1 in 200,000 young adults

Natural History & Prognosis

- Determined by associated cardiac anomalies or pulmonary artery hypertension
- Many can be conservatively managed

Treatment

- Revascularization of interrupted artery in infancy may prevent some degree of lung hypoplasia
- Hemoptysis: Angiographic embolization of systemic collaterals; pneumonectomy may be necessary

- 1. Leitman EM et al: Pulmonary arteries: imaging of pulmonary embolism and beyond. Cardiovasc Diagn Ther. 9(Suppl 1):S37-58, 2019
- 2. Williams EA et al: Proximal interruption of the pulmonary artery. J Thorac Imaging. 34(1):56-64, 2019

(Left) PA chest radiograph of an asymptomatic patient with proximal interruption of the left pulmonary artery shows a small left lung, a small left hilum (⇒), a right aortic arch ➡, and shift of the mediastinal structures to the left. (Right) Lateral chest radiograph of the same patient demonstrates absence of the left pulmonary artery \supseteq . The mediastinum is shifted posteriorly due to left lung hypoplasia and compensatory anterior herniation of the hyperinflated right lung.





(Left) Axial NECT of the same patient shows marked mediastinal shift to the left due to left lung hypoplasia. The left pulmonary artery is interrupted 🔁, and the right lung herniates anteriorly across the midline 🛃 due to compensatory hyperinflation. (Right) Coronal NECT of the same patient shows that the right pulmonary artery \implies is larger than the aortic arch $E\!\!>$, a finding that suggests pulmonary arterial hypertension, which is often found in association with proximal interruption of the pulmonary artery.





(Left) Composite image with PA (left) and lateral (right) chest radiographs of a patient with proximal interruption of the left pulmonary artery shows absence of the left pulmonary artery \supseteq . This case illustrates an uncommon variant in that the aortic arch \blacksquare is ipsilateral to the interrupted artery. (Right) Axial CECT of the same patient obtained for evaluation of pneumonia shows interruption of the left pulmonary artery \blacksquare and left lung consolidation 😂. Infection commonly affects the hypoplastic lung.









(Left) Axial CECT MIP image of a patient with proximal interruption of the left pulmonary artery shows asymmetric blood supply to the lungs. The left lung is supplied by bronchial ⊇ and intercostal ⊇ collateral vessels. (Right) Coronal CECT MIP image of the same patient shows enlarged bronchial arteries 🛃 that supply the hypoplastic left lung due to proximal interruption of the left pulmonary artery. Note dilatation of the right pulmonary artery 🔁. Affected patients may develop pulmonary hypertension.





(Left) Frontal pulmonary artery angiography of a patient with proximal interruption of the left pulmonary artery shows a small left lung, an enlarged right pulmonary artery \supseteq , and nonvisualization of the *left pulmonary artery.* (Right) Frontal angiography of a patient with hemoptysis and interrupted right pulmonary artery shows multiple enlarged systemic collateral arteries \bowtie supplying the right lung. Angiography and embolization may be required to treat recurrent or severe hemoptysis.





(Left) Anterior projection from a perfusion scintigram shows absence of perfusion to the right lung secondary to proximal interruption of the right pulmonary artery. (Right) Axial T2WI MR shows a normal pulmonary trunk, a normal left pulmonary artery, and proximal interruption of the right pulmonary artery ₽. MR imaging may be obtained in patients with proximal interruption of the pulmonary artery to evaluate associated congenital cardiac abnormalities.

TERMINOLOGY

- Abbreviations
 - Aberrant left pulmonary artery (ALPA)
 - Pulmonary artery sling (PAS)
- Definition
 - Originates from posterior right pulmonary artery and courses toward left hilum between trachea and esophagus

IMAGING

- Radiography
 - Mass effect on right lower trachea
 - Hyperinflation/atelectasis of right lung
 - Ovoid opacity (ALPA) between trachea and esophagus on lateral chest radiography
- CT/MR
 - Left pulmonary artery origin from posterior distal right pulmonary artery
 - ALPA course between trachea and esophagus

TOP DIFFERENTIAL DIAGNOSES

- Vascular ring
- Mediastinal mass
- Congenital proximal interruption of pulmonary artery

CLINICAL ISSUES

- Signs/symptoms
 - o Stridor, wheezing, recurrent pneumonia
 - Dysphagia, failure to thrive
- Associated conditions
 - o Tracheobronchial abnormalities (40-60%)
 - Congenital heart disease (15-85%)
- Demographics
 - o 2/3 of affected patients present on 1st day of life
 - Isolated ALPA reported in asymptomatic adults
- Treatment
 - o Surgical ligation and reanastomosis of ALPA
 - o Tracheoplasty for associated tracheal anomalies

(Left) Axial CECT MIP reformatted image of a 48year-old woman with aberrant left pulmonary artery (ALPA) shows the left pulmonary artery origin \square from the right pulmonary artery 🔁. The anomalous vessel partially encases the stenotic distal trachea 🖂. (Right) Coronal CECT miniP reformatted image of the same patient shows long-segment tracheal stenosis \supseteq due to complete cartilaginous rings and a right upper lobe tracheal bronchus \blacksquare . These tracheobronchial anomalies are commonly associated with ALPA.











Abbreviations

- Aberrant left pulmonary artery (ALPA)
- VACTERL: Nonrandom association of vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula/atresia, renal, and limb anomalies

Synonyms

- Anomalous pulmonary artery
- Pulmonary artery sling (PAS)

Definitions

 ALPA arises from posterior right pulmonary artery and courses between trachea and esophagus toward left hilum

IMAGING

General Features

- Best diagnostic clue
- Left pulmonary artery between trachea and esophagus
- Location
 Middle or visceral mediastinum
- Size
 - ALPA may be smaller than normal left pulmonary artery

Radiographic Findings

- Right-sided mass effect on lower trachea
- Leftward deviation of lower trachea
- Right lung hyperexpansion or atelectasis
 Vascular compression of trachea and right bronchi
- Ovoid opacity (ALPA) between trachea and esophagus on lateral chest radiography

Fluoroscopic Findings

- Upper Gl
 - Anterior impression on midesophagus
 - Rightward deviation of esophagus

CT Findings

- CECT
 - Left pulmonary artery origin from posterior distal right pulmonary artery
 - Courses between trachea and esophagus toward left lung
 - Normal pulmonary artery branching
 - No normal vascular connection between pulmonary trunk and left lung
 - Associated findings
 - Tracheobronchial anomalies (40-60%)
 - Complete cartilaginous tracheal rings
 - Tracheomalacia, atelectasis, or hyperinflation
 - Tracheal bronchus
 - Congenital heart disease in children (15-85%)

Imaging Recommendations

- Best imaging tool
 - Cross-sectional imaging with CT or MR for assessment of vascular anatomy
- Protocol advice
 - Contrast-enhanced CT
 - MR with black or bright blood sequences

DIFFERENTIAL DIAGNOSIS

Vascular Ring

Posterior to esophagus

Mediastinal Mass

• Rarely located between trachea and esophagus

Congenital Proximal Interruption of Pulmonary Artery

• Small hemithorax and small ipsilateral hilum

PATHOLOGY

General Features

- Etiology
 - Embryologic failure of formation of 6th aortic arch leads to anomalous origin of left pulmonary artery
- Associated abnormalities
 - Frequent association with tracheobronchial anomalies (Ring-Sling complex)
 - Association with congenital heart disease (15-85%) and other anomalies
 - Other associated anomalies: Imperforate anus, vertebral anomalies, VACTERL association

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Respiratory symptoms in infancy
 - Stridor most common; occasional apnea
 - Wheezing, recurrent pneumonia
- Other signs/symptoms
 - Dysphagia; failure to thrive

Demographics

- Age
 - o 2/3 of affected patients present on 1st day of life
 - Isolated ALPA reported in asymptomatic adults

Treatment

- Surgical ligation of ALPA and reanastomosis to normal location
- Tracheoplasty for associated tracheal stenosis

DIAGNOSTIC CHECKLIST

Consider

 ALPA in asymptomatic adult with ovoid opacity between trachea and esophagus on lateral radiography

Image Interpretation Pearls

- Anterior impression on esophagus on esophagram
- ALPA course between trachea and esophagus on CT or MR

- Escalon JG et al: Congenital anomalies of the pulmonary arteries: an imaging overview. Br J Radiol. 92(1093):20180185, 2019
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- 4. Fiore AC et al: Surgical treatment of pulmonary artery sling and tracheal stenosis. Ann Thorac Surg. 79(1):38-46; discussion 38-46, 2005

TERMINOLOGY

- Pulmonary arteriovenous malformation (PAVM)
- Communication between pulmonary artery(ies) and pulmonary vein(s), right-to-left shunt

IMAGING

- Radiography
 - Nodule with feeding artery(ies) and draining vein(s)
- CT/MR
 - Sharply defined round or ovoid nodule with feeding artery(ies) and draining vein(s)
 - Simple (80%): 1 or more feeding arteries from same segmental artery
 - Complex (20%): Multiple feeding arteries from different segmental arteries
- Transthoracic contrast echocardiography: Evaluation of cardiac and intrapulmonary shunts
- Nuclear medicine (Tc-99m labeled macroaggregates): Estimation of size of right-to-left shunt

TOP DIFFERENTIAL DIAGNOSES

- Meandering pulmonary vein
- Pulmonary vein varix
- Pulmonary artery pseudoaneurysm
- Solitary pulmonary nodule

PATHOLOGY

• Multiple AVMs highly suggestive of hereditary hemorrhagic telangiectasia

CLINICAL ISSUES

- Asymptomatic: Single PAVM feeding artery < 2 mm
- Symptomatic: 40-60 years of age
 - Hemorrhage, paradoxical embolism

DIAGNOSTIC CHECKLIST

• Consider PAVM for lung nodule with associated tubular opacities representing feeding artery and draining vein

(Left) PA chest radiograph of 34-year-old woman shows a right mid lung zone perihilar nodule 🔁 with a tubular opacity 🔁 that courses from the nodule to the hilum. (Right) Composite image with axial CECT in lung (left) and soft tissue (right) window of the same patient shows a lobulated intensely enhancing right lower lobe nodule 🔁 with feeding and draining vessels \supseteq , consistent with a pulmonary arteriovenous malformation.





(Left) Coronal CTA MIP reformatted image of a 50year-old woman shows a right lower lobe pulmonary arteriovenous malformation (nidus) 🔁 with a single feeding artery 🔁 and a draining vein 🔁. The draining vein is typically larger than the feeding artery. (Right) Composite image with coronal CECT MIP reformatted image in lung (left) and soft tissue (right) window of an 85-yearold woman shows a small *middle lobe pulmonary* arteriovenous malformation 🔁 with a feeding artery and draining vein.





Abbreviations

Pulmonary arteriovenous malformation (PAVM)

Definitions

- Direct communication between pulmonary artery(ies) and pulmonary vein(s), right-to-left shunt
 - Congenital (80-90%): Isolated or related to hereditary hemorrhagic telangiectasia (HHT)/Osler-Weber-Rendu syndrome
 - Acquired (10-20%): Hepatopulmonary syndrome, postsurgical, post-traumatic, post-infectious (actinomycosis, schistosomiasis), metastases, following surgery for complex cyanotic congenital heart disease

IMAGING

General Features

- Best diagnostic clue
- Nodule(s) with feeding artery(ies) and draining vein(s)
 Location
- Peripheral lower lobes, middle lobe, lingula (50-70%)
 Size
- Variable: 1-5 cm in diameter

Radiographic Findings

- Radiography
 - Sensitivity for PAVMs: 50-70%
 - o Ovoid or round nodule with feeding and draining vessels
 - Complex PAVM may mimic consolidation

CT Findings

- Round or ovoid nodule with **feeding artery(ies) and** draining vein(s)
 - **Simple** (80%): 1 or more feeding arteries from same segmental artery
 - **Complex** (20%): Multiple feeding arteries from different segmental arteries
 - Diffuse PAVM (5% of complex PAVMs): Innumerable feeders, frequently lobar

MR Findings

• MRA: Similar to CT for detection; may be used as adjunct for pre-embolization planning

Echocardiographic Findings

• Transthoracic contrast echocardiography (TTCE): Screening test of choice for PAVM, evaluation of cardiac and intrapulmonary shunts; presence of bubbles in left heart following 3 cardiac cycles or more after first appearance in right heart

Nuclear Medicine Findings

• Tc-99m MAA: Right-to-left shunt size estimate

Imaging Recommendations

- Best imaging tool
- CECT with MIP reformatted images; dual-energy CT
- Pulmonary angiography for treatment, not for diagnosis

DIFFERENTIAL DIAGNOSIS

Meandering Pulmonary Vein

- Often misdiagnosed as PAVM
- Lack of nidus or dilated pulmonary artery; tortuous vessel corresponds to pulmonary vein with abnormal course; no shunt

Pulmonary Vein Varix

• Dilated pulmonary vein; no arterial communication

Pulmonary Artery Pseudoaneurysm

• Usually at bifurcation; no draining vein

Solitary Pulmonary Nodule

• More commonly lung cancer, granuloma, hamartoma

PATHOLOGY

General Features

- Genetics
 - HHT: Autosomal dominant disorder, mutations in *ENG* gene (HHT type 1) and *ACVRL1* gene (HHT type 2)

Gross Pathologic & Surgical Features

• Draining vein usually 1-2 mm larger than feeding artery

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic: Single PAVM feeding artery < 2 mm
 - Symptomatic: 40-60 years of age
 - Hemorrhage: Pulmonary hemorrhage or hemothorax (10%), epistaxis from nasal telangiectasia in 95% of HHT (median age: 12 years)
 - CNS complications (40%): Paradoxical embolism, cerebral abscess
- Other signs/symptoms
 - Desaturation, exercise intolerance, cyanosis, and clubbing with large PAVMs

Demographics

- Age: 10% of cases in infancy or childhood
- M:F = 1:2

Diagnosis

- Blood test for identification of mutation (80% of patients); genetic screening
- Screening of risk patients with TTCE; CECT for positive screening

Natural History & Prognosis

• Growth postulated in puberty and pregnancy

Treatment

- Catheter embolization: Asymptomatic with feeding artery ≥ 3 mm or any symptomatic patient
 - o Follow-up CECT post-therapy every 3-5 years

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 Saboo SS et al: Pulmonary arteriovenous malformations: diagnosis. Cardiovasc Diagn Ther. 8(3):325-37, 2018

TERMINOLOGY

- Partial anomalous pulmonary venous return (PAPVR)
- Congenital anomaly: 1-3 pulmonary veins drain into systemic vein or right atrium; left-to-right shunt

IMAGING

- Distribution in adults
 - o Left upper lobe (47%), right upper lobe (38%)
 - Right lower lobe (13%), Left lower lobe (2%)
- Radiography
 - Left upper lobe PAPVR: Lateralization of aortopulmonary reflection
- CT
 - Left upper lobe PAPVR drains to left brachiocephalic via vertical vein
 - Right upper lobe PAPVR drains to superior vena cava
- MR
 - o Allows identification of PAPVR and sinus venosus ASDo Allows shunt quantification (QP/QS)

TOP DIFFERENTIAL DIAGNOSES

- Persistent left superior vena cava
 - May simulate vertical vein
 - o Often associated with dilated coronary sinus
 - Left superior pulmonary vein posterior to left atrial appendage
- Lateralization of aortic-pulmonary reflection
 - o Mediastinal lipomatosis
 - o PAPVR vertical vein, persistent left superior vena cava
 - Mediastinal lymphadenopathy

CLINICAL ISSUES

- Often asymptomatic with only 1 anomalous vein
- Symptoms relate to shunt size: Dyspnea, palpitations, chest pain, tachycardia, edema, systolic murmur
- Surgical correction for symptomatic PAPVR &/or QP/QS > 2:1, vascular rings, congenital heart disease
- Outcome depends on associated conditions (e.g., sinus venosus atrial septal defect)

(Left) PA chest radiograph of a patient with left upper lobe partial anomalous pulmonary venous return shows soft tissue 🔁 lateral to the aortic arch \supseteq and lateralization of the aortic-pulmonary reflection, a subtle yet abnormal finding. (Right) Composite image with axial CECT of the same patient shows the vertical vein \blacksquare coursing lateral to the aortic arch. Note absence of the left superior pulmonary vein from its normal location \blacksquare , anterior to the left mainstem bronchus and posterior to the left atrial appendage.





(Left) Curved coronal CECT reformatted image of the same patient shows a vertical vein 🛃 that arises from segmental left upper lobe pulmonary veins to drain into the ipsilateral left brachiocephalic vein 🔁 (Right) Coronal CECT 3D SSD reformatted image of the same patient shows the left upper lobe partial anomalous pulmonary venous return 🔿, the most common form of partial anomalous pulmonary venous return in the left hemithorax. When isolated, the left-to-right shunt is small and typically asymptomatic.





Abbreviations

• Partial anomalous pulmonary venous return (PAPVR)

Synonyms

• Left upper lobe vertical vein: Left upper lobe PAPVR draining into left brachiocephalic vein

Definitions

• Congenital anomaly: 1-3 pulmonary veins drain into systemic vein or right atrium; left-to-right shunt

IMAGING

General Features

- Best diagnostic clue
 - Direct drainage of pulmonary vein into: Superior vena cava, inferior vena cava, right atrium, or left brachiocephalic vein
- Location
 - Distribution in adults
 - Left upper lobe, most common (47%)
 - Right upper lobe (38%)
 - Right lower lobe (13%)
 - Left lower lobe (2%)

Radiographic Findings

- Radiography
 - Frequently normal
 - Left upper lobe PAPVR: Vertical vein may cause lateralization of aortic-pulmonary reflection
 - o If significant shunt
 - Cardiomegaly, right heart enlargement
 - Pulmonary artery enlargement
 - Increased number and size of pulmonary vessels (shunt vascularity)

CT Findings

• CECT

• Left upper lobe PAPVR

- Drains to left brachiocephalic vein via vertical vein, may drain into coronary sinus, hemiazygos, subclavian, or subdiaphragmatic veins
- Absence of left superior pulmonary vein from normal location (i.e., posterior to left atrial appendage)

• Right upper lobe PAPVR

- Middle lobe pulmonary vein also typically involved
- Drains into superior vena cava, occasionally into azygos vein, right atrium, inferior vena cava, hepatic vein, or portal vein
- Often associated with sinus venosus atrial septal defect (ASD), rarely with ostium primum ASD

• Right lower lobe PAPVR

- Scimitar syndrome: Right lower lobe, occasionally middle &/or upper lobe pulmonary veins drain into inferior vena cava
- May drain directly into right atrium (rare) when associated with sinus venosus ASD

• Bilateral upper lobe PAPVR uncommon (4% of cases)

- If significant left-to-right shunt
 - Right heart enlargement

- Pulmonary artery > 3 cm (pulmonary hypertension)
- Ancillary findings: Persistent left superior vena cava, azygos continuation of inferior vena cava

MR Findings

- MR equivalent to CT for characterization of PAPVR
- MR superior to CT for identification of ASD
- Allows shunt quantification (QP/QS)
 - 2 or more anomalous pulmonary veins &/or sinus venosus ASD may result in significant left-to-right shunt

Echocardiographic Findings

- Echocardiography frequently diagnostic
- Consider cardiac MR or CT for equivocal cases

Imaging Recommendations

- Best imaging tool
 - CT and MR equivalent for detection of PAPVR

DIFFERENTIAL DIAGNOSIS

Persistent Left Superior Vena Cava

- May mimic vertical vein
- Typically associated with dilated coronary sinus
- Left superior pulmonary vein anterior to left mainstem bronchus and posterior to left atrial appendage

Lateralization of Aortic-Pulmonary Reflection

- Mediastinal lipomatosis, most common cause
- Vascular: Vertical vein (PAPVR), persistent left superior vena cava
- Mediastinal lymphadenopathy

PATHOLOGY

Staging, Grading, & Classification

- Partial anomalous pulmonary venous **connection**: Anomalous vein connection with systemic vein
- Partial anomalous pulmonary venous **drainage**: Anomalous vein delivers oxygenated blood to right atrium via sinus venosus ASD

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Frequently asymptomatic if only 1 anomalous pulmonary vein
 - Symptoms relate to shunt size: Dyspnea, palpitations, chest pain, tachycardia, edema, systolic murmur

Natural History & Prognosis

Outcome depends on associated conditions (e.g., sinus venosus ASD)

Treatment

• Surgical correction may be indicated for symptomatic PAPVR &/or QP/QS > 2:1, vascular rings, coexistent congenital heart disease

- 1. Pendela VS et al: Partial anomalous pulmonary venous return presenting in adults: a case series with review of literature. Cureus. 12(6):e8388, 2020
- 2. El-Kersh K et al: Partial anomalous pulmonary venous return: a case series with management approach. Respir Med Case Rep. 27:100833, 2019

(Left) PA chest radiograph of a patient with left upper lobe partial anomalous pulmonary venous return (PAPVR) shows obscuration of the aortic arch \supseteq due to the presence of an adjacent vertical vein 🛃. (Right) Coronal CTA MIP image of the same patient shows left upper lobe PAPVR draining into a vertical vein 🔁. This should be distinguished from persistent left superior vena cava, in which the left superior pulmonary vein courses anterior to the left mainstem bronchus and posterior to the left atrial appendage.





(Left) Axial CTA of a patient with right upper lobe PAPVR and and sinus venosus atrial septal defect (ASD) shows anomalous drainage of the right upper lobe pulmonary vein \implies into the superior vena cava. (Right) Axial CTA of the same patient shows the sinus venosus ASD 🖻. Note that the middle lobe pulmonary vein \blacksquare drains directly to the right atrium and contributes to the left-to-right shunt. The association with sinus venosus ASD is typically seen in right upper lobe PAPVR.





(Left) Axial CTA of the same patient shows enlargement of the right heart chambers and inversion of the interventricular septum, consistent with increased right heart pressures secondary to a significant left-to-right shunt. (Right) Axial CTA shows a sinus venosus ASD \supseteq and a right lower lobe pulmonary vein 🛃 that drains into the left atrium and contributes to the left-toright shunt produced by the sinus venosus ASD. (Courtesy S. Abbara, MD.)









(Left) PA chest radiograph of a patient with bilateral upper lobe PAPVR but no sinus venosus ASD shows cardiomegaly and markedly increased pulmonary vascularity (shunt vascularity). There is an abnormal soft tissue interface lateral to the aortic arch 🛃. (Right) Curved coronal CTA MIP reformatted image of the same patient shows left upper lobe 🔁 and right upper lobe ➡ pulmonary veins that drain into the left brachiocephalic vein and the superior vena cava, respectively.





(Left) Composite image with axial MRA shows bilateral upper lobe PAPVR. Note the left vertical vein \blacksquare and direct drainage of the right upper lobe pulmonary vein 🔁 into the superior vena cava. (Right) Four-chamber view of SSFP cine MR of the same patient shows dilatation of the right heart chambers and flattening of the interventricular septum in keeping with a significant left-to-right shunt. Cardiac MR allows quantification of the shunt with velocity encoded imaging.





(Left) Coronal anterior 3D reconstruction of an MRA of the same patient shows the vertical vein 🛃 into which all left upper lobe pulmonary vein branches drain. (Right) Coronal posterior 3D reconstruction of an MRA of the same patient shows the *right upper lobe pulmonary* vein 🛃 draining into the superior vena cava. While PAPVR is often asymptomatic, symptoms may arise in direct proportion to the amount of blood being shunted as in this patient with bilateral PAPVR.

Scimitar Syndrome

KEY FACTS

TERMINOLOGY

- Synonyms: Hypogenetic lung syndrome, pulmonary venolobar syndrome
- Partial or total anomalous pulmonary venous return of right lung to vena cava above or below diaphragm

IMAGING

• Radiography

- Curved tubular opacity (scimitar vein) descending toward midline, paralleling right heart border
- Small right hilum
- o Small right hemithorax, hyperlucent lung
- CT
 - Visualization of course and drainage of anomalous pulmonary vein
 - Drainage to infradiaphragmatic inferior vena cava
- **MR**: Equivalent to CT for scimitar vein characterization, allows shunt quantification

TOP DIFFERENTIAL DIAGNOSES

- Proximal interruption of pulmonary artery
- Pulmonary sequestration
- Meandering pulmonary vein
- Swyer-James-MacLeod syndrome

PATHOLOGY

• Congenital, sporadic

CLINICAL ISSUES

- Infantile form: Associated cardiovascular anomalies
- Pediatric/adult form: May be asymptomatic
- Surgical treatment: Symptomatic patients, significant shunts, associated anomalies

DIAGNOSTIC CHECKLIST

• Triad of respiratory distress, right lung hypoplasia, and heart dextroposition should suggest scimitar syndrome

(Left) PA chest radiograph of a patient with scimitar syndrome shows a small right lung (hypoplasia), a right basilar curvilinear opacity (scimitar vein) 🔁, and enlarged pulmonary arteries \square secondary to pulmonary hypertension. (Right) Lateral chest radiograph of the same patient shows a retrosternal band-like opacity 🔁 produced by rightward displacement and rotation of the heart, a frequent ancillary finding in lateral chest radiographs of patients with scimitar syndrome.





(Left) Composite image with axial CECT of the same patient at different levels shows pulmonary hypertension 🖂, an anomalous vein that courses inferomedially 🔁 to drain into the lower right atrium 🖾. In most cases, the scimitar vein drains into the inferior vena cava. (Right) Coronal oblique CECT MIP reformatted image of the same patient shows the anomalous (scimitar) vein as it courses inferiorly and medially rightarrow to drain into the the rightatrium \boxtimes , typical of the socalled scimitar syndrome.





Synonyms

- Hypogenetic lung syndrome
- Pulmonary venolobar syndrome

Definitions

- Partial or total anomalous pulmonary venous return of right lung to the inferior vena cava above or below the diaphragm
- Infantile and pediatric/adult variants
- Associated abnormalities in descending frequency
 - Abnormal right lung lobation and right lung hypoplasia (~ 100%)
 - Dextroposition of heart; right pulmonary artery hypoplasia (60%)
 - Systemic arterialization of right lower lung (60%)
 - Secundum atrial septal defect (40% overall, 80-90% in infantile variant)
 - Right diaphragmatic hernia (15%)
 - Horseshoe lung
 - Infantile: Ventricular septal defect, patent ductus, hypoplastic aortic arch, coarctation, tetralogy of Fallot, anomalous origin of left coronary artery, truncus arteriosus

IMAGING

General Features

- Best diagnostic clue
 - Curved vertical vein paralleling right heart border directed toward midline
 - o Shaped like Turkish sword (or scimitar)
- Location
 - Majority are right-sided
 - o Left-sided (extremely rare); drains into inferior vena cava
- Size
- o Variable

Radiographic Findings

- Radiography
 - Partial anomalous pulmonary venous return, 75%
 - Gently curved tubular opacity (scimitar vein) descending from right mid lung toward midline, parallels right heart border
 - Vein broadens as it courses toward diaphragm
 - Scimitar vein seen in 50% of patients overall, 70% of pediatric/adult, 10% of infantile
 - Less conspicuous small, multiple, or obscured veins in rest
 - Cardiovascular findings
 - Small right hilum
 - Shift of cardiomediastinal silhouette to right (dextroposition)
 - Cardiac rotation to right; retrosternal band-like interface on lateral chest radiograph

Pulmonary findings

- No lung abnormalities (10%)
- Small right hemithorax (hypoplasia), lung may be hyperlucent
- Reticular opacities with recurrent infection and bronchiectasis

• Other: Elevated hemidiaphragm

CT Findings

- CECT
- o papvr
 - Visualization of course and drainage of anomalous pulmonary vein
 - Drainage to infradiaphragmatic inferior vena cava (more common)
 - Less common drainage: Hepatic vein, portal vein, azygos vein, coronary sinus, right atrium
- Cardiovascular findings
 - Pulmonary artery: Normal, hypoplastic, or absent
 - Dilated right heart with left-to-right shunt
 - Enlarged pulmonary trunk (pulmonary hypertension)
 - Systemic arterialization of lung from descending aorta or upper abdominal aorta
- Pulmonary findings
- Right hypoplastic lung
- Mosaic perfusion of hypoplastic lung
- Bronchiectasis from recurrent infection
- Absent minor fissure, left bronchial isomerism
- Horseshoe lung: Lung bridge fusing lungs across posterior mediastinum; association with lethal cardiac anomalies
- Other findings: Bronchial diverticula, bronchogenic cyst, accessory diaphragm, diaphragmatic hernia

MR Findings

• Equivalent to CT for characterization of scimitar vein

- Superior to CT for assessment of congenital heart disease and aortic hypoplasia
- Allows shunt quantification, QP:QS with velocity-encoding sequences
- Disadvantages: Less useful for assessment of lung or bronchial anatomy

Echocardiographic Findings

- 1st approach to diagnosis and postsurgical follow-up
- Evaluation of shunts and estimation of pulmonary artery pressure

Angiographic Findings

• Gold standard for diagnosis, pressure measurements, determination of size of left-to-right shunt

Imaging Recommendations

- Best imaging tool
 - CT and MR for assessment of morphologic features including lung abnormalities
- Protocol advice
 - MR must include MRA and velocity-encoding imaging for shunt quantification
 - o CTA allows comprehensive morphologic characterization

DIFFERENTIAL DIAGNOSIS

Proximal Interruption of Pulmonary Artery

- Also associated with pulmonary hypoplasia
- No vertical (scimitar) vein
- Normal bronchial branching

Pulmonary Sequestration

- Systemic supply to sequestered lung, usually from descending thoracic or upper abdominal aorta
- No vertical (scimitar) vein
- Normal venous drainage in intralobar sequestration

Meandering Pulmonary Vein

- Anatomic variant
- Pulmonary vein "meanders" in lung but drains normally into left atrium

Swyer-James-MacLeod Syndrome

- No vertical (scimitar) vein
- Volume loss of affected lung
- Normal pulmonary venous anatomy

PATHOLOGY

General Features

- Etiology
- o Congenital
- Genetics
 - o Sporadic (most)
 - o Autosomal dominant (some cases)
- Associated abnormalities
 - Cardiovascular anomalies in infantile form
 - Atrial septal defect (80%)
 - Patent ductus arteriosus (75%)
 - Ventricular septal defect (30%)
 - Pulmonic stenosis (20%)
 - Aortic coarctation
 - Subaortic stenosis
 - Aortic arch hypoplasia
 - Tetralogy of Fallot
 - Persistent left superior vena cava
 - Cardiovascular anomalies in pediatric/adult form
 - Atrial septal defect, ostium secundum (20%)
 - Patent ductus arteriosus
 - Other: Persistent left superior vena cava, coronary artery fistula, azygos continuation of inferior vena cava, cor triatriatum
 - Airway anomalies: Bronchiectasis, left bronchial isomerism, hypoplasia/anomalies of segmentation of right bronchial tree
 - o Vertebral anomalies: Hemivertebra, scoliosis
 - Other: Bronchogenic cyst, accessory diaphragm, diaphragmatic hernia, horseshoe lung

Gross Pathologic & Surgical Features

- Typically single scimitar vein, occasionally multiple
- Scimitar vein drains right lung
 - Entire lung (2/3 of cases)
 - Right lower lobe (1/3 of cases)
- Course of scimitar vein: Anterior to right hilum
- Scimitar drainage
 - Infradiaphragmatic inferior vena cava (most common)
 - Less common: Hepatic veins, portal vein, azygos vein, coronary sinus, right atrium
- Lung morphology
 - Lobar agenesis to focal hypoplasia: Equal incidence of uni-, bi-, and trilobed right lung

- Pulmonary arterial supply
 - Absent, hypoplastic, or normal right pulmonary artery
 - o Systemic blood supply to right lower lobe

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Infantile form
 - Severe tachypnea, cyanosis, heart failure from left-toright shunt; resultant failure to thrive
 - Diagnosed within 1st months of life
 - Pediatric/adult form
 - Absent or mild symptoms
 - Frequently asymptomatic
 - □ Recurrent pneumonia, mild dyspnea, fatigue
 - Hemoptysis may occur with left-to-right shunt due to bronchial wall varices
 - Diagnosed within first 3 decades
- Other signs/symptoms
 - Infantile form
 - Average QP:QS is > 3.0
 - Pediatric/adult form
 - Mild deficits in vital capacity and FEV1 (~ 80% of predicted)
 - Average QP:QS is 2.0

Demographics

- Age
 - Bimodal: Infantile and pediatric/adult forms
- Sex
- o M:F = 1:2
- Epidemiology
 - o 1-3 cases per 100,000 births

Natural History & Prognosis

- Infantile form: Significant mortality, poor prognosis without treatment
- Pediatric/adult form: Milder form, good prognosis

Treatment

- In absence of pulmonary hypertension, medical treatment during infancy allows growth before surgical repair
- Indications for surgical treatment
 - Coexistent atrial septal defect, pulmonary hypertension, stenosis of scimitar vein
 - Symptomatic patients and asymptomatic patients with QP:QS shunt > 1.5:1

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Triad of respiratory distress, right lung hypoplasia, and heart dextroposition should suggest scimitar syndrome
- Scimitar vein may be subtle, identification requires careful evaluation of small hyperlucent right hemithorax

- Ali YZ et al: Scimitar syndrome. Eur Heart J Cardiovasc Imaging. 21(8):939, 2020
- 2. Diaz-Frias J et al: Scimitar Syndrome 2020

Scimitar Syndrome





(Left) Ap chest radiograph of a patient with scimitar syndrome shows an abnormal right mid and lower lung zone tubular structure (scimitar vein) \supseteq that courses inferomedially and morphologically resembles a scimitar, a Turkish sword. (Right) Coronal oblique NECT MIP reformatted image of the same patient shows the anomalous pulmonary vein as it curves to course inferomedially, the so-called scimitar vein morphology associated with the scimitar syndrome.





(Left) Coned-down PA chest radiograph of an adult patient with scimitar syndrome shows a scimitar vein \supseteq but no evidence of right pulmonary hypoplasia. (Right) Composite image with coronal MRA at various levels of the same patient shows the anomalous pulmonary vein 🚬, which drains the right lower lobe and anastomoses with the infradiaphragmatic inferior vena cava 赵. While frequently associated with pulmonary hypoplasia, milder forms of scimitar syndrome occur without associated right lung hypoplasia.





(Left) Composite image with axial SSFP (bright blood) MR at various levels of a patient with scimitar syndrome shows the scimitar vein ➡ as it drains into the

infradiaphragmatic inferior vena cava A. (Right) Coronal MRA 3D reconstruction of the same patient shows the right lower lobe scimitar vein a si it courses inferomedially to drain into the inferior vena cava. Angiographic techniques are superb in depicting the morphologic features of scimitar syndrome.

Pulmonary Varix

KEY FACTS

TERMINOLOGY

- Synonyms
 - o Pulmonary venous aneurysm
- Definition: Nonobstructive dilatation of one or more pulmonary veins at insertion into left atrium
 May be an isolated radiologic finding

IMAGING

Radiography

- Left atrial enlargement (LAE)
- Soft tissue opacity adjacent to LAE in expected location of pulmonary vein
- CT
 - Enlarged confluence of pulmonary vein(s)
 - Maximum enhancement in pulmonary venous phase
 - May be dilated 2-3x normal venous diameter
 - No soft tissue mass
- CECT is imaging modality of choice

TOP DIFFERENTIAL DIAGNOSES

- Unilateral common pulmonary vein
- Arteriovenous malformation
- Partial anomalous pulmonary venous return
- Meandering pulmonary vein
- Intralobar sequestration
- Portopulmonary venous anastomosis

CLINICAL ISSUES

- Symptoms/signs
 - Most patients are asymptomatic
 - ± association with mitral valve disease and pulmonary venous hypertension
 - Incidental imaging finding
- Treatment
 - Not clinically significant
 - Typically no therapy or follow-up required
 - o Surgical repair if progressive increase in size

(Left) Lateral chest radiograph of a 65-year-old man with known coronary artery disease and ischemic cardiomyopathy with postsurgical changes of coronary artery bypass graft and biventricular cardiac defibrillator shows a dense retrocardiac opacity 🔁 that likely represents a combination of left atrial enlargement and confluence of enlarged inferior pulmonary veins. (Right) Axial CECT of the same patient shows left atrial enlargement and a large varix *▶* of the right inferior pulmonary vein.





(Left) Axial CECT of a patient with an asymptomatic pulmonary varix demonstrates an abnormally dilated right inferior pulmonary vein 🔁 resulting in a right lower lobe pulmonary varix. For comparison purposes, note the normal diameter of the left inferior pulmonary vein 🔁. (Right) Axial CECT of the same patient at a different level shows additional varicose dilatation of venous tributaries in the right lower lobe].





Synonyms

• Pulmonary venous aneurysm

Definitions

- Nonobstructive dilatation of one or more pulmonary veins at insertion into left atrium (LA)
- May be isolated radiologic finding
- May be congenital or associated with acquired heart disease (e.g., mitral stenosis ± regurgitation)
- No enlarged feeding artery or arteriovenous communication
- May be mistaken for mediastinal, hilar, or pulmonary mass

IMAGING

General Features

- Best diagnostic clue
 - Left atrial enlargement (LAE) + enlarged confluence of pulmonary vein(s)
- Location
 - Typically affects an inferior pulmonary vein
- Size
 - May be dilated 2-3x normal venous diameter
- Morphology
 - Fusiform dilatation of one of major central pulmonary veins
 - At point of insertion into LA

Radiographic Findings

- Radiography
 - Soft tissue opacity adjacent to LAE
 - Expected location of pulmonary vein

CT Findings

- CECT
 - Maximum enhancement during pulmonary venous phase
 - No arteriovenous communication
 - Arteriovenous malformation characterized by efferent and afferent vessels and nidus
 - No soft tissue mass

Imaging Recommendations

- Best imaging tool
 - Contrast-enhanced CT is imaging modality of choice
- Protocol advice
 - Administer contrast to evaluate right and left cardiac chambers

DIFFERENTIAL DIAGNOSIS

Unilateral Common Pulmonary Vein

• Superior and inferior pulmonary veins share common insertion into LA; an anatomic variant

Arteriovenous Malformation

• Feeding pulmonary artery and draining pulmonary vein

Partial Anomalous Pulmonary Venous Return

• Anomalous pulmonary vein drains into systemic venous circulation

• Left-to-right shunt

Meandering Pulmonary Vein

- Typically unilateral single pulmonary vein with circuitous route in lung
- Drains normally into LA

Intralobar Sequestration

- Systemic feeding artery
- Typically pulmonary venous drainage
- Draining vein not necessarily enlarged

Portopulmonary Venous Anastomosis

- Unusual collateral pathway in portal hypertension
- Shunt between paraesophageal varices and LA via pulmonary vein

PATHOLOGY

Staging, Grading, & Classification

• Histologically benign

Gross Pathologic & Surgical Features

• Dilated pulmonary vein at insertion into LA

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Most patients are asymptomatic
 - Incidental imaging finding
- Other signs/symptoms
 - Associated with acquired heart disease
 - Mitral valve disease, typically stenosis
 - Pulmonary venous hypertension
 - Rarely congenital

Natural History & Prognosis

- Not clinically significant
- Not to be confused with mediastinal, hilar, or pulmonary nodule/mass
- Rupture is rare
- Size may decrease following treatment of pulmonary venous hypertension

Treatment

- Typically no treatment required
- Surgical repair if progressive increase in size

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Enlarged pulmonary vein ± acquired heart disease
- May decrease with Valsalva and enlarge with Müller maneuvers

Reporting Tips

• Finding of no clinical significance in most cases

- Shostak E et al: A diagnostic conundrum: progressive tubular lung mass in asymptomatic young woman. Chest. 155(5):e131-5, 2019
- Haddad J et al: Pulmonary varix: a case report. Rev Port Cardiol. 35(7-8):443.e1-4, 2016

TERMINOLOGY

• Meandering pulmonary vein (MPV): Anomalous course of pulmonary vein, drains portion of lung, drains into left atrium

IMAGING

- Radiography
 - o Tortuous pulmonary tubular opacity
 - Right-sided MVP may produce the scimitar sign and mimic scimitar syndrome
- CT
 - Identification and characterization of anomalous vessel as pulmonary vein; documentation of venous drainage into left atrium
 - Right-sided > left-sided MVP
- MRA
 - Identification and characterization of anomalous vessel as pulmonary vein; documentation of drainage into left atrium

TOP DIFFERENTIAL DIAGNOSES

- Scimitar syndrome
- Partial anomalous pulmonary venous return
- Pulmonary arteriovenous malformation
- Pulmonary varix

CLINICAL ISSUES

- Signs and symptoms
 - Typically incidental finding in asymptomatic patient
 - No hemodynamic abnormality or shunt
- Wide age range: Infancy to older adults
- Men and women; slight female predominance

DIAGNOSTIC CHECKLIST

- Consider MPV in asymptomatic patient with tortuous tubular pulmonary opacity
- CT for identification and characterization of MPV and exclusion of associated abnormalities

(Left) PA chest radiograph of an asymptomatic 35-year-old woman shows a left perihilar retrocardiac nodular opacity \square initially thought to represent an indeterminate pulmonary nodule. (Right) Composite image with axial CECT of the same patient shows that the nodular lesion corresponds to a meandering pulmonary vein 🔁 that crossed the interlobar fissure ➡ and drained into the left , atrium via the left inferior pulmonary vein 🖾 Meandering pulmonary veins follow a circuitous course but drain into the left atrium.





(Left) Composite image with PA chest radiograph (left) and CECT (right) of an asymptomatic 64-year-old woman shows a left upper lobe tubular opacity \blacksquare , which corresponded to a dilated meandering pulmonary vein 🔁 that drained into the left atrium (drainage not shown). (Right) Coronal CECT MIP reformatted image of a 68year-old woman shows a circuitous right lower lobe meandering pulmonary vein \blacksquare that drains into the left atrium 🔁 Note the scimitarlike morphology 🛃 of the inferior portion of the vein.





Abbreviations

• Meandering pulmonary vein (MPV)

Synonyms

• Pseudo-scimitar syndrome, scimitar variant

Definitions

- Anomalous course of pulmonary vein, drains portion of lung, drains into left atrium
- Anomalous unilateral single pulmonary vein (AUSPV): Single pulmonary vein drains entire lung

IMAGING

General Features

- Location
 - Right-sided (3/4) > left-sided MVP
 - o > 50% involve right inferior pulmonary vein
 - Bilateral MPV reported
- Size
 - Dilated vessel; variable size
- Morphology
 - Curvilinear tubular opacity

Radiographic Findings

- Pulmonary tubular or nodular opacity
 - Right-sided MVP may produce scimitar sign and mimic scimitar syndrome
 - Dilated vessel with circuitous course

CT Findings

- Identification and characterization of anomalous vessel as pulmonary vein
- Course of MPV, drainage into left atrium; may cross interlobar fissures

MR Findings

- MRA
 - Identification/characterization of anomalous vessel as pulmonary vein
 - o Course of anomalous vessel and drainage into left atrium

Imaging Recommendations

- Best imaging tool
 - o CECT for identification/characterization of MPV
- Protocol advice
 - o Volume-rendered and MIP reformations

DIFFERENTIAL DIAGNOSIS

Scimitar Syndrome

- Anomalous drainage of right lung to inferior vena cava via curved so-called scimitar vein
- Associations: Right lung hypoplasia, cardiac dextroposition, right pulmonary artery hypoplasia, anomalous systemic arterial supply to right lung
- Left-to-right shunt

Partial Anomalous Pulmonary Venous Return

- Anomalous drainage of pulmonary vein into right-sided circulation
 - Drainage to left brachiocephalic vein on left

- Drainage to vena cava on right
- Left-to-right shunt

Pulmonary Arteriovenous Malformation

- Direct communication of pulmonary artery(ies) with pulmonary vein(s) without intervening capillary bed
- Right-to-left shunt

Pulmonary Varix

- Localized pulmonary vein dilatation; no shunt
- May mimic pulmonary nodule on radiography

PATHOLOGY

General Features

- Etiology
 - Atresia/hypoplasia of pulmonary vein before completion of lung segmentation; larger portion of lung drains via remaining "meandering" vein
 - o Interruption of communication of embryologic common pulmonary vein with left atrium → persistence of primitive connections between pulmonary and systemic vessels → obliteration of pulmonary vein connections with systemic circulation
- Associated abnormalities
 - o May be isolated finding without associated abnormalities
 - Other associations: Hypoplastic right lung, hypoplastic pulmonary artery, cardiac dextroposition; coexistent scimitar vein, congenital heart disease

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Typically incidental finding in asymptomatic patient
 - No hemodynamic abnormality or shunt

Demographics

- Age
- Wide age range: Infancy to older adults
- Sex
 - Men and women; slight female predominance
- Epidemiology
 - Rare anomaly, few reported cases

Treatment

None required if isolated anomaly

DIAGNOSTIC CHECKLIST

Consider

 MPV in asymptomatic patient with tortuous tubular pulmonary opacity

Image Interpretation Pearls

• CT for identification and characterization of MPV and exclusion of associated abnormalities

- Lee M et al: Meandering pulmonary veins: two case reports. Medicine (Baltimore). 99(16):e19815, 2020
- 2. Sneha Harish C et al: Meandering pulmonary vein: a case report. J Radiol Case Rep. 14(3):7-13, 2020
- 3. Lin CT et al: Pulmonary venous anomalies causing misdiagnosis of pulmonary arteriovenous malformations. Clin Imaging. 47:96-100, 2018

TERMINOLOGY

• Accessory fissure surrounding a portion of the right upper lobe (RUL)

IMAGING

- Radiography
 - Azygos fissure: Thin curvilinear opacity convex toward chest wall; extends from right tracheobronchial angle to right lung apex
 - Azygos vein: Ovoid, tear-shaped opacity in inferior aspect of accessory fissure
 - Trigone: Triangular opacity that marks superior aspect of azygos fissure
- CT
 - Arcuate linear opacity that extends from posterolateral upper thoracic spine to superior vena cava (SVC)
 - Traverses lung before entering SVC

TOP DIFFERENTIAL DIAGNOSES

- Paratracheal lymphadenopathy
- Tortuous supraaortic vessels
- Right upper lobe atelectasis

PATHOLOGY

• Failure of normal azygos vein migration over right lung apex

CLINICAL ISSUES

• Azygos fissure: Seen in 1% of individuals

DIAGNOSTIC CHECKLIST

- Dense lung medial to fissure does not signify underlying disease
- Enlarged azygos vein should prompt assessment for
 Elevated central venous pressure and possible etiologies
 - SVC &/or inferior vena cava obstruction

(Left) PA chest radiograph shows an accessory azygos fissure manifesting as a thin curvilinear opacity \square , extending obliquely across the right apex and terminating in a teardrop-shaped opacity inferiorly \square caused by the azygos arch. Note the triangular-shaped "trigone" 🔁 at the superior aspect of the fissure. (Right) AP chest radiograph shows a left upper extremity PICC that crosses the midline with the tip in the azygos vein at the inferior aspect of the azygos arch \supseteq .





(Left) Composite image with axial CECT in lung (left) and soft tissue (right) window shows the azygos arch as it courses within the inferior aspect of the accessory azygos fissure and drains into the posterior aspect of the superior vena cava. (Right) Coronal CECT of a patient with a right pneumothorax shows air surrounding the two parietal pleura components \bowtie of the accessory azygos fissure and the azygos arch \supseteq at the inferior aspect of the fissure. The visceral pleura components have "fallen away" from the fissure.





Synonyms

• Azygos fissure

Definitions

- Anomalous intrapulmonary course of azygos vein that creates accessory fissure
 - o Includes 4 layers of non-fused parietal and visceral pleura (mesoazygos) invaginated into medial right upper lobe (RUL)
 - Vertical or curved oblique course of fissure
 - o Teardrop-shaped lower margin contains azygos vein
 - Trigone
 - Cranial aspect of fissure (triangular shape); determines size of lung medial to fissure
 - Included lung shape classified based on trigone position
 - □ Type A: Trigone located in lateral aspect of pulmonary apex
 - □ Type B: Trigone located at mid point of apex; fissure is relatively vertically oriented
 - □ Type C: Trigone located medially; fissure curves toward mediastinum
 - Fissure length varies with type: Longer in type A, shorter in types B and C
- Accessory fissure of variable size borders medial aspect of RUL

IMAGING

Imaging Recommendations

• Pathognomonic radiographic and CT appearance

Radiographic Findings

- Azvgos fissure: Thin curvilinear opacity in medial RUL coursing from right tracheobronchial angle to apex
- Azygos vein: Teardrop-shaped opacity in lowermost azygos fissure
- Trigone: Triangular opacity that marks superior aspect of azygos fissure
- Lung surrounded by fissure is normally aerated
- Bronchoarterial supply from branches of RUL apical and posterior segments
- Lung medial to fissure may exhibit increased opacity • Tortuous supraaortic arteries and veins
 - o Mediastinal lipomatosis
 - Enlarged thymus (young infants)

CT Findings

- Curvilinear opacity extending from posterolateral upper thoracic spine at T4 that joins superior vena cava (SVC)
- Traverses RUL before joining SVC
- Exclusion of pulmonary pathology medial to accessory fissure
- ± azygos vein calcification
- Migration of azygos vein to mediastinum
 - Previous pneumothorax may be contributing factor • Associated with elevated intrathoracic pressure and
 - shorter fissure
- Vanishing azygos fissure
 - Associated with migration of azygos vein

• Associated with apical fibrosis

DIFFERENTIAL DIAGNOSIS

Right Paratracheal Lymphadenopathy

• Thick right paratracheal stripe

Tortuous Supraaortic Vessels

 Mediastinal widening without tracheal narrowing or displacement

Right Upper Lobe Atelectasis

• Direct and indirect signs of volume loss

PATHOLOGY

General Features

- Etiology
 - Failure of normal azygos vein migration over right lung apex
- Associated abnormalities
- Dense lung medial to azygos fissure
 - Potential diagnostic pitfall that may simulate pathology
- Azygos vein dilatation
 - Elevated central venous pressure: Cardiac decompensation, tricuspid stenosis, acute pericardial tamponade, constrictive pericarditis
 - Acquired obstruction of SVC or inferior vena cava (IVC)
 - Intrahepatic and extrahepatic portal vein obstruction
 - Anomalous pulmonary venous return
 - Heterotaxy syndrome with polysplenia □ Polysplenia, azygos continuation of IVC, left SVC, left thoracic isomerism, abdominal heterotaxy, truncated pancreas
- Azygos vein migration to normal position in mediastinum
- Vanishing azygos fissure
 - Apical pulmonary fibrosis may retract fissure upward (short fissure)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic; usually incidental imaging finding

Demographics

- Epidemiology
 - o 1% of individuals

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Dense lung medial to fissure does not necessarily signify underlving disease
- Enlarged azygos vein should prompt assessment for elevated central venous pressure and potential etiologies

- Semionov A et al: Migration of the azygos vein from the azygos fissure to the mediastinum. Radiol Case Rep. 14(6):763-5, 2019
- Taydas O et al: Reentrance of azygos vein into azygos fissure after 2. pneumothorax. Eurasian J Med. 49(1):62-3, 2017

TERMINOLOGY

• Inferior vena cava (IVC) interrupted above renal veins, hepatic veins drain into right atrium, azygos vein carries venous return

IMAGING

• Radiography

- Enlarged azygos arch in right tracheobronchial angle
 - Dilated azygos arch: > 10 mm in upright position; > 15 mm in supine position
- Visualization of azygos vein
- ± heterotaxy with left isomerism
- CT
 - Absent suprarenal intrahepatic IVC
 - Hepatic veins drain directly into right atrium
 - Dilated azygos courses cephalad and drains into SVC
 - Dilated hemiazygos in hemiazygos continuation
 - Heterotaxy syndrome with spectrum of left-sided isomerism

TOP DIFFERENTIAL DIAGNOSES

- Superior vena cava obstruction
- Pulmonary artery hypertension
- High volume states
- Lymphadenopathy
- Intrahepatic IVC occlusion by tumor/thrombus

CLINICAL ISSUES

- Often asymptomatic
- Symptoms typically related to congenital heart disease
- Prognosis related to associated anomalies
- Inadvertent surgical ligation may be lethal

DIAGNOSTIC CHECKLIST

• Consider importance of diagnosing azygos/hemiazygos continuation prior to catheter-based interventions through IVC, such as right heart catheterization

(Left) Graphic shows typical anatomic features of azygos continuation, including absence of the inferior vena cava, hepatic vein drainage 🔁 directly into the right atrium, and an enlarged azygos vein \square that provides the abdominal venous drainage. (Right) PA chest radiograph of a 65-year-old woman with heterotaxy syndrome shows an obliquely oriented opacity *⊡* that obscures the azygoesophageal recess, a markedly dilated azygos arch *⊠*, and bilateral hyparterial bronchi, compatible with leftsided isomerism.











Synonyms

- Azygos continuation of inferior vena cava (IVC)
- Interruption of IVC
- Absence of hepatic segment of IVC with azygos continuation

Definitions

- Caused by persistence of embryonic right supracardinal vein and failure of development of suprarenal part of subcardinal vein
 - IVC interrupted above renal veins
 - Hepatic veins drain directly into right atrium
- Venous return to right atrium
 - Large azygos vein carries venous return
 - Occasionally, large hemiazygos vein carries venous return
 - Both azygos and hemiazygos veins may carry venous return to right atrium
- Azygos continuation of IVC associated with congenital heart disease and situs abnormalities, especially heterotaxy syndrome with polysplenia

IMAGING

General Features

- Best diagnostic clue
 - Dilated azygos or hemiazygos veins on CT with concurrent interruption of IVC above renal veins
- Size
 - o Azygos arch located in right tracheobronchial angle
 - Azygos dilatation
 - □ > 10-mm short-axis diameter in erect position
 - □ > 15-mm short-axis diameter in supine position

Radiographic Findings

- Posteroanterior (PA) radiograph
 - Focal enlargement of azygos arch in right tracheobronchial angle
 - Round or ovoid shape
 - Dilatation: > 10-mm diameter in the erect position or
 > 15 mm in the supine position
 - Visualization of azygos vein interface
 - Visualization of aortic nipple may occur with hemiazygos continuation of IVC
 - Heterotaxy syndrome with variable spectrum of leftsided isomerism and polysplenia
 - Spectrum of findings
 - Bilateral bilobed lungs
 - Bilateral hyparterial bronchi
 - Midline or transverse liver
- Lateral radiograph
 - Retrotracheal opacity &/or thickening of tracheoesophageal stripe
 - ± absence of retrocardiac IVC interface
 - Suprahepatic IVC may be present

CT Findings

- CECT
 - Absent suprarenal and intrahepatic IVC
 - Hepatic veins drain directly into right atrium

- Large posterior, paraspinal vessel that corresponds to azygos (right) or hemiazygos (left) continuation
- Dilated azygos vein courses cephalad and drains into posterior aspect of superior vena cava (SVC)
 Associated dilated azygos arch
- Dilated hemiazygos courses cephalad
 - Typically drains into left SVC and dilated coronary sinus
 - May cross midline and join azygos vein
 - Rarely drains to accessory hemiazygos, left superior intercostal, and left brachiocephalic veins
 - Dilated left-sided venous arch lateral to aorta in cases of typical drainage
- Heterotaxy syndrome with spectrum of leftisomerism findings
 - Situs ambiguus
 - Bilateral bilobed (left-sided morphology) lungs
 - Bilateral hyparterial (left-sided morphology) bronchi
 - Congenital heart disease
 Partial anomalous pulmonary venous return
 - □ Atrial septal defect
 - Atrioventricular canal defect
 - Abdominal findings
 - Multiple spleens
 - Midline or transposed abdominal viscera
 - Intestinal malrotation
 - □ Preduodenal portal vein
 - Truncated pancreas
 - Biliary atresia

MR Findings

- T1WI
 - Absent suprarenal and intrahepatic portion of IVC
 - Hepatic veins drain directly into right atrium
 - Large posterior, paraspinal vessel corresponding to azygos (right) or hemiazygos (left) continuation
 - Dilated azygos courses cephalad and drains to SVC
 Dilated azygos arch
 - Dilated hemiazygos courses cephalad along left side of spine
 - Typically drains to left SVC and dilated coronary sinus
 - May cross midline and join azygos
 - Rarely drains to accessory hemiazygos vein, left superior intercostal vein, and left brachiocephalic vein
 - Dilated left-sided venous arch lateral to aorta in typical drainage
 - Heterotaxy syndrome with spectrum of left-sided isomerism/polysplenia identical to CT findings
- MRA
 - Azygos continuation, interrupted IVC observed on venous phase

Imaging Recommendations

- Best imaging tool
 - Combination of chest radiography, echocardiography, and abdominal ultrasound are optimal initial imaging modalities, especially in children
 - Contrast-enhanced CT or MR are studies of choice to evaluate azygos continuation

DIFFERENTIAL DIAGNOSIS

Superior Vena Cava Obstruction

- Distal SVC occlusion by mass or thrombus
- Azygos serves as collateral pathway
- Enlarged azygos arch and azygos veinNormal IVC

Pulmonary Artery Hypertension

- Dilated right heart chambers and SVC
 Enlarged azygos arch
- Enlarged pulmonary trunk and central pulmonary arteries
- Normal IVC

High Volume States

- Enlarged heart and increased pulmonary vessels
 Enlarged azygos arch
- Normal or dilated IVC
- Pregnancy, sickle cell disease, renal disease

Lymphadenopathy

- Right paratracheal lymph node enlargement
- Normal azygos arch and vein are separate from enlarged lymph nodes
- Normal IVC

Occlusion of Intrahepatic IVC by Tumor or Thrombus

- Intravascular growth of tumor; especially hepatocellular carcinoma
- Normal infrahepatic IVC

Double Aortic Arch

- May mimic enlarged azygos arch and vein on radiography
- Double aortic arch distinct from normal azygos arch and vein
- IVC normal

PATHOLOGY

General Features

- Etiology
 - Persistence of embryonic right supracardinal vein
 - Failure of development of suprarenal subcardinal vein
- Genetics
 - May be sporadic and occur in isolation without other associated abnormalities
 - When associated with heterotaxy syndrome, studies suggest possible multifactorial inheritance patterns:
 Sporadic, autosomal dominant, autosomal recessive, and X-linked recessive
- Associated abnormalities
 - Heterotaxy syndrome with spectrum of leftisomerism findings
 - Bilateral hyparterial bronchi and bilobed lungs
 - Midline or transposed liver/abdominal viscera, intestinal malrotation, preduodenal portal vein, truncated pancreas
 - Polysplenia
 - Congenital heart disease (50%)
 - Azygos and hemiazygos continuation of IVC rare in asplenia

Gross Pathologic & Surgical Features

- Complicates surgical planning for
 - Esophagectomy
 - Liver transplantation
 - IVC filter placement
 - Abdominal aortic aneurysm repair
 - Catheterization

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Often asymptomatic
- Other signs/symptoms
 - o Symptoms related to associated congenital heart disease
 - May be associated with sick sinus syndrome

Demographics

- Age
 - o Variable, often diagnosed incidentally
 - Early diagnosis when associated with severe congenital heart disease
- Sex
 - No predilection
- Epidemiology
 - Prevalence of approximately 0.6%
 - 0.2-4.3% of cardiac catheterizations for congenital heart disease

Natural History & Prognosis

- Related to associated anomalies, particularly congenital heart disease
- Inadvertent ligation at surgery may be lethal

Treatment

• Related to associated anomalies, particularly congenital heart disease

DIAGNOSTIC CHECKLIST

Consider

• Importance of diagnosing azygos/hemiazygos continuation prior to catheter-based interventions through IVC, such as right heart catheterization

Image Interpretation Pearls

• Lateral chest radiograph may not show absence of retrocardiac IVC interface due to drainage of hepatic veins in that location

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(Left) Axial CECT of a 39-yearold man with azygos continuation of the inferior vena cava and left-sided isomerism shows a dilated hemiazygos vein 乏 that crosses the midline to join the dilated azygos vein 🖾. (Right) Axial CECT of the same patient shows a dilated azygos vein 🔁, multiple spleens in the left upper quadrant \supseteq , and a truncated pancreas \boxtimes , which are in the spectrum of anomalies seen in patients with heterotaxy syndrome and left-sided isomerism.





(Left) Axial CECT of a patient with azygos continuation of the inferior vena cava and heterotaxy syndrome shows a markedly enlarged azygos arch 🖂. (Right) Axial CECT of the same patient shows the enlarged azygos vein \square , the transverse liver, a right-sided gastric bubble 🖂, and polysplenia 🖾. The multiple spleens in patients with heterotaxy and polysplenia are always on the same side of the body as the stomach, and typically along the greater curvature.





(Left) Axial cine MR shows an enlarged hemiazygos vein 🔁 in a patient with heterotaxy syndrome and hemiazygos continuation of the inferior vena cava. Note dextrocardia \square , which is among the spectrum of congenital anomalies that may occur with heterotaxy syndromes. (Right) Axial cine MR of the same patient shows a hemiazygos arch \supseteq that connects the hemiazygos vein to a persistent left superior vena cava.

TERMINOLOGY

- Persistent left superior vena cava (PLSVC)
- Left superior vena cava (SVC) arises from confluence of ipsilateral subclavian and internal jugular veins
- Drains to coronary sinus, occasionally to left atrium ± unroofed coronary sinus [i.e., coronary sinus atrial septal defect (ASD)]

IMAGING

- Radiography
 - Lateralization of aortic-pulmonary stripe
 - Left vertical course of catheters and pacer leads
- CT/MR
 - o Vertical vessel in left superior mediastinum
 - Originates from confluence of left internal jugular and subclavian veins
 - Typically drains into dilated coronary sinus
 - Right SVC may be normal, small, or absent

TOP DIFFERENTIAL DIAGNOSES

- Left upper lobe partial anomalous pulmonary venous return (PLSVC)
 - Anomalous left upper lobe veins join vertical vein
 - Vertical vein courses in prevascular space of left mediastinum lateral to aortic arch
 - No enlargement of coronary sinus

CLINICAL ISSUES

- Usually asymptomatic
- Cyanosis: PLSVC draining to left atrium &/or ASD
- Most common congenital thoracic venous anomaly
 0.3-0.5% of general population
- Treatment: None if isolated; surgical correction if significant shunt

DIAGNOSTIC CHECKLIST

• Consider PLSVC in patient with central catheter or pacer lead with left vertical course lateral to aortic arch

(Left) Graphic shows the typical appearance of persistent left superior vena cava ➡ with vertical course and drainage into coronary sinus \square , associated right superior vena cava 🔁, and bridging vein 🛃. (Right) PA chest radiograph of an asymptomatic patient with persistent left superior vena cava shows lateralization of the aortic-pulmonary reflection \square , a nonspecific finding that can also be seen in partial anomalous pulmonary venous return, lymphadenopathy, and mediastinal lipomatosis.





(Left) Composite image with axial CTA shows a persistent left superior vena cava \supseteq , which courses along the left mediastinal border. There is also a right-sided superior vena cava 🔁. Often no communication (i.e., bridging vein) is identified between the two vena cavas. (Right) Axial CTA of the same patient shows the persistent left superior vena cava \boxdot that courses along the left mediastinal border between the left atrial appendage and the superior pulmonary vein. The coronary sinus 🖂 is often dilated in these cases.





Abbreviations

• Persistent left superior vena cava (PLSVC)

Definitions

- Left superior vena cava (SVC) arises from confluence of ipsilateral subclavian and internal jugular veins
- Typically drains to coronary sinus, occasionally to left atrium ± unroofed coronary sinus [i.e., coronary sinus atrial septal defect (ASD)]

IMAGING

General Features

- Best diagnostic clue
 - Vertical vessel lateral to aortic arch associated with coronary sinus dilatation
- Size
 - o Variable

Radiographic Findings

- Radiography
 - May be normal
 - Lateralization of aortic-pulmonary stripe
 - Normally there is no soft tissue structure lateral to aortic arch
 - May also occur in left upper lobe partial anomalous pulmonary venous return (PAPVR); radiographically indistinguishable entities
 - Central catheter or pacemaker/defibrillator lead with left vertical course lateral to aortic arch

CT Findings

- CECT
 - Vertical vessel coursing along left superior mediastinum
 - Originates from confluence of left internal jugular and subclavian veins
 - Receives drainage from left superior intercostal vein
 - Courses inferiorly in prevascular space
 - □ Lateral to aortic arch and pulmonary trunk
 - □ Anterior to left mainstem bronchus
 - May be difficult to identify, as it courses posterior to left atrium
 - Drainage
 - Most into coronary sinus; frequently dilated
 May drain into left atrium
 - Always constitutes right-to-left shunt of variable size
 - May be associated with unroofed coronary sinus; coronary sinus ASD, left-to-right shunt
 - Right SVC may be normal, small, or absent
 - Left brachiocephalic (bridging vein) frequently absent (65%)
 - May receive drainage from left hemiazygos system, particularly with hemiazygos continuation

MR Findings

Equivalent to CT for morphologic assessment
 Same findings as in CT

- Allows shunt quantification in cases of drainage to left atrium &/or coronary sinus ASD
 Velocity encoding sequences
- Superior to CT for assessment of associated congenital heart disease

Angiographic Findings

- DSA
 - Injection through left-sided catheter opacifies vessel that courses inferiorly into coronary sinus and right atrium

Imaging Recommendations

- Best imaging tool
- CT and MR are equivalent for morphologic assessment
- Protocol advice
 - Injection in left arm for optimal vessel opacification

Echocardiographic Findings

- Dilated coronary sinus
- Confirmed by use of saline contrast (bubble study)
- Criteria
 - Dilated coronary sinus on 2-dimensional echocardiography without evidence of elevated rightsided filling pressures
 - Enhancement of dilated coronary sinus before right atrium after saline contrast infusion into left arm vein
 - Normal contrast transit with opacification of right atrium before coronary sinus when saline contrast injected into right arm vein

DIFFERENTIAL DIAGNOSIS

Dilated Coronary Sinus

- Other etiologies
 - o Elevated right atrial pressure (most common)
 - Coronary arteriovenous fistula
 - o PAPVR
 - Coronary sinus ASD (unroofed coronary sinus)

Left Upper Lobe Partial Anomalous Pulmonary Venous Return

- Anomalous left upper lobe veins join vertical vein
- Vertical vein courses cephalad in prevascular space of left mediastinum lateral to aortic arch
- Absence of left superior pulmonary vein from normal location anterior to left mainstem bronchus
- No enlargement of coronary sinus
- Normal to enlarged left brachiocephalic vein and right SVC
- Cephalic (not caudal) direction of blood flow on MRV

Lateralization of Aortic-Pulmonary Stripe

- Other etiologies
 - Mediastinal lipomatosis (most common)
 - Left upper lobe PAPVR (i.e., vertical vein)
 - Lymphadenopathy
 - Neoplasm (e.g., lung cancer)

Enlarged Left Superior Intercostal Vein

- Courses horizontally along lateral margin of aorta
- Typically smaller than left SVC
- Provides anastomotic connection between left brachiocephalic vein and accessory hemiazygos vein

Lymph Node

• Not tubular on contiguous images

PATHOLOGY

General Features

- Etiology
 - Persistence of left superior cardinal vein
- Genetics
 - No known genetic predisposition
 - Higher prevalence in patients with congenital heart disease
- Associated abnormalities

Congenital heart disease

- Present in 40% of all cases of PLSVC
- More common with absent right SVC
 ASD
 - □ Bicuspid aortic valve
 - □ Aortic coarctation
 - Coronary sinus ostial atresia
 - 🗆 Cor triatriatum
- PLSVC occurs in 30-50% of patients with heterotaxy syndrome

Staging, Grading, & Classification

- Unroofed coronary sinus ASD classification
 - Type I: Completely unroofed with PLSVC
 - Type II: Completely unroofed without PLSVC
 - Type III: Partially unroofed mid portion
 - Type IV: Partially unroofed terminal portion

Gross Pathologic & Surgical Features

- Subtypes
 - Right and left SVC
 - Most common
 - Bridging vein may or may not be present (absent in 65%)
 - PLSVC and absent right SVC
 - Related to regression of caudal right superior cardinal vein
- Termination: Right atrium (80-90%); left atrium (~ 10%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Usually asymptomatic
- Other signs/symptoms
 - Cyanosis may occur with PLSVC that drains to left atrium &/or ASD
 - Risk of paradoxical embolism or cerebral abscess when associated with ASD, unroofed coronary sinus, or direct communication of vein to left atrium
 - Rarely, cardiac arrhythmias due to atrioventricular nodal stretching in setting of catheter placement
 - Rarely, left ventricular outflow obstruction due to incomplete occlusion of mitral valve
 - Congenital heart disease
 - May exhibit symptoms related to ASD or heterotaxy syndrome

- Challenging placement of pulmonary artery catheter; imaging guidance recommended
- Challenging placement of pacemakers and implantable cardioverter defibrillators
 - Complications: Arrhythmia, cardiogenic shock, cardiac tamponade, coronary sinus thrombosis
- PLSVC: Relative contraindication for administration of retrograde cardioplegia

Demographics

- Age
 - Usually incidental finding at any age
 - Patients with complex associated congenital anomalies may present early in life
- Sex
 - No predilection
- Epidemiology
 - Most common congenital thoracic venous anomaly
 - Left SVC occurs in 0.3-0.5% of general population
 - Prevalence: 3-10% in children with congenital heart disease
 - In congenital heart disease, PLSVC often drains directly into left atrium
 - Drainage into top of left atrium usually between left atrial appendage and pulmonary veins
 - Coronary sinus often absent or unroofed, producing intraatrial communication

Natural History & Prognosis

• Related to associated congenital anomalies

Treatment

• None if isolated; surgical correction if significant shunt

DIAGNOSTIC CHECKLIST

Consider

- Left arm contrast injection for optimal opacification of PLSVC
- Evaluation for associated congenital anomalies in patients with PLSVC

Image Interpretation Pearls

• Suggest diagnosis in patient with central catheter or pacemaker lead that follows left vertical course lateral to aortic arch

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(Left) Coronal CTA of the same patient shows the relationship of the persistent left superior vena cava 🛃 to the left pulmonary artery 🖾. Normally, no soft tissue should be identified lateral to the aortic arch or the pulmonary artery. (Right) Curved coronal CTA of the same patient shows the entire course of the persistent left superior vena cava 🛃. The dilated coronary sinus 🔁 is a characteristic finding that helps differentiate persistent left superior vena cava from left upper lobe partial anomalous pulmonary venous return.





(Left) Curved coronal CTA of a patient with persistent left superior vena cava shows a bridging vein \blacksquare that connects the left superior vena cava to the right superior vena cava. A bridging vein between the left and right superior vena cavas is absent in approximately 65% of affected patients. (Right) Axial SSFP MR of a patient shows a persistent left superior vena cava *Æ* lateral to the aortic arch. In this case, the left superior vena cava drained into the left atrium with a coronary sinus atrial septal defect (i.e., unroofed coronary sinus).





(Left) Axial SSFP MR of the same patient shows a coronary sinus 🔁 of normal size. Multiplanar imaging through the coronary sinus is recommended to demonstrate the unroofing. Velocityencoded sequences may be necessary to establish the presence of a right-to-left shunt. (Right) Oblique coronal MRA of the same patient shows a short-axis view of the coronary sinus 🛃 with unroofing and communication D with the left atrium. MR is superior to CT in confirming and quantifying the right-toleft shunt.

TERMINOLOGY

• Aberrant right subclavian artery (ARSA): Arises from distal left aortic arch, courses posterior to trachea and esophagus, and to the right

IMAGING

- Radiography
 - o Often normal
 - Frontal radiograph: Oblique opacity from left aortic arch and extending superiorly to the right (60%)
 - Lateral radiograph: Opacity in Raider triangle; indents posterior tracheal wall
- Esophagram: Oblique posterior indentation on esophagus
- CT
 - Last branch of 4-branch vessel left aortic arch
 - Courses posterior to trachea and esophagus, extends superiorly and crosses midline from left to right
 - Diverticulum of Kommerell: Dilated origin of ARSA

TOP DIFFERENTIAL DIAGNOSES

- Right aortic arch
- Double aortic arch
- Foregut duplication cyst
- Esophageal abnormality: Neoplasm, achalasia, foreign body
- Substernal thyroid goiter or ectopic thyroid

CLINICAL ISSUES

- Most common congenital anomaly of aortic arch
- Most patients asymptomatic; dysphagia, cough, dyspnea from tracheal/esophageal compression
- Treatment
 - No treatment required if asymptomatic
 - o Severe symptoms may require surgery

DIAGNOSTIC CHECKLIST

• Identification of ARSA is important for surgical planning, especially during thyroid/parathyroid surgery

(Left) Graphic shows the anatomic course of an aberrant left subclavian artery \square , which arises as the last branch of a left aortic arch, crosses the midline typically behind the trachea and esophagus, and continues towards the right. (Right) Axial curved CECT of an asymptomatic 55-year-old woman shows an aberrant right subclavian artery 🔁 that arises from a diverticulum of Kommerell 🔁, which originates from the proximal descending thoracic aorta and follows a characteristic retroesophageal course.





(Left) Composite image with lateral chest radiograph (left) and left anterior oblique esophagram (right) of the same patient shows an illdefined retrotracheal opacity rightarrow that corresponds to theposterior esophageal indentation 🔁. (Right) Coronal contrast-enhanced MRA shows an aberrant right subclavian artery 🔁 that arises from the proximal aspect of the descending thoracic aorta and crosses the midline to supply the right upper extremity.





Synonyms

• Aberrant right subclavian artery (ARSA)

IMAGING

General Features

- Best diagnostic clue
 - Artery that arises from distal left aortic arch, courses posterior to trachea and esophagus, and to the right
- Location
 - Most commonly retroesophageal and anterior to spine
 - Between esophagus and trachea (15%)
 - Anterior to trachea (5%)

Radiographic Findings

- Radiography
 - Chest radiograph often normal
 - Frontal radiograph
 - Oblique opacity arising from left aortic arch and extending superiorly to the right (60%)
 - Ill-defined opacity overlying medial right sub-clavicular region
 - Lateral radiograph
 - Opacity in Raider triangle (retrotracheal space)
 - Obscuration of aortic arch (60%)
 - Indentation on posterior tracheal wall (50%)

Fluoroscopic Findings

- Esophagram
 - Oblique posterior indentation on esophagus oriented superiorly toward right shoulder

CT Findings

• ARSA: 4th and final branch of left-sided aortic arch

- Courses posterior to esophagus and trachea, extends superiorly from left to right crossing midline
 Esophageal compression usually apparent
- No brachiocephalic artery
- Diverticulum of Kommerell
 - Dilated origin of ARSA; tapering tubular structure arising from posterior aspect of aortic arch
 - ± thrombus or calcification

Imaging Recommendations

- Best imaging tool
 - Contrast-enhanced CT or MRA are optimal for visualization and characterization of ARSA

DIFFERENTIAL DIAGNOSIS

Mass in Retrotracheal Space

- Vascular
 - Right aortic arch
 - Double aortic arch
- Foregut duplication cyst
- Esophageal abnormality
 - Neoplasm (benign or malignant)Achalasia
 - Foreign body
- Mediastinal thyroid goiter or ectopic thyroid tissue

PATHOLOGY

General Features

- Etiology
 - Involution of embryonic right 4th aortic arch between left carotid and left subclavian arteries
- Associated abnormalities
 - Congenital heart disease
 - Down syndrome (trisomy 21), Edwards syndrome (trisomy 18)
 - Anomalous right laryngeal nerve (non-recurrent laryngeal nerve, coursing directly into larynx)
 - Thoracic duct may terminate on the right

Gross Pathologic & Surgical Features

- ARSA course on pathology series
 - Retroesophageal (80%), retrotracheal (15%), pretracheal (5%)
- Diverticulum of Kommerell (60%)
- Aberrant left subclavian artery
 - Right aortic arch
 - Non-mirror image branching: Last branch off aorta, no increased incidence of congenital heart disease
- Mirror image branching: Left subclavian artery is 1st branch off aorta; high incidence of congenital heart disease
 - Most common: Tetralogy of Fallot, ventricular septal defect (VSD), truncus arteriosus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Most patients asymptomatic
- Other signs/symptoms
 - o Dysphagia lusoria from esophageal compression
 - Dyspnea and cough from tracheal compression

Demographics

- Epidemiology
 - Most common aortic arch anomaly; incidence ~ 0.5-2%

Natural History & Prognosis

• Morbidity and mortality related to surgical repair

Treatment

- None unless symptomatic
- Mild symptoms: Dietary modification
- Major symptoms may require surgery

DIAGNOSTIC CHECKLIST

Consider

- Identification of ARSA is important for surgical planning, especially during thyroid/parathyroid surgery
 - Awareness of non-recurrent right laryngeal nerve
 - Possible compression of left recurrent laryngeal nerve by aberrant artery (Ortner syndrome)

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Right Aortic Arch

KEY FACTS

TERMINOLOGY

- Right aortic arch (RAA)
 - Aortic arch located to right of trachea
- Common variations
 - RAA with aberrant left subclavian artery (ALSA) ± Kommerell diverticulum (KD)
 - RAA with mirror-image branching

IMAGING

- Radiography
 - Right paratracheal opacity + indentation on right tracheal margin on frontal radiography
 - KD: Retroesophageal opacity with indentation on posterior tracheal margin on lateral chest radiograph
- CT
 - RAA with ALSA with retroesophageal course ± KD
 - RAA with mirror-image branching
 - RAA with left descending aorta with retroesophageal aortic segment

TOP DIFFERENTIAL DIAGNOSES

- Double aortic arch
- Mediastinal mass

CLINICAL ISSUES

- RAA with ALSA
 - Most patients are asymptomatic
 - o Some patients with KD may have dysphagia or stridor
- RAA with mirror-image branching
 Cyanotic congenital heart disease
- RAA with left descending aorta (circumflex aorta)
 - Ductus ligament between pulmonary artery and ALSA constitutes vascular ring
- Treatment
 - Symptomatic RAA with ALSA/KD may require division of ligamentum via left thoracotomy

DIAGNOSTIC CHECKLIST

• RAA with ALSA and no KD is usually incidental finding

(Left) PA chest radiograph of a patient with a right aortic arch and an aberrant left subclavian artery shows that the right aortic arch manifests as a rounded right paratracheal opacity \implies that indents the right trachea. (Right) Lateral chest radiograph of the same patient shows normal posterior tracheal morphology \blacksquare . The coexistent aberrant left subclavian artery was not associated with a Kommerell diverticulum, as evidenced by absence of a posterior tracheal indentation on lateral radiography.





(Left) Composite image with axial CTA shows a right aortic arch 🛃, an aberrant left subclavian artery 🔁, a right descending thoracic aorta, and an incidental persistent left superior vena cava 🔁, which drained into the coronary sinus (not shown). (Right) Coronal CTA of the same patient shows the aberrant left subclavian artery 🔁 arising as the last aortic branch. As there is no Kommerell diverticulum, there is no ductus ligament, and therefore, this anomaly does not constitute a vascular ring.





Abbreviations

- Right aortic arch (RAA)
- Left aortic arch (LAA)

Definitions

- Aortic arch located to right of trachea
- Common variations
 - RAA with aberrant left subclavian artery (ALSA) ± Kommerell diverticulum (KD)
 - Branches: Left common carotid, right common carotid, right subclavian, aberrant left subclavian
 - KD
 - Saccular dilatation at proximal ALSA
 - Implies presence of ligamentum arteriosum and vascular ring
 - RAA with mirror-image branching: Left brachiocephalic, right common carotid, and right subclavian
- Uncommon variations
 - o RAA with left descending aorta (circumflex aorta)
 - RAA with isolation of left subclavian artery
 - RAA with aberrant brachiocephalic artery
 - o RAA with unilateral absence of pulmonary artery

IMAGING

General Features

- Best diagnostic clue
 - Indentation of right tracheal margin by RAA

Radiographic Findings

- Radiography
 - General features
 - Right paratracheal opacity
 - Indentation on right tracheal margin
 - RAA with ALSA
 - Associated KD
 - Retroesophageal opacity
 - Indentation on posterior tracheal margin
 - May simulate LAA on frontal projection
 - RAA with mirror-image branching
 - ± dextrocardia
 - High association with congenital heart disease
 - RAA with unilateral absence of pulmonary artery
 - Hypoplastic ipsilateral hemithorax; contralateral hyperinflation
 - Absent or grossly ↓ pulmonary vascular markings

CT Findings

- RAA with ALSA
 - 4 great arteries in following order: Left common carotid, right common carotid, right subclavian, ALSA
 - ALSA with retroesophageal course
 - KD: Bulbous dilatation at origin of ALSA
- RAA with mirror-image branching
 - 3 great arteries in following order: Left brachiocephalic, right common carotid, right subclavian
 - Rarely, blind-ending aortic diverticulum (similar to KD)
- RAA with left descending thoracic aorta (circumflex aorta)
 Retroesophageal aortic segment

- RAA with isolation of left subclavian artery
 - 3 great vessels in following order: Left common carotid, right common carotid, right subclavian
 - Blind origin left subclavian artery; connected to aortic arch by ductus ligament

MR Findings

• Same accuracy as CT for assessment of variant anatomy

DIFFERENTIAL DIAGNOSIS

Double Aortic Arch

- Differentiation on radiography may be not possible; KD may simulate LAA
- CT and MR diagnostic
 - Patent RAA and LAA with larger RAA and smaller LAA
 - Double aortic arch (DAA) with atretic LAA
 - Inferior tethering of left subclavian artery
 - Aortic diverticulum more common in DAA

Mediastinal Mass

• Right paratracheal lymphadenopathy &/or mass may simulate RAA on radiography

PATHOLOGY

General Features

- Etiology
 - Embryologic considerations
 - RAA with ALSA: Vascular interruption between left common carotid and left subclavian arteries
 - RAA with mirror-image branching: Vascular interruption distal to left subclavian artery
- Associated abnormalities
 - RAA with ALSA ± KD: Low incidence of congenital heart disease
 - RAA with mirror-image branching: High incidence of congenital heart disease (~ 98%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - RAA with ALSA
 - Patients with KD may have dysphagia or stridor

Natural History & Prognosis

• Determined mostly by coexisting congenital heart disease

Treatment

- Symptomatic RAA with ALSA/KD
 Requires division of ligamentum via left thoracotomy
- RAA with mirror-image branching
 - Treatment of associated congenital heart disease

DIAGNOSTIC CHECKLIST

Consider

• RAA with ALSA and no KD is usually incidental finding

SELECTED REFERENCES

 Prabhu S et al: Anatomic classification of the right aortic arch. Cardiol Young. 30(11):1694-701, 2020 (Left) PA chest radiograph of an asymptomatic patient shows a right aortic arch that manifests as a right paratracheal opacity \blacksquare that indents the right lateral tracheal margin. (Right) Lateral chest radiograph of the same patient shows a posterior tracheal indentation $\square,$ that corresponds to a Kommerell diverticulum, which suggests that mirrorimage branching is not present and that there is a vascular ring, which may or may not be symptomatic.





(Left) Composite image with axial CTA shows a right aortic arch, a right descending aorta, an aberrant left subclavian artery, and a Kommerell diverticulum 🔁. Note mild esophageal dilatation 🔁 proximal to the Kommerell diverticulum. (Right) Sagittal CTA of the same patient shows posterior tracheal indentation by the Kommerell diverticulum \supseteq , which implies the presence of a ductus ligament and a vascular ring. While most affected patients are asymptomatic, Kommerell diverticulum may be associated with dysphagia.





(Left) Oblique coronal CTA of the same patient shows a bulbous configuration 🔁 at the origin of the aberrant left subclavian artery, a Kommerell diverticulum. The latter results from the associated ligamentum arteriosum. The resultant vascular ring may be associated with dysphagia. (Right) Composite image with anterior (left) and posterior (right) CTA 3D reformations of the same patient shows a right aortic arch, an aberrant left subclavian artery \blacksquare , and the bulbous Kommerell diverticulum 🔁.





Right Aortic Arch





(Left) Composite image with axial CTA shows a right aortic $arch \blacksquare, a retroesophageal$ left descending thoracic aorta (circumflex aorta) ₽, a blindending aortic diverticulum \bowtie , and mirror-image branching. (Right) Composite image with coronal CTA of the same patient shows a right aortic arch 🖂, a left brachiocephalic trunk 🚬, a blind-ending aortic diverticulum \mathbf{E} , and a left descending thoracic aorta 🖂 The circumflex aorta implies the presence of a vascular ring, which is often loose and may be symptomatic.





(Left) Axial CTA of a patient who presented with stridor shows a right aortic arch 🔁 with mirror-image branching, a blind-ending aortic diverticulum 🖂, and a rightsided descending thoracic aorta 🛃. (Right) Posterior CTA 3D reformation of the same patient shows a blindending aortic diverticulum 🖂 associated with a right aortic arch. This anomaly may mimic a double aortic arch with an atretic left aortic arch. The latter can be excluded given absence of inferior tethering of the left subclavian artery. (Courtesy R. Reina, MD.)





(Left) Axial CECT shows a right aortic arch \blacksquare associated with isolation of the left subclavian artery and enlarged arterial collateral vessels 🔁. (Right) Coronal CECT of the same patient shows the blind origin of the left subclavian artery and a cord-like structure that extends from it to the aortic wall and represents a ductus ligament \blacksquare , which forms a loose vascular ring. Extensive arterial vascular collaterals ᠫ supply the left subclavian artery.
Double Aortic Arch

KEY FACTS

TERMINOLOGY

- Congenital aortic arch anomaly
- Most common symptomatic vascular ring (55%)

IMAGING

• Radiography

- Bilateral tracheal indentations
- Right arch indentation typically higher and more pronounced than left
- Lateral chest radiograph: Anterior and posterior tracheal compression at level of arch

• CT/MR

- 4 artery sign: Symmetric takeoff of 4 aortic branches on axial image at thoracic inlet
- o 2 arches encircle trachea and esophagus
- Right aortic arch typically larger and more superior
- Severe tracheal compression at level of double arch
- Descending thoracic aorta typically on left

TOP DIFFERENTIAL DIAGNOSES

- Right arch with aberrant left subclavian artery and other arch abnormalities
- Aberrant left pulmonary artery
- Innominate artery compression syndrome
- Nonvascular masses

CLINICAL ISSUES

- Symptoms/signs
 - o Typically manifests early in life, soon after birth
 - o Inspiratory stridor, worsens with feeding
 - May be minimally symptomatic incidental finding
- Treatment: Thoracotomy with division of smaller of 2 arches

DIAGNOSTIC CHECKLIST

• 4 artery sign on axial image at thoracic inlet should suggest double aortic arch

(Left) Axial CECT of an adult with double aortic arch status post repair of congenital heart disease shows that the $common \ carotid \Longrightarrow and$ subclavian arteries 🔁 arise from their respective arches (4 artery sign). A Blalock-Taussig conduit from the left subclavian artery to pulmonary artery is present ► (Right) Axial CECT of the same patient shows that the right (R) and left (L) arches have equal size and encircle and narrow the trachea \blacksquare and esophagus 🔁. The Blalock-Taussig conduit 🔁 courses caudally.





(Left) Axial CECT of the same patient shows the more inferior left (L) arch joining with the right arch posteriorly \blacksquare to form the descending aorta. The Blalock-Taussig conduit \triangleright courses caudally. (Right) Axial CECT of the same patient shows the ascending aorta (A), which divides superiorly into right and left aortic arches. The descending aorta (D) courses inferiorly in the midline. The trachea 🔁 and esophagus \blacksquare are encircled and compressed. The Blalock-Taussig conduit 🔁 courses caudally to the left pulmonary artery.





Definitions

- Congenital aortic arch anomaly
 - o Persistent right and left 4th embryonic aortic archeso Complete vascular ring encircles trachea and esophagus
- Most common symptomatic vascular ring (55%)
- May occur with or without other congenital abnormalities
- Often isolated anomaly in adults

IMAGING

General Features

- Best diagnostic clue
- Right and left aortic arches that compress tracheaLocation
 - Ascending aorta divides into right and left arches
 - Right aortic arch typically larger and more superior
 - Each arch gives rise to respective carotid and subclavian arteries
 - Symmetric **4 artery** sign
 - No brachiocephalic artery
 - Arches anastomose posterior to esophagus
 - Right arch courses behind esophagus to join left
 - Descending thoracic aorta is typically contralateral to dominant arch
 - Dominant right: Descending aorta on left
 - Dominant left: Descending aorta on right
- Part of left arch may be atretic; patent portions remain connected by fibrous band

Radiographic Findings

- Radiography
 - Soft tissue on both sides of mid trachea
 Paratracheal contour abnormality
 - Bilateral tracheal indentations. mid tracheal stenosis
 - Trachea may be deviated by dominant arch
 - Trachea may be in abnormal midline position
 - Right arch indentation typically higher and more pronounced than left
 - Lateral chest radiograph: Anterior and posterior tracheal compression at level of aortic arch
 - Symmetric lung aeration; no unilateral air-trapping

Fluoroscopic Findings

- Esophagram
 - Frontal view: Bilateral indentations on contrast-filled esophagus, often at different levels
 - Lateral view: Oblique or nearly horizontal posterior indentation

CT Findings

- CTA
 - **4 artery** sign: Symmetric takeoff of 4 aortic branches on axial image at thoracic inlet
 - 2 anterior carotid arteries
 - 2 posterior subclavian arteries
 - 2 arches encircle trachea and esophagus
 - Smaller of 2 arches may be partially atretic
 - May be difficult/impossible to differentiate from right aortic arch with aberrant left subclavian artery (LSA)

• Severe tracheal compression at level of double arch

MR Findings

- As specific as CTA for morphologic characterization
- Additional benefit of no ionizing radiation
- Axial and coronal images are most helpful
 - Imaging protocol
 - Black blood images
 3D Gadolinium MRA
 - ECG and respiratory navigator-gated 3D steady statefree precession (SSFP)

Echocardiographic Findings

- Echocardiogram
 - Suprasternal notch view shows 2 aortic arches, each with separate carotid and subclavian arteries
 - Often insufficient for preoperative diagnosis
- Color Doppler
 In countries with good prenatal care: Antenatal diagnosis of < 25% of vascular rings

Angiographic Findings

Conventional angiography
 Rarely required with use of CT and MR

Imaging Recommendations

- Best imaging tool
 - Radiography remains primary initial step for evaluating patients with suspected vascular ring
 - Absence of tracheal compression excludes vascular ring
 - Esophagram rarely obviates need for CT or MR
 - Some asymptomatic arch anomalies initially diagnosed by esophagram
 - CT or MR: Confirm diagnosis and depict anatomic variations
- Protocol advice
 - Axial and coronal reformations
 - Multidetector CTA performed more expeditiously than MR; typically with no need for sedation &/or intubation
 - CT shows airway compromise better than MR

DIFFERENTIAL DIAGNOSIS

Right Arch With Aberrant Left Subclavian Artery and Other Arch Abnormalities

- Difficult to differentiate radiographically if associated with diverticulum of Kommerell
- Differentiation easier with cross-sectional imaging

Aberrant Left Pulmonary Artery

- Compression on anterior esophagus and posterior trachea on radiography
- Often associated with tracheomalacia and congenital heart disease (CHD)

Innominate Artery Compression Syndrome

- Anterior tracheal compression
- No esophageal compression

Nonvascular Masses

• Neoplasm or foregut cyst may compress trachea

- Lymphadenopathy: Benign entities (e.g., sarcoidosis) or malignant processes (metastatic lymphadenopathy, lymphoproliferative process)
- Enteric duplication, thymic, and bronchogenic cysts
 - Often do not compress tracheaLow attenuation, near water
 - Contrast enhanced MR shows fluid content and enhancing mural component

Azygos Continuation of Inferior Vena Cava

- Right paratracheal contour abnormality (azygos) and wide mediastinum
- No tracheal impression
- Associated with heterotaxy syndrome

PATHOLOGY

General Features

- Etiology
 - Branchial arch development begins by second week of gestation and continues until seventh week
 - o 6 paired arches connect paired dorsal and ventral aortas
 - All arches are not present at same time
 - Normal left aortic arch formed by regression of right aortic arch, right sided ductus, and right dorsal aorta
 - Abnormal persistence or regression of various segments leads to various malformations
 - Double aortic arch: Both right and left fourth branchial arches persist, one on each side of trachea
- Genetics
 - o 1/3 of all vascular rings associated with genetic disorders
 - 22q11 microdeletion, trisomy 21, CHARGE syndrome (coloboma, heart anomaly, atresia choanae, growth restriction, genital and ear abnormalities), VACTERL association (vertebral defect, anal atresia, cardiac defect, tracheoesophageal fistula, renal anomalies and limb abnormalities)
 - o 1/2 have additional congenital cardiac pathology
 - Ventricular septal defect (most common)
 - Tetralogy of Fallot
 - Atrioventricular septal defect
 - Double outlet right ventricle
 - Hypoplastic left heart syndrome
 - 10-15% of patients with double aortic arch have chromosome 22q11 deletion
- Associated abnormalities
 - Typically isolated lesion
 - o 20% have additional CHD
- Pathophysiology
 - Severe airway and esophageal compression
 - Tracheomalacia is common
- No hemodynamic sequelae, unless associated CHD

Gross Pathologic & Surgical Features

- Complete vascular ring encircles trachea and esophagus
 Dominant right arch, left descending aorta: 75%
 - Dominant left arch, right descending aorta: 20%
 - Arches equal in size: 5%
- Smaller of 2 arches may be partially atretic

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Inspiratory stridor (60%)
 - Recurrent upper respiratory tract infection (27%)
 - o Cough (20%)
 - Dysphagia once child is old enough to take solid food (15%)
 - May be minimally symptomatic, incidental finding on imaging
- Other signs/symptoms
 - Apneic attacks
 - o "Seal bark" cough

Demographics

- Age
 - o Patients typically present early in life, soon after birth
 - Other vascular rings may be more common but less symptomatic (e.g., aortic abnormalities associated with aortic diverticulum; Kommerell)

Treatment

- Thoracotomy with division of smaller of 2 arches, atretic segments, and ligamentum arteriosum
 - Rare complication: Aortoesophageal fistula
 - Associated with prolonged esophageal tube placement
- < 30% have persistent symptoms postoperatively
 - Tracheobronchomalacia ± extrinsic compression
 - Midline/circumflex descending aorta
 - Previously ligated arch
- 11% of patients require 2nd surgery to repair airway
 - Aortopexy or other vascular suspension procedures
 - Tracheal ring resection and airway reconstruction
- Imaging plays critical role in surgical planning
- Surgical approach depends on position of dominant aortic arch
 - Dominant right aortic arch repaired through left thoracotomy
 - Dominant left aortic arch repaired through right thoracotomy

DIAGNOSTIC CHECKLIST

Consider

• Look for signs of atretic arch segment that does not opacify on CTA or MRA and does not show flow void on MR

Image Interpretation Pearls

• 4 artery sign on axial image at thoracic inlet should suggest double aortic arch

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- 2. Priya S et al: Congenital anomalies of the aortic arch. Cardiovasc Diagn Ther. 8(Suppl 1):S26-44, 2018
- 3. Hanneman K et al: Congenital variants and anomalies of the aortic arch. Radiographics. 37(1):32-51, 2017
- 4. Backer CL et al: Vascular rings. Semin Pediatr Surg. 25(3):165-75, 2016

Double Aortic Arch





(Left) Axial CTA of an infant with stridor secondary to an isolated double aortic arch shows that the common carotid \supseteq and subclavian arteries \blacksquare symmetrically arise from their respective arches (4 artery sign) and encircle the trachea and esophagus. (Right) Axial CTA of the same infant shows a dominant right arch \blacksquare and a smaller left arch \blacksquare . The arches encircle the trachea and esophagus. Severe tracheal narrowing resulted in stridor. Residual thymic tissue is normal for age.





(Left) Coronal CTA of the central airways of the same infant shows that the trachea is moderately compressed between the arches \blacksquare . Moderate stenosis of the right mainstem bronchus \implies is not related to the vascular ring and likely represents bronchomalacia. (Right) AP esophagram of the same infant shows typical indentations from the higher dominant right arch \blacksquare , the lower left arch \square , and the left-sided proximal descending aorta ➡. Affected infants may present with difficulty feeding.





(Left) Coronal 3D reformatted image (posterior view) of the same infant shows the right $arch \blacksquare superior to the$ smaller left arch 🛃. The arches join posteriorly to form the descending aorta 🔁 A double aortic arch may be an isolated anomaly. (Right) Graphic shows the morphology of double aortic arch with arches arising from the ascending aorta 🛃 to form a complete vascular ring that encircles and compresses the trachea \square and the esophagus \blacksquare . The right arch is typically larger and more superior.

Aortic Coarctation

KEY FACTS

TERMINOLOGY

- Congenital aortic stenosis typically just distal to left subclavian artery origin
- From Latin term coarctatus: Contracted or tightened

IMAGING

- Radiography
 - Inferior rib notching, figure 3 sign
 - Ill-defined or obscured aortic arch
 - Left ventricular hypertrophy ± calcified bicuspid aortic valve
- Esophagram: Reverse figure 3 sign
- **CTA**
- Identification of location and severity of stenosis
- Focal shelf-like narrowing of posterior/lateral aorta distal to left subclavian origin
- Enlarged collateral arteries
- MR
 - Contrast-enhanced 3D MRA for vessel morphology

TOP DIFFERENTIAL DIAGNOSES

- Pseudocoarctation
- Takayasu arteritis
- Interrupted aortic arch
- Traumatic pseudoaneurysm

PATHOLOGY

 Associations: Bicuspid aortic valve, ventricular septal defect (VSD), patent ductus arteriosus (PDA), Turner syndrome

CLINICAL ISSUES

- Surgical correction used for infants
- Balloon angioplasty used for children and adults
- Stent placement typically for recoarctation

DIAGNOSTIC CHECKLIST

- Search for subtle signs of coarctation in any young patient with hypertension
- Enlarged collateral vessels imply significant stenosis

(Left) Coned-down PA chest radiograph shows inferior rib notching, a classic radiographic sign of aortic coarctation produced by benign pressure erosion from collateral vasculature. (Courtesy L. Heyneman, MD.) (Right) Composite image with PA chest radiographs that shows the figure 3 sign (left) produced by an upper convexity 🛃 due to a tortuous left subclavian artery, an indentation \blacksquare due to the coarctation, a lower convexity *▶* due to a dilated poststenotic aorta, and an obscured aortic arch (right).





(Left) Composite image with axial CTA proximal to (left) and at the coarctation (right) shows typical features that include focal stenosis at the $coarctation \blacksquare$ and dilated internal mammary \blacksquare and intercostal \square arteries that provide collateral circulation. (Right) Oblique CTA MIP reformatted image of the same patient optimally demonstrates the aortic coarctation \blacksquare , the poststenotic aortic dilatation *▶*, as well as a tortuous dilated internal mammary $artery \blacksquare$ and intercostal collateral vessels.





Abbreviations

• Aortic coarctation, coarctation of aorta (CoA)

Definitions

- Congenital aortic stenosis typically just distal to left subclavian artery origin
- From Latin coarctatus: Contracted or tightened

IMAGING

General Features

- Best diagnostic clue
 - Inferior rib notching on radiography
- Location
 - May occur anywhere in aorta or at multiple sites
 Preductal, ductal, postductal
- Size
 - o Long-segment stenosis referred to as tubular hypoplasiao Focal &/or diffuse

Radiographic Findings

• Radiography

• Inferior rib notching (Roesler sign)

- Large collateral intercostal arteries: Pressure erosion
- Rare before 5 years of age
- Ribs 3-8; ribs 1-2 spared; supplied by costocervical trunk; does not anastomose with distal aorta
- May regress post repair
- Unilateral rib notching may indicate aberrant subclavian artery

• Figure 3 sign in up to 50% of cases

- Proximal convexity: Dilated left subclavian artery
- Indentation at coarctation
- Distal convexity: Poststenotic descending aorta
- $\circ\;$ Ill-defined or obscured aortic arch
- Left ventricular hypertrophy ± calcified bicuspid aortic valve
- Esophagram
 - Reverse figure 3 sign: Esophageal compression by dilated left subclavian artery and poststenotic dilated descending aorta

CT Findings

- CTA
 - Multiplanar reformatted images (sagittal oblique), 3D volume-rendered images
 - $\circ~$ Identification of location and severity of stenosis
 - Focal shelf-like narrowing of posterior/lateral aorta just distal to left subclavian origin
 - Enlarged collateral arteries: Internal mammary, intercostal, thyrocervical, thyroacromial arteries

MR Findings

- Contrast-enhanced MRA
 - Assessment of vessel morphology; identification of enlarged collateral arteries
- Velocity-encoded cine (VENC)
 - Flow-sensitive phase-contrast technique and timeresolved velocity-encoded 3D phase contrast (4D flow MR)

• Estimation of pressure gradients and flow volumes

Cardiac MR

- Diagnosis of associated cardiac anomalies
- Assessment of bicuspid aortic valve; quantification of stenosis &/or regurgitation

Angiographic Findings

- Assessment of vessel morphology and direct measurement of pressure gradient
 - o < 20 mm Hg: Mild coarctation
 - o > 20 mm Hg: Suggests need for intervention
 - Role in treatment rather than in diagnosis

Imaging Recommendations

- Best imaging tool
 - Echocardiography in infancy
 - CTA or MR in older child or adult
 - MR for follow-up evaluations

DIFFERENTIAL DIAGNOSIS

Pseudocoarctation

- Older adult with elongated and kinked aorta related to atherosclerosis
- No hemodynamically significant stenosis, no collateral vessels

Takayasu Arteritis

- Inflammatory narrowing of unknown etiology
- Narrowing &/or occlusion of aorta and branch vessels, rarely isolated to aortic isthmus

Interrupted Aortic Arch

- Complete absence of continuity between 2 aortic segments
- Nearly always manifests in neonates

Traumatic Pseudoaneurysm

- History of trauma, healed rib, and other skeletal fractures
- Descending aorta narrowing may coexist with pseudoaneurysm

Inferior Rib Notching Differential

- Neurofibromatosis
- Venous collaterals (superior vena cava obstruction)
- Decreased pulmonary blood flow (tetralogy of Fallot, pulmonary atresia)
- Blalock-Taussig shunt (1st and 2nd ribs)

PATHOLOGY

General Features

- Etiology
 - Abnormal development of embryologic left 4th and 6th aortic arches
 - Muscular theory: Migration of tissue from ductus arteriosus to aortic wall and subsequent contraction
 - Hemodynamic theory
 - → aortic blood flow during fetal development may prevent proper aortic growth

- → incidence of coarctation in disorders with ↓ ductal flow (e.g., tetralogy of Fallot)
- Genetics
 - Association with Turner syndrome (CoA in up to 20%)
- Associated abnormalities
 - Bicuspid aortic valve (in 50-85%)
 - Ventricular septal defect
 - Patent ductus arteriosus
 - Sinus venosus-type atrial septal defect (ASD)
 - Shone syndrome: Aortic coarctation, subaortic stenosis, parachute mitral valve, supravalvular mitral membrane
 - Cerebral aneurysms

Staging, Grading, & Classification

- No agreed upon classification; previously described classifications discouraged due to overlapping manifestations
- **Simple coarctation**: Isolated lesion; just distal to left subclavian artery origin (postductal)
- **Complex coarctation**: Associated with other intracardiac anomalies; manifests in infancy; often preductal

Gross Pathologic & Surgical Features

- Obstructing membrane or tissue ridge near aortic isthmus
- May develop cystic medial necrosis adjacent to coarctation site; predisposition to aneurysm or dissection

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Neonates
 - Asymptomatic if coarctation not severe or patent ductus arteriosus
 - Severe coarctation or closed ductus arteriosus: Heart failure, lower body hypoperfusion, renal dysfunction, acidosis
 - Decreased femoral pulses, associated murmurs
 - Children and adults
 - Usually asymptomatic unless severe hypertension
 - May have claudication and chest pain with exercise
 - Differential hypertension between upper and lower extremities, diminished femoral pulses
 - Murmur associated with bicuspid aortic valve
 - Turner syndrome: Short webbed neck, broad chest, pigmented facial nevi, short 4th metacarpals

Demographics

- Age
 - Based on degree of stenosis and associated abnormalities
- Sex
 - o M:F = 2:1
- Epidemiology
 - o Incidence: 2-6 per 10,000 births
 - o 5-8% of cases of congenital heart disease

Natural History & Prognosis

- Without repair
 - o Average age of death: 35-42 years
 - o 75% mortality by age 46

- Aortic dissection/rupture, heart failure, myocardial infarct, cerebral hemorrhage
- With repair
 - Approximately 90% survival at 20 years; ↓ survival with
 ↑ age at repair
 - Recoarctation (2-14%): Associated with younger age at surgery
 - Postoperative aneurysm (↑ risk after patch aortoplasty)
 - ↓ long-term survival; hypertension, coronary artery disease, dissection
- Pregnancy-related issues
 - Outreated coarctation: ↑ risk of dissection and intracranial hemorrhage
 - Treated coarctation: ↑ rate of miscarriage and preeclampsia

Treatment

- Indications for treatment
 - o Infant with severe stenosis and heart failure
 - Longstanding hypertension
 - Hemodynamically significant stenosis (gradient > 20 mm Hg)
 - Extensive collateral flow
 - Female patient contemplating pregnancy
- Surgical correction: First-line treatment for infants
 - Resection with end-to-end anastomosis: Higher risk of spinal artery injury and restenosis
 - Left subclavian flap aortoplasty: Sacrifice left subclavian artery and vertebral artery (to avoid subclavian steal)
 - Bypass graft: Used if area of narrowing is too long for end-to-end repair
 - Acute complications
 - Paradoxic hypertension, recoarctation, hypertension, paraplegia from spinal artery damage, recurrent laryngeal or phrenic nerve injury, subclavian steal
 - Late complications: Aortic aneurysm, recurrent coarctation, hypertension
- Balloon angioplasty
 - First-line treatment for native coarctation or recoarctation in older children and adults
 - Not for infants due to ↑ rate of recurrence
 - Acute complications rare: Dissection, stroke
 - Late complications: Recoarctation, aneurysm, endocarditis, hypertension
- Stent placement: Generally reserved for recoarctation
 - Complications: Acute rupture, dissection, stent fracture or migration, aneurysm

DIAGNOSTIC CHECKLIST

Consider

• Search for subtle signs of coarctation in any young patient with hypertension

Image Interpretation Pearls

• Enlarged collateral vessels imply significant stenosis

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- Erben Y et al: Multicenter experience with endovascular treatment of aortic coarctation in adults. J Vasc Surg. 69(3):671-9.e1, 2019

Aortic Coarctation





(Left) Volume rendered 3D CTA of a patient with aortic coarctation shows the use of this technique for morphologic assessment of aortic coarctation and for providing an overall view of chest wall vascular collaterals. 3D reformatted images may help clinicians and surgeons to better understand the tridimensional configuration of the lesion. (Right) Sagittal oblique MR SSFP cine (bright blood) sequence shows the aortic morphology and the area of stenosis 🛃. Spindephasing jets may be seen in regions of stenosis.





(Left) Axial CECT of a patient with aortic coarctation (not shown) shows a ventricular septal defect 乏, a known associated abnormality. (Right) DSA of a patient undergoing cerebral angiography for subarachnoid hemorrhage shows the catheter tip proximal to a severe aortic coarctation \supseteq . Because of their association with intracranial aneurysms, aortic coarctations may be incidentally discovered during conventional angiography. Note dilated thyrocervical and costocervical trunk branches $\overline{}$





(Left) Axial CTA of a patient who underwent surgical repair of aortic coarctation demonstrates postoperative recoarctation ≥ and a poststenotic aortic aneurysm ≥. (Right) Axial CECT of a patient who underwent surgical repair of an aortic coarctation shows a postoperative pseudoaneurysm ≥. Such pseudoaneurysm scan subsequently be excluded with an endovascular stent graft ≥, as in this case.

Atrial Septal Defect

KEY FACTS

TERMINOLOGY

• Atrial septal defect (ASD)

IMAGING

- Radiography
 - o Cardiac silhouette usually normal
 - Shunt vascularity
 - Pulmonary edema and pleural effusions
 - Pulmonary artery hypertension
- Cardiac gated CTA
 - Direct visualization of ASD
 - o Determination of direction and extent of shunt
 - Associated abnormalities
- MR
 - Evaluation of shunt volume and direction
 - Evaluation of valvular function
 - o Assessment of pressure gradients across valves

TOP DIFFERENTIAL DIAGNOSES

- Ventricular septal defect
- Patent ductus arteriosus
- Pulmonary artery hypertension

CLINICAL ISSUES

- Usually asymptomatic in early life
- Becomes symptomatic with advancing age
- 90% of patients are symptomatic by 40 years
 Exertional dyspnea, fatigue, palpitations, and heart failure
- Surgical repair
 - Open repair with extracorporeal support most common
 - Minimally invasive approaches
- Percutaneous transcatheter therapy
 - o Small ostium secundum defects most amenable
 - Fewer complications compared to surgical repair

(Left) PA chest radiograph of a patient with an atrial septal defect (ASD) demonstrates enlargement of the bilateral pulmonary arteries 🖂. (Right) Lateral chest radiograph of the same patient shows hilar enlargement due to enlarged pulmonary arteries. Patients with ASD may develop pulmonary artery hypertension, which manifests as enlargement of the pulmonary trunk and pulmonary arteries, pruning of peripheral pulmonary artery branches, and enlargement of the right atrium and right ventricle.





(Left) Axial CECT of the same patient demonstrates a sinus venosus ASD with communication between the right and left atria 🔁. Sinus venosus is the least common type of ASD after ostium secundum and ostium primum types. (Right) Axial CECT of the same patient shows partial anomalous pulmonary venous return as the right superior pulmonary vein 🖂 drains into the superior vena cava 🖾. Partial anomalous pulmonary venous return is one of the most common conditions associated with ASD.





Abbreviations

• Atrial septal defect (ASD)

IMAGING

General Features

- Best diagnostic clue
 - Normal cardiac silhouette and shunt vascularity on chest radiography
- Location
 - Ostium secundum (75%)
 - Mid interatrial septum
 - Oval defect bordered by fossa ovalis
 - o Ostium primum (15-20%)
 - Anterior/inferior interatrial septum
 - Located adjacent to atrioventricular (AV) valves
 - o Sinus venosus (5-10%)
 - Superior interatrial septum near superior vena cava
 - Posterior to fossa ovalis
 - o Coronary sinus (<1%)
 - Due to unroofing of coronary sinus
 - Persistent left superior vena cava

Radiographic Findings

- Radiography
 - o Cardiac silhouette usually normal
 - Left atrium typically normal in size
 - Differentiates ASD from ventricular septal defect and patent ductus arteriosus
 - May be enlarged in severe mitral regurgitation
 - Enlarged right atrium and right ventricle may be seen in pulmonary artery hypertension

• Shunt vascularity

- Pulmonary edema and pleural effusions
- Pulmonary artery hypertension
 - Enlarged pulmonary trunk and pulmonary arteries
 - Pruning of peripheral pulmonary artery branches
 - Enlarged right atrium and right ventricle

CT Findings

- Cardiac gated CTA
 - Direct visualization of ASD
 - o Determination of direction and extent of shunt
 - o Associated abnormalities
 - Partial anomalous pulmonary venous return
 Pulmonary vein draining into superior vena cava
 - Usually involves right upper lobe
 - □ Strongest association with sinus venosus ASD
 - Coronary sinus ASD with persistent left superior vena cava and unroofing of coronary sinus (depending of contrast phase, actual ASD can be seen e.g., flow of contrast from opacified coronary sinus to less opacified left atrium)

MR Findings

- Phase contrast and cine MR
 - o Assessment of shunt volume and direction
 - Assessment of valvular function
 - o Determination of pressure gradients across valves

Echocardiographic Findings

• Echocardiogram

- Direct visualization of ASD: 2-dimensional (2D) imaging subcostal approach
- o Mitral valve prolapse may be visualized
- Anterior systolic motion of interventricular septum
- Gooseneck deformity of ostium primum defect: Subxiphoid long-axis view of left ventricular outflow tract (LVOT)
- Enlarged pulmonary trunk and right ventricle in pulmonary artery hypertension
- Color Doppler
 - Direct visualization of ASD

Angiographic Findings

- Cardiac catheterization
 A Performed when echocardiography is in
 - Performed when echocardiography is inconclusive or to evaluate associated abnormalities
 - Extension of catheter across defect
- Left ventricular angiography
 - Evaluation of mitral valve prolapse and extent of mitral regurgitation
 - o Gooseneck deformity in ostium primum defect
 - Best seen on right anterior oblique (RAO) view

Imaging Recommendations

- Best imaging tool
 - Cardiac gated CTA or MR to visualize defect

DIFFERENTIAL DIAGNOSIS

Ventricular Septal Defect

- Left-to-right intracardiac shunt
- Enlarged cardiac silhouette
 - Left atrium and left ventricle
- Shunt vascularity
- Pulmonary edema
- Pulmonary artery hypertension
 - Enlarged pulmonary trunk and pulmonary arteries
 - Pruning of peripheral pulmonary artery branches
 - Enlarged right ventricle

Patent Ductus Arteriosus

- Persistent connection between descending thoracic aorta and proximal left pulmonary artery
- Left-to-right intracardiac shunt
- Enlarged cardiac silhouette
- Left atrium and left ventricle
- Enlarged aortic arch
 - Distinguishes patent ductus arteriosus from ventricular septal defect
- Shunt vascularity
- Pulmonary edema
- Pulmonary artery hypertension
 - Enlarged pulmonary trunk and pulmonary arteries
 - Pruning of peripheral pulmonary artery branches
 - Enlargement of right ventricle

Pulmonary Artery Hypertension

- Enlarged pulmonary trunk and central pulmonary arteries
- CTA: Enlarged pulmonary trunk > 30 mm

- HRCT
 - o Pre-capillary etiologies: Emphysema, fibrosis, honeycomb lung
 - o Post-capillary etiologies: Centrilobular ground-glass nodules, pulmonary edema, pleural effusions • Chronic PAH: Patchy, ground-glass opacities
- Pre-capillary etiologies: Chronic pulmonary emboli,
- congenital left-to-right shunts, lung disease, idiopathic Post-capillary etiologies: Left heart failure and mitral stenosis

PATHOLOGY

General Features

- Etiology
 - Congenital cardiac anomaly characterized by defects within interatrial septum
 - o Ostium secundum
 - Incomplete adhesion of septum secundum to flap valve of foramen ovale
 - Ostium primum
 - Incomplete fusion of septum primum with endocardial cushion
 - Sinus venosus
 - Abnormal fusion of sinus venosus and right atrium
 - o Coronary sinus
 - Unroofing of coronary sinus
- Genetics
 - o Ellis van Creveld
 - Skeletal dysplasia with common atrium
 - Autosomal recessive pattern of inheritance
 - o Holt-Oram syndrome
 - ASD and upper extremity anomalies
 - Autosomal dominant pattern of inheritance
 - o Trisomv 21
 - Associated with ostium primum defects
 - Other syndromes
 - Familial ASD associated with progressive AV block □ Autosomal dominant pattern of inheritance
- Associated abnormalities
 - Mitral valve abnormalities
 - Double-orifice mitral valve
 - □ 2% of ostium primum defects
 - Right upper lobe partial anomalous pulmonary venous return
 - Strongest association with sinus venosus ASD

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Usually asymptomatic in early life
 - Some patients may be symptomatic
 - □ Exertional dyspnea
 - □ Fatigue
 - □ Recurrent respiratory infections
 - □ Congestive heart failure
 - Typically becomes symptomatic with advancing age
 - 90% of patients with ASD are symptomatic by age 40
 - Exertional dyspnea
 - Fatigue

- Palpitations
- Heart failure
- Pulmonary artery hypertension
 - Dyspnea on exertion, fatigue, syncope, chest pain
- Eisenmenger syndrome
 - Symptoms related to polycythemia
 - Headache, fatigue, and marked dyspnea

Demographics

- Sex
 - o F:M = 2:1
- Epidemiology
 - o 10% of all congenital cardiac anomalies
 - Most common congenital cardiac anomaly in adults

Natural History & Prognosis

- 20% close spontaneously during 1st year of life
- Spontaneous closure in adulthood is unlikely
- 1% become symptomatic during 1st year of life 0.1% mortality
- ASD may result in pulmonary artery hypertension • May be reversible if treated early
 - Development of Eisenmenger syndrome
 - Reversal of left-to-right shunt
- 25% lifetime mortality if unrepaired

Treatment

- Medical therapy
- Limited to atrial arrhythmias and volume overload
- Surgical repair
 - Indications: Right ventricular overload, pulmonary flow:systemic flow > 1.5
 - Contraindications: Pulmonary flow:systemic flow < 0.7, severe pulmonary artery hypertension
 - Open repair with extracorporeal support most common
 - Direct closure and patch repair
 - o Minimally invasive approaches
 - Types
 - □ Limited thoracotomy
 - □ Hemisternotomy
 - □ Submammary approach
 - No difference in morbidity and mortality
- Percutaneous transcatheter therapy
 - Use of atrial septal occluder device
 - Small ostium secundum defects most amenable
 - Success rates approach 96%
 - Fewer complications and decreased hospitalization time compared to surgical repair

DIAGNOSTIC CHECKLIST

Consider

• ASD in setting of normal cardiac silhouette and shunt vascularity on chest radiography

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Atrial Septal Defect





(Left) Axial cardiac gated CTA demonstrates a small defect \square in the interatrial septum, consistent with an ASD. Cardiac gated CTA not only enables direct visualization of an ASD, but may also provide information regarding the direction and extent of the intracardiac shunt. (Right) Axial cine MR demonstrates a sinus venosus defect **→**. ASD accounts for approximately 10% of all congenital cardiac anomalies, but is the most common congenital cardiac anomaly diagnosed in adults.





(Left) PA chest radiograph of a patient with a treated ASD shows an atrial septal occluder device in the anatomic location of the interatrial septum 之. (Right) Lateral chest radiograph of the same patient confirms the location of the occluder device in the interatrial septum 🔁 Atrial septal occluder devices are placed percutaneously and are associated with fewer complications and decreased hospitalization time when compared to surgical repair.





(Left) Axial CECT of a patient with a history of ASD and subsequent repair shows an atrial septal occluder device in the interatrial septum 🖂 Small ostium secundum ASDs are most amenable to percutaneous transcatheter therapy, as in this case. (Right) Graphic shows placement of an atrial septal occluder introduced into the right atrium via inferior vena cava approach. The device is expanded within the ASD 🛃 . Its double-disc morphology secures it in place with resultant closure.

KEY FACTS

TERMINOLOGY

• Ventricular septal defect (VSD)

IMAGING

- Radiography
 - Chest radiographs may be normal with small defects
 - Cardiac enlargement with larger defects
 - Left atrial enlargement: Distinguishes VSD and patent ductus arteriosus (PDA) from atrial septal defect (ASD)
 - Aortic arch normal in size: Distinguishes VSD from PDA
 - Enlarged pulmonary vasculature
 - Findings of pulmonary artery hypertension
- **CT and MR**: Direct visualization of VSD
- MR
 - Ventricular volume, mass, function
 - Shunt volume and direction
 - o Valvular function
 - Pressure gradients across valves

TOP DIFFERENTIAL DIAGNOSES

- Atrial septal defect
- Patent ductus arteriosus
- Pulmonary artery hypertension

PATHOLOGY

• Most commonly congenital in etiology

CLINICAL ISSUES

- Patients with small defects may be asymptomatic
- Small VSDs typically close spontaneously
- Large VSDs require surgical correction
- Defects may result in pulmonary artery hypertension and Eisenmenger syndrome
- Treatment
 - Medical management of congestive heart failure and Eisenmenger syndrome
 - Surgical management: Closure and percutaneous device occlusion

(Left) Axial cardiac gated CTA demonstrates a defect 🔁 within the high aspect of the interventricular septum, which allows communication between the left and the right ventricles. (Right) Axial GRE MR of the same patient shows the defect \supseteq , which is consistent with a perimembranous type of ventricular septal defect. Perimembranous ventricular septal defects are the most common types of ventricular septal defect, and account for approximately 75% of cases.





(Left) Lateral chest radiograph of the same patient demonstrates enlargement of the left atrium \blacksquare , which extends posteriorly and produces mass effect on the anterior aspect of the tracheobronchial tree. (Right) Sagittal reformatted image from a cardiac gated CTA shows a supracristal ventricular septal defect 🔁 Ventricular septal defects account for approximately 20% of congenital cardiac anomalies.





Abbreviations

• Ventricular septal defect (VSD)

IMAGING

General Features

- Best diagnostic clue
 - Enlarged left atrium and ventricle and enlarged pulmonary vasculature on chest radiography
- Location
 - o Perimembranous (75%)
 - o Inlet (8-10%)
 - Muscular or trabecular (5-10%)
 - Outlet or supracristal (5%)
- Morphology
 - o Multiple defects may occur
 - More common in muscular or trabecular septum

Radiographic Findings

- Radiography
 - Chest radiographs may be normal in patients with small defects
 - Medium-sized defects
 - Mild enlargement of cardiac silhouette
 - Enlarged pulmonary vasculature

• Large defects

- Enlarged cardiac silhouette
 - □ Left ventricle
 - Left atrial enlargement: Distinguishes VSD and patent ductus arteriosus (PDA) from atrial septal defect (ASD)
- Aortic arch normal in size: Distinguishes VSD from PDA
- Enlarged pulmonary vasculature
- ± pulmonary edema
- ± pleural effusions
- Pulmonary artery hypertension (PAH)
 - Enlarged pulmonary trunk
 - Enlarged central pulmonary arteries
 - Pruning of peripheral pulmonary artery branches
 - Enlarged right ventricle

CT Findings

- Cardiac gated CTA
 - $\circ~$ Direct visualization of VSD
 - o Determination of direction and extent of shunting

MR Findings

- Phase contrast and cine MR
 - o Ventricular volume
 - Ventricular mass, ventricular function
 - Shunt volume and direction
 - o Valvular function
 - Pressure gradients across valves

Echocardiographic Findings

- Echocardiogram
 - Most VSDs identified and characterized by echocardiography
 - Direct visualization of defects

- Color Doppler
 - Helpful in detecting small defects
 - Direction and velocity of shunting

Angiographic Findings

- Small defects
 - Normal right heart pressures
 - o Normal pulmonary vascular resistance
- Large defects
 - Pulmonary flow > systemic flow
 - o Pulmonary and systemic systolic pressures equivalent
- Eisenmenger syndrome
 - Elevated systolic and diastolic pulmonary artery pressures
 - Desaturation of blood in left ventricle
 - Minimal left-to-right shunting

Imaging Recommendations

- Best imaging tool
 - Cardiac gated CTA or MR to visualize defect

DIFFERENTIAL DIAGNOSIS

Atrial Septal Defect

- Left-to-right intracardiac shunt
- Left atrium typically normal in size: Distinguishes ASD from VSD
- Enlarged pulmonary vasculature
- Pulmonary edema
- PAH
 - Enlarged pulmonary trunk and central pulmonary arteries
 - Pruning of peripheral pulmonary artery branches
 - Enlarged right ventricle

Patent Ductus Arteriosus

- Persistent connection between descending thoracic aorta and proximal left pulmonary artery
- Left-to-right intracardiac shunt
- Enlarged cardiac silhouette
 - Left atrium and left ventricle
- Enlarged aortic arch: Distinguishes PDA from VSD
- Enlarged pulmonary vasculature
- Pulmonary edema
- PAH
 - Enlarged pulmonary trunk and central pulmonary arteries
 - Pruning of peripheral pulmonary artery branches
 - Enlarged right ventricle

Pulmonary Artery Hypertension

- Enlarged pulmonary trunk and central pulmonary arteries
- CTA: Enlarged pulmonary trunk > 30 mm
- Imaging
- CECT
 - Enlarged pulmonary arteries: Pulmonary trunk > 30 mm, right interlobar pulmonary artery > 16 mm in men; > 14 mm in women
 - Peripheral pulmonary artery narrowing/dilatation
 - Pulmonary artery filling defects, intra-arterial soft tissue
 - Hypertrophied bronchial arteries

- o CT/HRCT
 - Centrilobular nodules, mosaic attenuation, interlobular septal thickening, bronchiectasis, subpleural peripheral opacities, ground-glass opacities, diffuse solid nodules

PATHOLOGY

General Features

• Etiology

Developmental Abnor<u>malities</u>

- Congenital
 - Most common etiology
 - 4 types described by location along interventricular septum
- Traumatic
 - Blunt or penetrating chest trauma
- Postmyocardial infarction
- Associated abnormalities
 - Tetralogy of Fallot, truncus arteriosus, double outlet right ventricle
 - Coarctation and tricuspid atresia less common

Staging, Grading, & Classification

- Interventricular septum divided into 2 parts
- Membranous part
 - Divided into atrioventricular and interventricular parts by apical attachment of septal leaflet of tricuspid valve
- o Muscular part
 - Divided into inlet, trabecular, and outlet components

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Patients with small defects may be asymptomatic
 - "Maladie de Roger"
 - Small, asymptomatic VSD
 - Development of symptoms depends on several factors
 - Size and location
 - Pulmonary arterial pressure
 - Left ventricular outflow resistance
 - Most common symptoms
 - Shortness of breath
 - Tachypnea
 - Failure to thrive
 - Tachycardia
 - o PAH
 - Dyspnea on exertion
 - Fatigue
 - Syncope
 - Chest pain
 - Eisenmenger syndrome
 - Symptoms related to polycythemia
 - Headache
 - Fatigue
 - Marked dyspnea
 - Physical examination
 - Holo- or pansystolic murmur
- Other signs/symptoms
 - Recurrent respiratory infections

Demographics

- Sex
 - o M:F = 1:1
- Epidemiology
 - o VSD accounts for 20% of all congenital cardiac anomalies
 - o Incidence: 2-6 of every 1,000 live births

Natural History & Prognosis

- Defects that spontaneously close or decrease in size early in life usually require no treatment
- Small VSDs typically close spontaneously
 Inlet VSDs rarely close spontaneously
- Large VSDs require surgical correction
- May result in PAH
 - May be reversible if treated early
 - Development of Eisenmenger syndrome
 - Reversal of left-to-right shunt

Treatment

- Medical management
 - Treatment of congestive heart failure
 - Diuretics
 - Afterload reduction
 - Treatment of Eisenmenger syndrome
 - Partial exchange transfusion
 - Endocarditis prophylaxis
 - Treatment of recurrent respiratory infections
- Surgical management
 - Pulmonary artery banding
 - Dilatable banding of pulmonary trunk ± branch vessels
 - May enable postponement of surgery
 - Constriction of VSD may be seen
 - Surgical closure
 - Indications
 - □ Symptomatic patients
 - □ Large defects
 - Elevated pulmonary vascular resistance
 - Minimally invasive surgical closure
 - Typically for perimembranous VSD
 - Percutaneous transcatheter device occlusion
 - Use of septal occluder device
 - Typically for perimembranous VSD
 - Complications
 - Complete heart block
 - Aortic regurgitation
 - Tricuspid regurgitation

DIAGNOSTIC CHECKLIST

Consider

• VSD in patient with left atrial and ventricular enlargement and prominent pulmonary vasculature on chest radiography

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Ventricular Septal Defect





(Left) Axial CECT demonstrates a small linear defect 🔁 within the interventricular septum that extends between the left and right ventricles, consistent with a small ventricular septal defect. (Right) Coronal CECT of the same patient demonstrates the small ventricular septal defect 🖂 Although routine chest CT may demonstrate ventricular septal defects, cardiac gated CTA can provide additional information regarding direction and extent of intracardiac shunting.





(Left) Axial cardiac gated CTA shows communication between the ventricles in the high aspect of the interventricular septum 🖂, consistent with a perimembranous type of ventricular septal defect, which is the most common type. (Right) PA chest radiograph of a patient with a history of ventricular septal defect demonstrates the presence of a septal occluder device \supseteq at the expected position of the defect between the right and left ventricles. Note that the heart is normal in size.





(Left) Lateral chest radiograph of the same patient shows the location of the occluder device Percutaneous transcatheter device occlusion is typically performed for management of perimembranous ventricular septal defects. (Right) Axial CECT of a patient with a history of prior surgical repair of a ventricular septal defect shows surgical sutures at the site of $closure \supseteq$. Indications for surgical closure of ventricular septal defect include symptoms, large defects, and elevated pulmonary vascular resistance.

KEY FACTS

TERMINOLOGY

- Bicuspid aortic valve (BAV)
- Bicuspid aortopathy
- BAV syndrome

IMAGING

- Radiography: Ascending aorta dilation: Contour abnormality of right cardiomediastinal silhouette
- **CT** and **MR** better than echocardiography for aortic measurement

TOP DIFFERENTIAL DIAGNOSES

- Aortic stenosis in tricuspid aortic valve
 3 leaflets and triangular systolic aperture
- Marfan syndrome
 - Effacement of sinotubular junction
- Aortic aneurysm
 - More common in aortic arch and descending aorta

PATHOLOGY

- Type 1 (~ 80%): Fusion of right and left coronary cusps (anterior-posterior BAV)
- Type 2 (~ 20%): Fusion of right and noncoronary cusps (right-left BAV)

CLINICAL ISSUES

- Type 1 BAV
 - Normal aortic shape and ↑ aortic root dimensions
 - Associated with aortic coarctation and less aortic valve pathology
 - o M:F = 2.7:1
- Type 2 BAV
 - More rapid progression of valvular disfunction, ascending aortic dilatation, larger arch diameters
 - ↑ prevalence of myxomatous mitral valve disease
 M:F = 1.3:1
- Aortic reconstruction when diameter > 4.5 cm

(Left) Graphic shows the morphologic features of the different types of bicuspid aortic valve. Approximately 80% are type 1, and 20% are type 2. Type 3 is very uncommon. (Right) Short-axis SSFP cardiac MR of a patient with type 1 bicuspid aortic valve without raphe shows a fish-mouth aperture \square of the aortic valve during systole. In this case, no significant stenosis is appreciated, and both coronary arteries arose from the anterior coronary sinus that resulted from fusion of the right and left coronary sinuses.





(Left) PA chest radiograph of a patient with bicuspid aortic valve shows an aneurysm of the ascending aorta that produces a characteristic contour abnormality of the superior right cardiomediastinal border 🔁 and represents the dilated aorta. This finding can also be seen in other etiologies of ascending aortic aneurysm, such as Marfan syndrome and atherosclerosis. (Right) Lateral chest radiograph of the same patient demonstrates filling of the retrosternal space 🔁 related to a dilated ascending aorta.





Abbreviations

• Bicuspid aortic valve (BAV)

Synonyms

- Bicuspid aortopathy
- BAV syndrome

Definitions

• Aortic valve with only 2 leaflets, usually of unequal size; fusion of 2 cusps forming ridge (raphe)

IMAGING

General Features

- Best diagnostic clue
 - Ascending aortic aneurysm on chest radiography of young patient without Marfan syndrome

Radiographic Findings

- Indirect findings
 - Visualization of calcified raphe is diagnostic but difficult to ascertain
 - Ascending aortic aneurysm: Contour abnormality of right cardiomediastinal silhouette

CT Findings

- CTA
 - **Calcifications** confined to raphe and base of cusps (commissures)
 - Often accurately differentiates between bicuspid and tricuspid aortic valves
 - Optimally assessed with cardiac gating and multiplanar reformations
 - BAV without raphe identified on diastolic short axis reformations
 - BAV with raphe better identified on systolic short axis (i.e., fish-mouth appearance)
 - Normal tricuspid valve has triangular aperture
 - Planimetry during mid systole (maximum aperture) allows for grading of aortic stenosis
- Cardiac gated CTA
 - Useful for assessment of preoperative coronary artery morphology

MR Findings

- Cardiac gated MR as accurate as echocardiography and CTA for morphologic diagnosis (including planimetry)
- Allows calculation of additional functional parameters in aortic stenosis
 - e.g., peak velocity
- Determination and quantification of aortic regurgitation
- Promising 4-dimensional MR evaluation can assess flow patterns

Echocardiographic Findings

- Specificity 96%, sensitivity 78%, accuracy 93%
- 2 cusps and 2 commissures on short axis
- Cusp redundancy and eccentric valve closure
- Single coaptation line between cusps during diastole
- May be obscured by severe fibrosis or calcification; falsenegative results may be produced by prominent raphe

Imaging Recommendations

Best imaging tool

- Echocardiography
- American College of Cardiology (ACC)/American Heart Association (AHA) follow-up recommendations
 - Echocardiographic follow-up
 - If sinuses of Valsalva, sinotubular junction, and ascending aorta are not well visualized, consider CT or MR
 - Follow-up intervals
 - Every year for severe stenosis or severe regurgitation
 - Every 1 or 2 years for moderate aortic stenosis or moderate aortic regurgitation
 - Every 3-5 years for mild aortic stenosis or mild aortic regurgitation
 - Every year if aortic root > 4 cm

DIFFERENTIAL DIAGNOSIS

Aortic Stenosis in Tricuspid Aortic Valve

- 3 leaflets and triangular systolic aperture
- Difficult to differentiate in heavily calcified and stenotic aortic valves
- Calcification typically extends to commissure

Marfan Syndrome

- Dilatation of ascending aorta with tricuspid aortic valve
- Effacement of sinotubular junction

Aortic Aneurysm

- More common in aortic arch and descending thoracic aorta
- Often associated with extensive atherosclerotic plaques

PATHOLOGY

General Features

- Etiology
 - Etiologies of aneurysm formation
 - Hemodynamic hypothesis
 - Orientation of systolic jet in BAV may lead to differential distribution of wall stress and remodeling of vessel wall
 - Abnormal systolic helical flow
 - □ Type 2 BAV more prone to significant aortic stenosis
 - Congenital hypothesis: Intrinsic congenital disorder of vascular connective tissue
- Genetics
- Exact genetic cause and inheritance pattern remain unknown
- Familial or hereditary BAV described in 10-30% of individuals
- Mutation in *NOTCH1* causes cardiac abnormalities, including BAV with severe calcifications
- Disruption of expression of fibroblast growth factor 8 in pharyngeal arch ectoderm and endoderm leads to BAV and other vascular abnormalities
- Associated with Turner syndrome and Loeys-Dietz syndrome

Associated abnormalities

- Aortic coarctation
 - BAV present in 50% of cases of coarctation

- Hypoplastic left heart syndrome
- Interrupted aortic arch: BAV present in 27%
- Aortic dilatation (20-85%)
- Intracranial arterial aneurysms (10%)

Staging, Grading, & Classification

- BAV leaflet morphology
 - Type 1 (~ 80%): Fusion of right and left coronary cusps (anterior-posterior BAV)
 - Without raphe (20.2%)
 - With raphe (59.1%)
 - Type 2 (~ 20%): Fusion of right and noncoronary cusps (right-left BAV)
 - Without raphe (9.3%)
 - With raphe (10.1%)
 - Type 3: Fusion of noncoronary and left coronary cusps
 Without raphe (0.5%)

• Morphology of aortic root

- Normal (type N)
 - Diameter sinuses of Valsalva > diameter sinotubular junction; diameter sinuses of Valsalva ≥ diameter mid ascending aorta
 - More common in type 1 BAV
- Ascending aortic dilatation (type A)
 - Diameter sinuses of Valsalva > diameter sinotubular junction; diameter sinuses of Valsalva < diameter mid ascending aorta
 - More common in type 2 BAV
- Effacement of sinotubular junction (type E)
 - Diameter sinuses of Valsalva ≤ diameter sinotubular junction
 - Infrequent in patients with dilated ascending aorta in BAV
 - Common in patients with dilated ascending aorta in Marfan syndrome

Gross Pathologic & Surgical Features

- Calcification increases with age; largely confined to raphe
- Left coronary artery dominance more common in BAV
- Short left main coronary artery
- Asymmetric leaflet size more prone to develop rapid calcification
- Unicuspid or quadricuspid aortic valves are rare

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic until aortic stenosis develops (2nd decade)
 - Aortic ejection click ± ejection systolic murmur
 - Aortic stenosis or regurgitation
 - Incidence of aortic stenosis: 15-71%
 - Incidence of aortic regurgitation: 1.3-3%
 - Angina, syncope, and heart failure: Peak incidence in 5th-6th decades
 - o Aortic dissection (9x risk): Chest pain
 - Incidence: 5%

- Aortic aneurysm (80x greater risk than general population)
 - − ↑ risk of dissection and rupture
- Infective endocarditis
 - Incidence 9.5-40%
- Sudden death
- Clinical profile
 - Type 1 BAV
 - Normal aortic shape and \uparrow aortic root dimensions
 - Associated with aortic coarctation and less aortic valve pathology
 - Type 2 BAV
 - Associated with more rapid progression of valve disfunction (i.e., aortic stenosis and regurgitation), ascending aortic dilatation, larger arch diameters
 ↑ prevalence of myxomatous mitral valve disease
 - Type 3 BAV: Uncommon

Demographics

- Age
 - Symptoms and complications of BAV stenosis increase with age
- Sex
 - Type 1 BAV (M:F = 2.7:1)
 - o Type 2 BAV (M:F = 1.3:1)
- Epidemiology
 - Most common congenital heart disease (0.5-2% of general population)
 - Most common reason for aortic valve replacement
 - o 50% of all adults with aortic stenosis have BAV

Treatment

• Close follow-up; ascending aortic reconstruction when diameter > 4.5 cm

DIAGNOSTIC CHECKLIST

Consider

- Ascending aortic aneurysms in young patients are common in Marfan syndrome and BAV
- Chest radiography is insensitive for detection of ascending aortic aneurysm
- Echocardiography: Standard initial evaluation with high sensitivity and specificity
- CT and MR
 - Helpful for assessment of complications
 - Consider cardiac gating if actual assessment of aortic valve required

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Bicuspid Aortic Valve





(Left) Short-axis cardiac CTA during diastole shows a type 1 bicuspid aortic valve without raphe. Early calcification along the commissures \supseteq eventually results in aortic stenosis. (Right) Composite image with axial (left) and oblique sagittal (right) cardiac CTA of the same patient shows ascending aorta dilatation 🔁 and preservation of the sinotubular junction 🛃 (type A morphology). Patients with type 1 bicuspid aortic valve tend toward a preserved ascending aortic shape (type N morphology) with larger sinuses of Valsalva.





(Left) Short-axis cardiac CTA MIP reformatted image of a patient with type 1 bicuspid aortic valve with raphe during mid diastole shows normal aperture of the aortic valve and a raphe \implies . (Right) Composite image with short-(left) and long- (right) axis cardiac CTA of a patient with type 2 bicuspid aortic valve without raphe \blacksquare shows the left coronary artery 🔁 arising from the left coronary sinus and dilatation of the ascending aorta 🔁 with effacement of the sinotubular junction 乏 (aortic type E morphology).





(Left) Short-axis MRA after intravenous gadolinium injection shows a bicuspid aortic valve type 2 without a raphe and dilatation of the coronary sinuses. (Right) Posterior 3D reformation from C+ MRA of the same patient shows dilatation of the ascending aorta and the aortic arch with preservation of the sinotubular junction \blacksquare (aortic type A morphology). *Type 2 bicuspid aortic valve* exhibits a female predominance, larger aortic arch dimensions, and myxomatous mitral valve disease.

Pulmonic Stenosis

KEY FACTS

TERMINOLOGY

- Pulmonic stenosis (PS)
- Lesion resulting in obstruction of right ventricular outflow tract (RVOT)

IMAGING

- **Radiography**: Enlargement of pulmonary trunk and left pulmonary artery
- CT
 - Poststenotic dilation of pulmonary trunk and left pulmonary artery
 - Thickened, immobile valve leaflets ± calcification
 - o Small valvular annulus
 - Pericardial calcification involving aorta and pulmonary trunk may rarely produce acquired PS
- MR
 - Determination of presence and extent of PS
 - Doming or windsock appearance of pulmonic valve
 - Narrowing of valve orifice

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary artery hypertension
- Idiopathic dilatation of pulmonary trunk
- Proximal interruption of pulmonary artery

PATHOLOGY

- Majority of cases are congenital in etiology
- Acquired: Rheumatic heart disease, carcinoid syndrome, infective endocarditis
- Severity of PS determined by pressure gradient across pulmonic valve or pulmonic valve area

CLINICAL ISSUES

- Treatment
 - Trivial and mild PS: Observation and endocarditis prophylaxis prior to surgical procedures
 - Moderate and severe PS: Balloon valvuloplasty or surgical valvotomy

(Left) Axial CECT of a patient with congenital pulmonic valve stenosis demonstrates dilatation of the pulmonary $trunk \supseteq$ and left pulmonary artery \square , which are the most common abnormalities identified on imaging studies. (Right) Coronal CECT of the same patient shows thickening of the pulmonic valve leaflets *⊡*. Although thickening and calcification of the valve leaflets are most reliably identified on cardiac gated CTA, these findings may be visible on routine chest CT, as in this case.





(Left) Oblique sagittal RVOT SSFP cardiac MR shows a focal region of signal dephasing 🗩 arising from the pulmonic valve, consistent with severe pulmonic stenosis. Thickening of the pulmonic valve leaflets D is also noted. Patients with moderate and severe pulmonic stenosis are typically treated with balloon valvuloplasty or surgical valvulotomy. (Right) Graphic shows the morphologic features of pulmonic stenosis characterized by diffuse pulmonic valve leaflet thickening \supseteq and marked valve orifice stenosis (insert).





Pulmonic Stenosis

TERMINOLOGY

Abbreviations

• Pulmonic stenosis (PS)

Definitions

• Lesion resulting in obstruction of right ventricular outflow tract (RVOT) + poststenotic dilatation of pulmonary trunk and left pulmonary artery

IMAGING

General Features

- Best diagnostic clue
- Enlarged pulmonary trunk and left pulmonary arteryLocation
 - o Valvular (90%)
 - o Subvalvular
 - o Supravalvular

Radiographic Findings

- Radiography
 - Most common abnormality is enlarged pulmonary trunk
 - Convexity along left mediastinal border inferior to aortic arch
 - Enlarged left pulmonary artery may be present
 - Right ventricular enlargement

CT Findings

- CECT
 - Poststenotic dilatation of pulmonary trunk and left pulmonary artery
 - Right ventricular enlargement
 - o Thickened valve leaflets ± calcification
 - Focal pericardial calcification involving aorta and pulmonary trunk reported as unusual cause of acquired PS
- Cardiac gated CTA
 - Thickened, immobile valve leaflets
 - May exhibit calcification
 - o Small valvular annulus
 - Hypoplasia of supravalvular pulmonary trunk may be present

MR Findings

- MRA
- Enlarged pulmonary trunk and left pulmonary artery
- MR cine
 - Evaluation of pulmonic valve morphology
 - Thickening ± fusion of valve leaflets
 - Narrowing of valve orifice
 - Doming or windsock appearance of pulmonic valve
- Phase contrast imaging
 - Determination of presence and extent of PS
 - Determination of volume flow rates across pulmonic valve

Echocardiographic Findings

- Echocardiogram
 - Thickening of valve leaflets

- Restricted systolic motion and reduced mobility of valve leaflets
- o Doming or windsock appearance of pulmonic valve
- Poststenotic dilatation of pulmonary artery
- Color Doppler
 - o Systolic high-velocity flow jet in pulmonary outflow tract

Angiographic Findings

- Conventional
 - Not indicated in mild or moderate PS
 Patients with severe PS usually undergo cardiac catheterization for confirmatory pressure assessment
 Concomitant balloon valvuloplasty may be performed
 - Useful for evaluating morphology of pulmonary outflow tract, pulmonary arteries, and right ventricle

DIFFERENTIAL DIAGNOSIS

Pulmonary Artery Hypertension (PAH)

- Enlarged pulmonary trunk and central pulmonary arteries
- CTA: Enlarged pulmonary trunk > 30 mm
- HRCT
 - Pre-capillary etiologies
 - Emphysema
 - Fibrosis
 - Honeycomb lung
 - Post-capillary etiologies
 - Centrilobular ground-glass nodules
 - Pulmonary edema
 - Pleural effusions
 - Chronic PAH
 - Patchy ground-glass opacities
- Pre-capillary etiologies
 - Chronic pulmonary emboli,
 - Congenital left-to-right shunts,
 - Idiopathic PAH
- Post-capillary etiologies
 - Left heart failure and mitral stenosis

Idiopathic Dilation of Pulmonary Trunk

- Congenital dilatation of pulmonary trunk ± involvement of left and right pulmonary arteries
- Pulmonary and cardiac causes of pulmonary artery enlargement must be excluded
- Normal pressures in pulmonary artery and right ventricle
- Enlarged pulmonary artery may appear as rounded opacity along left mediastinal border
 - o May mimic mediastinal mass

Proximal Interruption of Pulmonary Artery

- Failed development of proximal pulmonary artery
- Small ipsilateral lung and hilum on chest radiography
- Absence of pulmonary artery on CT
- Visualization of ipsilateral collateral systemic and bronchial arteries
- Mosaic attenuation may be seen on HRCT

Aberrant Left Pulmonary Artery

- a.k.a. pulmonary artery sling
- Congenital anomaly in which left pulmonary artery arises from right pulmonary artery

- Forms "sling" around trachea as it passes between trachea and esophagus
- May be associated with abnormalities of tracheobronchial tree and cardiovascular system
- May appear as nodular opacity projecting between trachea anteriorly and esophagus posteriorly on lateral chest radiographs
- CT and MR useful for definitive diagnosis

PATHOLOGY

General Features

- Etiology
 - Congenital
 - Most common etiology of PS
 - Isolated in 80% of cases
 - Additional forms of congenital heart disease present in 20% of cases
 - Acquired
 - Rheumatic heart disease
 - □ Associated with mitral and aortic valvular disease
 - Carcinoid syndrome
 - □ Associated with tricuspid valvular disease
 - Infective endocarditis
- Genetics
 - Generally considered to be multifactorial in origin
 - Familial forms have been described
 - May be associated with genetic disorders
 - Valvular PS
 - □ Noonan syndrome
 - Supravalvular PS
 - Congenital rubella syndrome
 - □ Williams syndrome
- Associated abnormalities
 - Atrial septal defect (ASD)
 - Ventricular septal defect (VSD)
 - Patent foramen ovale (PFO)
 - Tetralogy of Fallot

Staging, Grading, & Classification

- Severity classification by pressure gradient across pulmonic valve
 - Trivial stenosis (gradient < 25 mm Hg)
 - Mild stenosis (gradient 25-50 mm Hg)
 - Moderate stenosis (gradient 50-80 mm Hg)
 - Severe stenosis (gradient > 80 mm Hg)
- Severity classification by pulmonic valve area
 - o Normal: 2.5-4.0 cm²
 - o Mild PS: < 1 cm²
 - Severe PS: < 0.5 cm²

Gross Pathologic & Surgical Features

- Thickening of valve leaflets • Calcification may be present
- Partial fusion of commissures
- Valve is typically dome-shaped or conical in configuration
- Narrowing of central orifice

Microscopic Features

• Thickening of valve leaflets

• Dysplastic valves may be composed of myxomatous tissue: Present in 10-15% of patients with valvular PS

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Presentation depends on severity of symptoms
 - Mild PS: Typically asymptomatic
 - Moderate or severe PS
 - □ Signs and symptoms of systemic venous congestion
 - □ Mimics heart failure
- Other signs/symptoms
 - Cyanosis in setting of concomitant PFO or ASD

Demographics

- Age
- Age of presentation depends on severity of obstruction
- Sex
 - o M:F = 1:1
- Epidemiology
 - Represents 10% of all congenital cardiac defects
 - o 8-12% of all congenital cardiac defects in children
 - Isolated PS with intact ventricular septum is 2nd most common defect

Natural History & Prognosis

- Severity of stenosis determines morbidity and mortality
 - Mild to moderate PS is usually well tolerated
 - Severe PS
 - Decreased cardiac output,
 - Right ventricular hypertrophy
 - Heart failure
 - Cyanosis may develop

Treatment

- Trivial and mild PS: Observation and endocarditis prophylaxis prior to surgical procedures
- Moderate and severe PS: Balloon valvuloplasty or surgical valvotomy
 - Mild pulmonic regurgitation and right ventricular dilatation may develop following valvuloplasty

DIAGNOSTIC CHECKLIST

Consider

 PS in patients with pulmonary trunk and left pulmonary artery enlargement

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Pulmonic Stenosis





(Left) PA chest radiograph of a patient with congenital pulmonic valve stenosis demonstrates marked enlargement of the pulmonary $trunk \supseteq$ and left pulmonary artery 🔁. (Right) Axial CECT of the same patient shows marked enlargement of the pulmonary trunk \supseteq and left pulmonary artery 🔁, representing post-stenotic dilatation distal to the site of stenosis. These findings are typically identifiable on both radiography and crosssectional imaging.





(Left) Axial CECT of a patient with congenital pulmonic valve stenosis shows marked thickening of the pulmonic valve leaflets 🔂 Although valve thickening and calcification may be visible on routine CT, gated examinations employing CT or MR are necessary to assess valve mobility. (Right) Axial CECT of the same patient demonstrates marked thickening of the wall of the right ventricular outflow tract $\overline{\supseteq}$, which may be seen on CT or MR.





(Left) Sagittal RVOT magnitude MR shows linear hypointensity 🔁 arising from the pulmonic valve, consistent with severe pulmonic stenosis. Severity of pulmonic stenosis may be classified according to the pressure gradient across the pulmonic valve or the pulmonic valve area. (Right) Oblique axial "black blood" FSE STIR MR through the pulmonary trunk demonstrates thickening of a leaflet \blacksquare of the pulmonic valve and right ventricular hypertrophy 🛃 secondary to pulmonic stenosis.

Heterotaxy

KEY FACTS

TERMINOLOGY

• Heterotaxy: Abnormal arrangement of thoraco-abdominal organs across left-right axis: Isomerism of atrial appendages

IMAGING

- Best clue: Cardiac apex contralateral to gastric bubble
- 2 classic forms, but much overlap
 - o Right isomerism: Bilateral right-sidedness (asplenia)
 - o Left isomerism: Bilateral left-sidedness (polysplenia)
- Radiography: Chest radiograph useful as preliminary survey; assessment of central tracheobronchial tree
 Bilateral hyparterial/eparterial bronchi: Reliable predictor
- Bilateral hyparterial/eparterial bronchi: Reliable predictor of isomerism
- **CT**: Characterization of atrial appendage morphology and visceral situs abnormalities
- Echocardiography and MR: Evaluation of cardiac chamber anomalies
- **Upper GI series**: Infants with heterotaxy for exclusion of intestinal malrotation

TOP DIFFERENTIAL DIAGNOSES

- Situs inversus
- Mislabeled images

CLINICAL ISSUES

• Long-term prognosis usually determined by severity of cardiovascular anomalies

DIAGNOSTIC CHECKLIST

- Classification schemes
 - "Heterotaxy syndrome" followed by description of specific anatomy in parentheses
 - Van Praagh segmental method
- Consider heterotaxy syndrome with left isomerism in asymptomatic or minimally symptomatic patient with radiographic findings of bilateral hyparterial bronchi and azygos continuation of inferior vena cava
- Atrial appendage differentiation is often difficult; alternatively, rely on tracheobronchial morphology

(Left) PA chest radiograph of a patient with heterotaxy syndrome demonstrates an abnormal right mediastinal interface 🛃 due to azygos continuation of the inferior vena cava. Note bilateral hyparterial bronchi 🔁, consistent with left isomerism. (Right) Lateral chest radiograph of the same patient shows absence of the normal inferior vena cava interface ➡. This is a common finding in heterotaxy, typically associated with left isomerism. The minor fissure is also absent, consistent with bilateral bilobed lungs.





(Left) Composite image of the same patient with axial CECT shows an enlarged azygos $arch \blacksquare$ (top) and dilatation of the azygos vein 🛃 (bottom). Azygos continuation of the inferior vena cava is a common finding in heterotaxy syndrome. (Right) Coronal CECT of the same patient shows bilateral hyparterial bronchi. The upper lobe bronchi arise below the respective pulmonary arteries \blacksquare , consistent with left isomerism. The enlarged azygos arch 🔁 is consistent with azygos continuation of the inferior vena cava.





Heterotaxy

TERMINOLOGY

Synonyms

- Isomerism of atrial appendages
- Situs ambiguus (term discouraged; known anatomic location)

Definitions

- Situs
 - Position of cardiac atria and viscera relative to midlineIndependent of cardiac apex position
- Situs solitus
 - Normal position of cardiac atria and viscera
- Situs inversus
 - Mirror image of normal position
- Isomerism
 - Equal parts (bilateral left- or right-sidedness)
- Heterotaxy
 - Abnormal arrangement of thoraco-abdominal organs across left-right axis
- Cardiac position
 - Refers to global location of heart in chest
 - Left (levoposition), midline (mesoposition), right (dextroposition)
- Levocardia and dextrocardia: Location of cardiac apex
 - Levoversion: Situs inversus with levocardia
 - o Dextroversion: Situs solitus with dextrocardia

IMAGING

General Features

- Best diagnostic clue
 - Suspect heterotaxy if cardiac apex is contralateral to gastric bubble

Radiographic Findings

- Tracheobronchial morphology (hyparterial or eparterial bronchi): Reliable predictor of isomerism in absence of optimal imaging of atrial morphology
- Cardiac apex may be ipsilateral or contralateral to gastric bubble
 - Levocardia or dextrocardia
- Dilated azygos vein from azygos continuation of inferior vena cava
- Lateral chest radiograph may or may not show absence of inferior vena cava interface

CT Findings

• Situs solitus

- Right side: Systemic atrium, trilobed lung, eparterial bronchus, liver
- Left side: Pulmonary atrium, bilobed lung, hyparterial bronchus, aorta, cardiac apex, single spleen, gastric bubble
- Situs inversus
 - Left side: Systemic atrium, trilobed lung, eparterial bronchus, liver
 - Right side: Pulmonary atrium, bilobed lung, hyparterial bronchus, aorta, cardiac apex, single spleen, stomach
- Heterotaxy
 - 2 classic forms: Asplenia and polysplenia; inconsistent features

• Right isomerism (classically asplenia)

– Bilateral right atrial appendages

- Triangular/pyramidal shape with broad base, crista terminalis, pectinate muscles extend to atrioventricular junction
- Absent coronary sinus
- Bilateral minor fissures
- Bilateral trilobed lungs
- Bilateral eparterial bronchi: Upper lobe bronchus above ipsilateral pulmonary artery
- o Left isomerism (classically polysplenia)
 - Bilateral left atrial appendages
 - Narrow base, tubular shape, pectinate muscles confined to appendage
 - Presence of coronary sinus
 - No minor fissures
 - Bilateral bilobed lungs
 - Bilateral hyparterial bronchi: Upper lobe bronchus below ipsilateral pulmonary artery
 - Interrupted inferior vena cava with azygos/hemiazygos continuation
- Midline transverse liver, discordant location of stomach and cardiac apex

MR Findings

- Excellent modality to evaluate patients with heterotaxy; no ionizing radiation
- Direct evaluation of atrial morphology (situs)
- Evaluation of other congenital heart disease

Fluoroscopic Findings

- Upper Gl
 - o Malrotation
 - Frequent finding in heterotaxy
 - Displacement of duodenal/jejunal junction below duodenal bulb

Echocardiographic Findings

• Diagnosis and characterization of cardiovascular anomalies

Imaging Recommendations

- Best imaging tool
 - Chest radiography useful as preliminary survey
 - CT for characterization of visceral situs abnormalities
 - Echocardiography and MR for evaluation of cardiovascular anomalies
 - Upper GI series in infant with heterotaxy to exclude intestinal malrotation

DIFFERENTIAL DIAGNOSIS

Situs Inversus

- Complete reversal of thoraco-abdominal organs
- Congenital heart disease in 3-5%
- Kartagener syndrome (20%)
 - Structural abnormality of cilia
 - Bronchiectasis, chronic sinusitis, situs inversus

Mislabeled Images

- Most common cause of misinterpretation
- Confirm accuracy of image labeling with technologists prior to diagnosis of situs abnormalities

PATHOLOGY

General Features

Genetics

- Most occur sporadically
- Evidence of both autosomal and X-linked inheritance; likely multifactorial
- Associated abnormalities

Heterotaxy

- Classic asplenia and polysplenia categories misleading
- Extensive overlap of abnormalities
 - □ Discordance in > 20% of patients with heterotaxy
- Right isomerism (asplenia)
 - More severe (cyanotic) congenital heart disease:
 Atrioventricular canal, transposition of great arteries, total anomalous pulmonary venous return, single ventricle, double outlet right ventricle
 - 🗆 Right aortic arch, dextrocardia
 - Midline liver and gallbladder
 - Gastrointestinal malrotation
- Left isomerism (polysplenia)
 - Less severe congenital heart disease: Left-to-right shunt (atrial septal defect, ventricular septal defect), partial anomalous pulmonary venous return, transposition of great arteries
 - Interrupted inferior vena cava with azygos/hemiazygos continuation
 - Biliary atresia
 - Midline liver and gallbladder
 - Gastrointestinal malrotation
 - Truncated pancreas

Staging, Grading, & Classification

- "Heterotaxy syndrome" followed by description of specific anatomy in parentheses
 - Example: Heterotaxy syndrome (bilateral trilobed lungs, dextrocardia, asplenia)
- Van Praagh segmental approach to congenital heart disease
 - o 3-step approach
 - (1) Determination of viscero-atrial situs: S (solitus), I (inversus), A (ambiguus)
 - (2) Determination of ventricular loop orientation: D (dextro; normal), L (levo; reversed)
 - (3) Determination of great vessel orientation: S (situs), I (inverted), D-transposition of great arteries, Ltransposition of great arteries
 - Segmental analysis coded with 3 letters, that address each of 3 steps (e.g., normal would be S, D, S)
 - Atrioventricular and ventriculoarterial connections, and other malformations also reported

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Range: Severe cardiac anomalies in infants to asymptomatic adults
- Midgut volvulus due to malrotation in heterotaxyOther signs/symptoms
 - Asplenia: Howell-Jolly bodies on blood smear

Demographics

- Age
 - Right isomerism likely to manifest in infancy due to severe congenital heart disease
 - Left isomerism may be incidental finding in adult
- Epidemiology
 - o Heterotaxy: 1/10,000 live births
 - o Situs inversus: 0.01%

Natural History & Prognosis

- Asplenia: Immunosuppressed for encapsulated bacteria
- Long-term prognosis usually determined by cardiac defects
 - Incidence of congenital heart disease
 - o Situs solitus: < 1%
 - Situs solitus + dextrocardia (dextroversion): 95%
 - Situs inversus: 3-5%
 - Situs inversus + levocardia (levoversion): 99%
 - o Left isomerism: 90%
 - o Right isomerism: 99%

Treatment

- Surgical repair of cardiac anomalies
- Prophylactic Ladd procedure to prevent midgut volvulus is controversial
- Prophylactic antibiotics for asplenia
- Pneumococcal vaccination for asplenia

DIAGNOSTIC CHECKLIST

Consider

 Heterotaxy syndrome with polysplenia in asymptomatic or minimally symptomatic patient with radiographic findings of bilateral hyparterial bronchi and azygos continuation of inferior vena cava

Image Interpretation Pearls

- Discordance between cardiac apex and abdominal situs suggests congenital heart disease
- Visceroatrial concordance rule
 - Liver should be ipsilateral to right atrium
 - Stomach should be ipsilateral to left atrium, but not to degree seen with liver and right atrium
- Atrial appendage differentiation often difficult; use tracheobronchial morphology

Reporting Tips

- Classification schemes of asplenia and polysplenia discouraged due to extensive overlap
- Alternative schemes
 - "Heterotaxy syndrome" followed by description of specific anatomy in parentheses
 - Example: Heterotaxy syndrome (bilateral trilobed lungs, dextrocardia, asplenia)
 - o Van Praagh segmental method

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Heterotaxy





(Left) PA chest radiograph shows bilateral hyparterial bronchi 🔁 and azygos $continuation \blacksquare of the inferior$ vena cava, cardiomegaly, and pulmonary artery enlargement. (Right) Horizontal long-axis (4chamber) bright blood cine MR of the same patient shows azygos continuation 🔁 of the inferior vena cava and bilateral atrial enlargement. A spin dephasing jet 🗾 is present in the right atrium due to a small atrial septal defect. Patients with heterotaxy have an increased incidence of congenital heart disease.





(Left) PA chest radiograph of an asymptomatic patient demonstrates discordance of the cardiac apex and the gastric bubble ⊇, highly indicative of heterotaxy syndrome. Note enlarged azygos arch ⊇ from azygos continuation of the inferior vena cava. (Right) Axial CECT of the same patient shows a midline liver ⊇ with the major hepatic lobe on the left, a right-sided stomach ⊇, polysplenia ⊇, and azygos continuation ⊡ of the inferior vena cava.





(Left) PA chest radiograph shows a right eparterial bronchus 🛃 and a left hyparterial bronchus \square , consistent with normal situs. Note enlargement of the azygos arch 🖘 and mild cardiomegaly. (Right) Axial CECT of the same patient shows polysplenia \square and azygos 🔁 and hemiazygos 乏 continuation of the inferior vena cava. Azygos continuation is frequently associated with polysplenia, but the presence of polysplenia in the abdomen does not necessarily denote left isomerism in the chest.

KEY FACTS

TERMINOLOGY

• Congenital absence of pericardium; may be partial or complete

IMAGING

Radiography

- Lung interposition between pulmonary trunk and aortic arch
- Lung interposition between left hemidiaphragm and base of heart
- Conspicuous left atrial appendage
- Leftward shift of cardiac silhouette
- CT: Leftward shift and rotation of heart
 - Absence of visible pericardium in affected region
- MR: Absence of hypointense pericardial line
 Excessive mobility of myocardium
 - Large difference in heart volume between end-systole and end-diastole in affected patients

TOP DIFFERENTIAL DIAGNOSES

- Pericardial cyst
- Pericardial effusion
- Loculated pleural effusion
- Left ventricular aneurysm

PATHOLOGY

• Interruption of vascular supply to developing pericardium during embryogenesis

CLINICAL ISSUES

- Most complete defects are clinically insignificant
- Subtype of partial absence (foramen-type defects) may be lethal
- Treatment: Surgical closure or enlargement of defect

DIAGNOSTIC CHECKLIST

• Consider absence of pericardium in cases of interposition of lung between pulmonary trunk and aortic arch

(Left) Sagittal graphic shows herniation of the left atrial $appendage \square through a$ partial pericardial defect. While usually an incidental finding, the herniated structures may strangulate. (Right) Axial CECT demonstrates complete shift of the heart into the left hemithorax. No visible pericardium is present. Leftward shift and rotation of the heart and absence of a visible pericardium in the affected region are characteristic findings of congenital absence of the pericardium.





(Left) PA chest radiograph of a patient with partial absence of the pericardium shows the cardiac silhouette shifted to the left ("Snoopy's nose") and a small amount of lung interposed between the aortic arch \square and the pulmonary trunk 🖂 (Right) Axial CECT of the same patient demonstrates interposition of the lung \supseteq between the pulmonary trunk 🔁 and the ascending thoracic aorta 🔁. A left minor fissure is incidentally identified.





Definitions

• Congenital absence of pericardium; may be partial or complete

IMAGING

General Features

- Location
 - Partial defects usually occur along left lateral ventricular wall

Radiographic Findings

- Radiography
 - Lung interposition between pulmonary trunk and aortic arch
 - Lung interposition between left hemidiaphragm and base of heart
 - Leftward shift of cardiac silhouette ("Snoopy's nose")
 - Classically described in complete absence of pericardium
 - May not be seen in younger patients with complete absence
 - May also be seen in partial absence of left pericardium
 - **Conspicuous left atrial appendage** ("Snoopy's ear")
 - Common in partial absence of left pericardium

CT Findings

- NECT
 - Lung interposition between pulmonary trunk and ascending aorta
 - Leftward shift and rotation of heart
 - Absence of visible pericardium in affected region

MR Findings

- Absence of hypointense pericardial line
- Excessive myocardium mobility
- Large difference in heart volume between end-systole and end-diastole in affected patients

Echocardiographic Findings

- Echocardiogram
 - Enlarged left atrial appendage
 - Heart hypermobility
 - Abnormal ventricular septal motion
 - Swinging heart motion

Imaging Recommendations

- Best imaging tool
 - CT and MR findings are diagnostic

DIFFERENTIAL DIAGNOSIS

Pericardial Cyst

- Cardiophrenic angle mass abutting heart
- Imperceptible cyst wall
- Water-attenuation content on CT
- Fluid signal intensity content on MR

Pericardial Effusion

- Globular symmetric enlargement of cardiopericardial silhouette on frontal chest radiography: Water bottle sign
- > 2-mm water density stripe between retrosternal and subepicardial fat on lateral chest radiography
 Fat pad sign, Oreo cookie sign

Loculated Pleural Effusion

- Typically separate from uninvolved pericardium
- Typically water attenuation on CT

Left Ventricular Aneurysm

- Rare complication of myocardial infarction
- ± calcification

PATHOLOGY

General Features

- Etiology
 - Interruption of vascular supply to developing pericardium during embryogenesis
- Associated abnormalities
 - Atrial septal defect, patent ductus arteriosus, mitral valve stenosis, tetralogy of Fallot

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Complete absence: Usually asymptomatic
 - Partial absence: Nonexertional paroxysmal chest pain, tachycardia, palpitations

Demographics

- Epidemiology
 - Prevalence: 0.002-0.004%

Natural History & Prognosis

- Most complete defects are clinically insignificant
- Subtype of partial absence may be lethal
 - Foramen-type defects may result in herniation of left atrial appendage or left ventricle that results in myocardial strangulation

Treatment

- Surgical
 - Closure of pericardial defect, enlargement of pericardial defect to prevent cardiac strangulation, pericardiectomy, pericardioplasty

DIAGNOSTIC CHECKLIST

Consider

• Absence of pericardium when there is lung interposition between the pulmonary trunk and the aortic arch, particularly if associated with cardiac leftward shift

- Fadl SA et al: Comprehensive review of pericardial diseases using different imaging modalities. Int J Cardiovasc Imaging. 36(5):947-69, 2020
- Lopez D et al: Congenital absence of the pericardium. Prog Cardiovasc Dis. 59(4):398-406, 2017
- Parmar YJ et al: Congenital abnormalities of the pericardium. Cardiol Clin. 35(4):601-14, 2017

Poland Syndrome

KEY FACTS

TERMINOLOGY

- Definition
 - Pectoral aplasia-syndactyly syndrome
 - Congenital unilateral partial or total absence of pectoralis major muscle

IMAGING

- Radiography
 - Unilateral hyperlucency
 - Absence of normal axillary fold on affected side
 - Rib deformities that range from hypoplasia to aplasia (60%)
- CT/MR
 - Absence or hypoplasia of pectoral girdle musculature
- Associated abnormalities
 - Hypoplasia of affected hand
 - Hypoplastic middle phalanx
 - Rib deformities

TOP DIFFERENTIAL DIAGNOSES

- Technical factors and artifacts
- Swyer-James-MacLeod syndrome
- Radical mastectomy/prosthesis
- Chest wall soft tissue mass

CLINICAL ISSUES

- Asymptomatic cosmetic deformity
- Reported increased incidence of leukemia, non-Hodgkin lymphoma, lung cancer, breast cancer, leiomyosarcoma

DIAGNOSTIC CHECKLIST

- Consider conditions involving lung parenchyma, airway, pulmonary vasculature, pleural space, chest wall, and technical factors in patients with unilateral hyperlucent hemithorax
- Evaluate patients with Poland syndrome for occult lung cancer (reported increased incidence)

(Left) AP chest radiograph of a 64-year-old man shows asymmetric hyperlucency of the right hemithorax in comparison to the left. The finding is subtle and nonspecific and could be easily overlooked. (Right) Axial CECT of the same patient shows complete asymmetric hypoplasia of the right pectoralis major and minor musculature ⊇, which are characteristic findings of Poland syndrome.





(Left) Axial NECT of a patient who presented with pneumonia 🔁 shows complete absence of the right pectoralis musculature \supseteq , consistent with Poland syndrome. CT and MR are sensitive imaging modalities for assessment of chest wall abnormalities. (Right) Coronal NECT of a 63-year-old man with Poland syndrome shows complete hypoplasia of the right pectoralis major and minor musculature 🖂. Note a left-sided rib osteochondroma protruding into the thoracic cavity 🖂, an incidental finding.





Synonyms

• Pectoral aplasia-syndactyly syndrome

Definitions

• Congenital unilateral partial or total absence of pectoralis major muscle (rarely bilateral)

IMAGING

General Features

- Best diagnostic clue
 - Clinical suspicion: Syndactylism + deformity of pectoral muscle

Radiographic Findings

- Unilateral hyperlucency
- Absence of normal axillary fold on affected side
- Rib deformities that range from hypoplasia to aplasia (60%)
- Ipsilateral hand abnormalities that range from hypoplastic phalanges to syndactyly

CT Findings

- Unilateral absence or hypoplasia of pectoral girdle musculature
- Hypoplastic ipsilateral breast

Imaging Recommendations

- Best imaging tool
 - Chest radiography usually sufficient to document thoracic abnormality
 - CT and MR: More sensitive for identification soft tissue abnormalities

DIFFERENTIAL DIAGNOSIS

Technical Factors and Artifacts

- Malaligned grid
- Abnormal image density extending outside thorax

Swyer-James-MacLeod

- Unilateral hyperlucent lung
- Diminutive pulmonary vasculature in affected lung
- Mosaic attenuation on inspiratory CT and expiratory airtrapping on affected side

Radical Mastectomy/Prosthesis

- Absent or altered breast shadow
- Surgical clips in axilla (often)
- History of breast cancer

Chest Wall Soft Tissue Mass

• Increased, often asymmetric density of affected side

PATHOLOGY

General Features

- Etiology
 - Non-genetic congenital abnormality of unknown etiology
 - Most popular postulated theory: Chest wall abnormality secondary to unilateral subclavian artery hypoplasia

- Associated abnormalities
 - o Skeletal dysostoses affecting hand
 - Range from shortened phalanges to syndactyly
 - Pectus excavatum deformity
 - o Anomalies of ipsilateral upper limb

• Other anomalies

- Absence of pectoralis minor muscleHypoplasia of latissimus dorsi and serratus anterior
- muscles – Hypoplasia or aplasia of nipple &/or breast
- Lung herniation
- Hypoplasia of hemithorax &/or ribs
- Dextrocardia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic cosmetic deformity
- Other signs/symptoms
 - Reported increased incidence of leukemia, non-Hodgkin lymphoma, lung cancer, breast cancer, leiomyosarcoma

Demographics

- Sex
 - o M > F (3:1)
- Epidemiology
 - True incidence/prevalence difficult to predict
 - Variable between groups (male vs. female)
 - Prevalence: Ranges from 1/7,000 to 1/100,000 live births

Treatment

- Muscle flaps and breast implants: Correction of muscle deficiency and breast hypoplasia
- Chest wall reconstruction if thoracic skeleton involved
- Homologous preservation of costal cartilage: Improves chest wall stability
- Bone grafts or prosthetic mesh: Reconstruction of aplastic ribs

DIAGNOSTIC CHECKLIST

Consider

- Etiologies of unilateral hyperlucent hemithorax
- Conditions involving lung parenchyma, airway, pulmonary vasculature, pleural space, chest wall
 - In adult woman consider mastectomy
 - Exclude technical factors and artifacts

Image Interpretation Pearls

- Evaluate patients with Poland syndrome for occult lung cancer (reported increased incidence)
- Chest radiography, CT, and MR for identification of absent or hypoplastic ipsilateral ribs and scoliosis

- Parenti VG et al: Imaging findings in Möbius-Poland syndrome. Radiol Case Rep. 15(4):379-81, 2020
- Mak SM et al: Imaging of congenital chest wall deformities. Br J Radiol. 20150595, 2016
- Dillman JR et al: Expanding upon the unilateral hyperlucent hemithorax in children. Radiographics. 31(3):723-41, 2011

Pectus Deformity

KEY FACTS

TERMINOLOGY

- Pectus excavatum: Sternum depressed; anterior ribs protrude anterior to sternum
- Pectus carinatum: Anterior protrusion of sternum; congenital or acquired

IMAGING

- Right heart border frequently obscured; depressed sternum replaces aerated lung at right heart border
- Heart displaced to left and rotated (mitral configuration), may cause spurious cardiomegaly
- Degree of sternal depression best evaluated on lateral chest radiography

TOP DIFFERENTIAL DIAGNOSES

- Right middle lobe atelectasis
- Right middle lobe pneumonia
- Cardiophrenic angle mass

PATHOLOGY

- Pectus excavatum: Mitral valve prolapse (20-60%)
- Pectus carinatum: Cyanotic congenital heart disease

CLINICAL ISSUES

- Pectus excavatum and carinatum: Usually asymptomatic
- Pectus excavatum: 1 in 300-400 births; most common chest wall abnormality (90%)
- Family history of pectus deformity in 20-40% of cases
- Scoliosis in 21% of patients with pectus excavatum and in 11% of patients with pectus carinatum
- M:F = 4:1

DIAGNOSTIC CHECKLIST

- Consider pectus excavatum in asymptomatic patients with obscuration of right heart border on PA chest radiography
- Degree of sternal depression optimally appreciated on lateral chest radiography

(Left) PA chest radiograph of a 29-year-old woman with pectus excavatum shows obscuration of the right heart border 🔁, which can be misinterpreted as middle lobe pneumonia. Horizontal 🔁 posterior ribs and vertical/oblique orientation 🔁 of anterior ribs are characteristic associated findings. (Right) Lateral chest radiograph of the same patient shows no middle lobe consolidation, which confirms absence of pneumonia and optimally demonstrates the degree of posterior sternal depression 🖂





(Left) Lateral chest radiograph of a 59-year-old woman shows anterior sternal protrusion characteristic of pectus carinatum 🔁. Sagittal and coronal CT reformatted images are useful for evaluation of abnormalities of the sternum and costal cartilages. (Right) Axial CECT of a 59-year-old woman shows compression and displacement of the heart \supseteq by a depressed sternum 🖾. These findings correlate with obscuration of the right heart border on frontal chest radiography.





Synonyms

- Pectus excavatum: Funnel chest
- Pectus carinatum: Chicken breast or pouter pigeon breast

Definitions

- Pectus excavatum: Sternum depressed; anterior ribs protrude anterior to sternum
- Pectus carinatum: Anterior protrusion of sternum; congenital or acquired

IMAGING

Radiographic Findings

• Radiography

• Pectus excavatum

- Right heart border frequently obscured; depressed sternum replaces aerated lung at right heart border
- Horizontal posterior ribs and vertical oblique orientation of anterior ribs on frontal radiograph
- Heart displaced to left and rotated (mitral configuration), may cause spurious cardiomegaly
- Degree of sternal depression optimally visualized on lateral radiograph
- Pectus carinatum: 3 different types
 - Chondrogladiolar protrusion (chicken breast): Anterior displacement of sternum and symmetric concavity of costal cartilages (most common)
 - Lateral depression of ribs on one or both sides of sternum (frequently associated with Poland syndrome)
 - Chondromanubrial prominence (pouter pigeon breast): Upper anterior protrusion of manubrium and depression of sternal body (least common)

CT Findings

- Severity of defect quantified on CT or MR (Haller index)
 - "Haller index" = transverse thoracic diameter/AP thoracic diameter
 - o "Haller index" > 3.25 considered for surgical correction

DIFFERENTIAL DIAGNOSIS

Right Middle Lobe Atelectasis

- Obscuration of right heart border without cardiac displacement to left
- Other signs of volume loss

Right Middle Lobe Pneumonia

• Consolidation on lateral chest radiograph

Cardiophrenic Angle Mass

• Well-defined cardiophrenic mass

PATHOLOGY

General Features

- Etiology
 - Pathogenesis unclear
- Genetics
 - o Pectus excavatum: Familial history (40%)
 - o Pectus carinatum: Familial history (26%)

- Associated abnormalities
 - Musculoskeletal abnormalities: Marfan syndrome, Ehlers-Danlos syndrome, Noonan syndrome, osteogenesis imperfecta
 - o Scoliosis (15-20%)
 - Pectus excavatum: Mitral valve prolapse (20-60%); nontuberculous mycobacterial infection with predominant involvement of right middle lobe and lingula (Lady Windermere syndrome)
 - Pectus carinatum: Cyanotic congenital heart disease

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Pectus excavatum and carinatum: Usually asymptomaticOther signs/symptoms
 - Pectus excavatum and carinatum: Nonspecific chest or back pain
 - Pectus excavatum: Exercise-induced decreased respiratory reserve or pain along costal cartilages
 - Pectus excavatum: Occasionally, cardiac symptoms/signs (pulmonic murmur, mitral valve prolapse, Wolff-Parkinson-White syndrome)

Demographics

- Sex
- o M:F = 4:1
- Epidemiology
 - Family history of pectus deformity in 20-40% of cases
 - Pectus excavatum: 1 in 300-400 births; most common chest wall abnormality (90%)
 - Pectus carinatum: Less frequent by ratio of approximately 1:5; 5-7% of chest wall deformities

Natural History & Prognosis

• Scoliosis in 21% of patients with pectus excavatum and 11% of patients with pectus carinatum

Treatment

- Surgical correction
- o Haller index > 3.25
- Respiratory or cardiovascular regurgitationPsychosocial factors and cosmesis
- Nuss procedure is preferred surgical correction; 1-3 curved metal bars inserted behind sternum to push it to normal position

DIAGNOSTIC CHECKLIST

Consider

 Pectus excavatum in asymptomatic patient with obscuration of right heart border on PA radiography

Image Interpretation Pearls

• Degree of sternal depression optimally appreciated on lateral chest radiography

- Rodríguez-Granillo GA et al: Preoperative multimodality imaging of pectus excavatum: state of the art review and call for standardization. Eur J Radiol. 117:140-8, 2019
- Mak SM et al: Imaging of congenital chest wall deformities. Br J Radiol. 20150595, 2016

Kyphoscoliosis

KEY FACTS

TERMINOLOGY

• Complex 3-dimensional rotational curvature of spine

IMAGING

- Scoliosis: > 10° lateral deviation of spine from central axis
- Cobb angle: Scoliotic curve's angle
- Idiopathic kyphoscoliosis
 - Usually convex to right
 - o Most cases, no kyphosis (hypokyphosis)
 - Difficult chest radiographic interpretation in severe cases due to thoracic and cardiac rotation
- Neurofibromatosis type 1
 - Sharply angled at thoracolumbar junction
 - Lateral thoracic meningocele
 - Neurofibromas may extend into spinal canal
- Pott disease
 - Erosive scalloping of anterolateral vertebral bodies
 - Collapse of intervertebral disc space
 - o Angular kyphotic deformity and gibbus formation

- Ankylosing spondylitis
 - Kyphosis, squared vertebral bodies
 - Vertebral syndesmophytes, usually T9 to T12
- Mitral valve prolapse
 - o Idiopathic scoliosis (25%)
 - o Straight back syndrome (33%)

TOP DIFFERENTIAL DIAGNOSES

- Neurofibromatosis type 1
- Infectious spondylitis
- Neuromuscular etiology

CLINICAL ISSUES

- Restrictive lung disease
- Pulmonary artery hypertension; cor pulmonale
- Respiratory failure
- Treatment of scoliosis
- Observation, orthosis
- Surgical correction and stabilization

(Left) PA chest radiograph of a 51-year-old woman shows typical features of idiopathic scoliosis, which manifests as a right convex scoliosis ₽. The lateral chest radiograph (not shown) demonstrated hypokyphosis. (Right) PA chest radiograph of a 73-year-old woman status post thoracoplasty $\stackrel{\frown}{\Longrightarrow}$ for tuberculosis shows a right convex scoliosis \triangleright at the cervicothoracic spine that developed as a result of the chest wall surgery.





(Left) AP chest radiograph of a 63-year-old man with ankylosing spondylitis shows the typical bamboo spine ≥ deformity that results from spinal ankylosis. (Right) Sagittal NECT of a patient with ankylosing spondylitis shows typical findings of kyphosis, squared vertebral bodies ≥, syndesmophytes ≥, and spinal ankylosis.





- Abbreviations
- Neurofibromatosis type 1 (NF1)

Synonyms

- Scoliosis
- Kyphosis
- Gibbus deformity

Definitions

• Complex 3-dimensional rotational curvature of spine

IMAGING

General Features

- Best diagnostic clue
 - Abnormal spinal curvature on anteroposterior and lateral radiographs
- Location
 - Cervical and thoracic spine more commonly affected
- Size
 - Partial or entire spine involvement
- Morphology
 - o Scoliosis: > 10° lateral deviation of spine from central axis
 - **Cobb angle**: Scoliotic curve's angle
 - Calculated by selecting upper and lower end vertebrae in curve
 - Erecting perpendiculars to their transverse axes
 - At their point of intersection, angle is measured

Radiographic Findings

- Idiopathic kyphoscoliosis
- Usually convex to right
- o Most cases, no kyphosis (hypokyphosis)
- Chest radiograph difficult to interpret in severe cases because of rotation of thorax and heart
- Neurofibromatosis type 1 (von Recklinghausen disease)
 - Short-segment angular scoliosis
 - Kyphosis more pronounced than scoliosis
 - Involves 5 vertebrae or fewer in primary curve
 - Sharply angled at thoracolumbar junction
 - Intervertebral foramina enlargement
 - Lateral thoracic meningocele, neurofibromas that extend into spinal canal
 - Lateral thoracic meningocele
 - Herniation of meninges through intervertebral foramen
 - Kyphoscoliosis with meningocele on convex side
 - Round, well-defined, paravertebral mass
 - Right > left
 - Rib erosion and erosion of adjacent neural foramen
 - Multiple meningoceles in 10%
 - Vertebral body scalloping
 - Anterior, posterior, lateral
 - Wedge-shaped vertebrae
 - Hypoplastic or pressure remodeled pedicles
 - Transverse process spindling
 - o Spondylolisthesis, spinal clefts, osteolysis
 - o Unstable spine, leads to subluxation or dislocation

- Spinal fusion complicated by pseudoarthrosis, curve progression
- Inferior rib notching; twisted, ribbon-like upper ribs
- Pectus excavatum
- Infectious spondylitis: Kyphosis, paraspinal mass, bone destruction, disc space loss
- Pott disease (tuberculous spondylitis)
 - L1 vertebra corpus is most common site; 3 or more contiguous vertebrae
 - Erosive scalloping of anterolateral surfaces of vertebral bodies (gouge defect)
 - Collapse of intervertebral disc space
 - o Progressive vertebral collapse with anterior wedging
 - Angular kyphotic deformity and gibbus formation
 - o Paravertebral "cold" abscesses, may calcify
- Congenital: Hemivertebra, fused ribs; may lead to scoliosis
- Senile osteoporotic kyphosis: Compression fractures of multiple vertebrae and cortical thinning
- Ankylosing spondylitis
 - Kyphosis, squared vertebral bodies
 - o Vertebral syndesmophytes, usually T9 to T12
 - Interspinous ossification
 - Ossification of costotransverse joints
 - Manubriosternal joint erosion or fusion

CT Findings

- CECT
 - Lateral thoracic meningocele
 - Well-circumscribed, low-attenuation paravertebral masses
 - Peripheral rim enhancement may occur
 - CT myelography: Fills with intrathecal contrast
 - Neurofibromas
 - May show very low attenuation (10-20 HU)

MR Findings

- NF1
 - o Lateral meningoceles, dural ectasia
 - Shows cerebrospinal fluid content of meningoceles
 - o Neurofibromas
 - T1WI: Low to intermediate signal intensity; T1 C+ (enhance with contrast)
 - T2WI: Often heterogeneous high signal intensity regions due to myxoid tissue or cystic degeneration; central low signal intensity due to collagen and fibrous tissue

Echocardiographic Findings

- Echocardiogram
 - Mitral valve prolapse in idiopathic scoliosis (25%) and straight back syndrome (33%)

Imaging Recommendations

- Best imaging tool
 - Radiography: Serial imaging to assess for progression
 Assessment of skeletal maturity
 - Complex cases: MR or CT with multiplanar reconstructions
- Protocol advice
- Prococol advice
- Upright standing anteroposterior and lateral radiography, entire spine
 - Sitting radiography for patients who cannot stand
Kyphoscoliosis

- Supine radiography for patients who cannot sit
- Close surveillance during greatest growth (puberty, early adolescence)
- MR to detect peri/intraspinal abnormalities

DIFFERENTIAL DIAGNOSIS

Neurofibromatosis Type 1

• Stigmata of neurofibromatosis

Infectious Spondylitis

• Disc space involvement, vertebral destruction, sepsis

Neuromuscular Etiology

- Upper motor neuron lesions: Cerebral palsy, syringomyelia, spinal cord trauma
- Lower motor neuron lesions: Poliomyelitis, spinal muscular atrophy
- Myopathic conditions: Arthrogryposis, muscular dystrophy, other myopathies

Congenital

- Hemivertebrae, fused ribs, spina bifida, Klippel-Feil syndrome
- VATER complex (vertebral, anorectal, tracheal, esophageal, renal anomalies)

Post Thoracoplasty

• Chest wall deformity, surgical history

Radiation Treatment for Childhood Malignancy

• Hypoplasia of ipsilateral pedicles in radiation port

PATHOLOGY

General Features

- Etiology
 - Majority are idiopathic
- Genetics
 - Various diseases associated with scoliosis: Friedrich ataxia, Morquio syndrome, Ehlers-Danlos, Marfan syndrome, muscular dystrophy
 - o NF1: Autosomal dominant
- Associated abnormalities
 - Scoliosis associated with pectus excavatum or carinatum

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Most patients are symptom free; many discovered at school screening
 - Indications for CT or MR
 - Abnormal neurological examination
 - Painful scoliosis; neck pain and headache
 - Clinical signs of dysraphism; weakness, pes cavus, ataxia
 - Neuromuscular disease: Poor cough reflex
 - Susceptibility for pneumonia
- Cardiac symptoms
 - Pulmonic murmur, mitral valve prolapse, syncope, Wolff-Parkinson-White syndrome
 - o Ankylosing spondylitis: Aortic valve stenosis

- o NF1
 - Hypertension, aortic coarctation, coronary artery disease
 - Pulmonic valve stenosis, atrial septal defect, ventricular septal defect, hypertrophic cardiomyopathy
- Respiratory symptoms
 - Kyphoscoliosis
 - Decreased lung and chest wall compliance
 - Hypoventilation, hypoxic vasoconstriction, hypercapnia
 - Pulmonary artery hypertension; cor pulmonale
 - Restrictive lung disease, respiratory failure
 - o NF1
 - Interstitial lung disease, basilar predominance
 - Pulmonary artery hypertension
 - Upper lobe bullae, honeycombing, pneumothorax
 - Ankylosing spondylitis

Demographics

- Age
 - Age at presentation
 - Congenital
 - Infantile (< 3 years)
 - Juvenile (3-10 years)
 - Adolescent (> 10 years)
- Sex
 - o Idiopathic scoliosis: M:F = 1:4
- Epidemiology
 - Idiopathic scoliosis
 - Prevalence 1-3% for curves > 10°
 - 80% of severe cases are idiopathic
 - NF1 (50% of patients with kyphosis)
 - Neuromuscular diseases
 - 90% of males with Duchenne muscular dystrophy
 - 60% of patients with myelodysplasia
 - 20% of children with cerebral palsy

Natural History & Prognosis

- Most severe in nonambulatory patients; progression in neuromuscular disorders
- Juvenile idiopathic scoliosis: Nearly 90% of curves progress, almost 70% require surgery
- Longstanding severe kyphoscoliosis
 - Pulmonary artery hypertension
 - Respiratory failure associated with Cobb angle > 100°

Treatment

• Scoliosis: Observation, orthosis, surgical correction, stabilization

- Ishihara Y et al: Age-related progression of degenerative lumbar kyphoscoliosis: a retrospective study. Spine Surg Relat Res. 4(3):229-36, 2020
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- Grissom LE et al: Thoracic deformities and the growing lung. Semin Roentgenol. 33(2):199-208, 1998

Kyphoscoliosis





(Left) Coronal T2WI MR of a 20-year-old patient with neurofibromatosis type 1 shows dextroscoliosis that extends from T3 to T7 and right-sided lateral thoracic meningoceles 🕰. Meningoceles in this condition typically occur at the convex side of the scoliotic curve. (Right) Sagittal STIR MR of the same patient shows dural ectasia with posterior scalloping 🛃 of the T3 through T7 vertebral bodies, which are typical imaging features of patients with neurofibromatosis type 1.





(Left) Coronal CECT of a 30year-old patient with neurofibromatosis shows a large right paravertebral mass 🛃 that was proven to represent a neurofibroma. The lesion extended into the T7 neural foramen (not shown). Neurofibromas typically occur at the concave side of the scoliosis 🛃. (Right) PA chest radiograph of a 23-year-old man with Duchenne muscular dystrophy shows an S-shaped scoliosis \supseteq of the thoracic and lumbar spine, the result of muscular wasting.





(Left) Coronal NECT of a 29year-old woman with HIV infection and Pott disease shows bilateral large paravertebral soft tissue masses 🛃, lytic and sclerotic lesions at T8-T10, and compression deformity of T10 A. (Right) Sagittal NECT of the same patient shows disc space narrowing and gibbus deformity at the T9-T10 level \blacksquare and erosion of the anterior inferior endplate of T9 🔼, consistent with osteomyelitis and discitis. Percutaneous biopsy cultures grew Mycobacterium tuberculosis.

Morgagni Hernia

KEY FACTS

TERMINOLOGY

- Anterior diaphragmatic hernia
- Intrathoracic migration of abdominal contents via retrosternal defect

IMAGING

- Radiography
 - Well-defined right cardiophrenic angle mass ± air-filled bowel
 - o Lateral radiograph confirms retrosternal location
- CT
 - Hernia sac containing mesenteric vessels, fat ± bowel, viscera
 - o Coronal and sagittal images for optimal visualization
 - Assessment of complications
- MR
 - o Allows direct multiplanar imaging
 - Optimal resolution of diaphragm and defect

TOP DIFFERENTIAL DIAGNOSES

- Mediastinal fat (common)
- Cardiophrenic angle mass

PATHOLOGY

- Defect related to maldevelopment of septum transversum (precursor of diaphragm)
- Most defects small, contain only omental fat
- Herniated contents are covered by a pleuroperitoneal sac (> 90%)

CLINICAL ISSUES

- Typically asymptomatic
- Potential for incarceration or strangulation if hernia contains bowel

DIAGNOSTIC CHECKLIST

• Consider Morgagni hernia in patient with cardiophrenic mass containing bowel on radiography or omental fat with mesenteric vessels ± viscera on CT/MR

(Left) PA chest radiograph of a young adult woman with substernal chest pressure shows a large, smoothly marginated right cardiophrenic angle mass 🔁 that obscures the right heart border. (Right) Composite image with lateral chest radiograph (left) and sagittal NECT (right) of the same patient shows the retrosternal location of the mass \square , the diaphragmatic defect \blacksquare , and the herniated fat and mesenteric vessels \bowtie , consistent with Morgagni hernia.





(Left) Axial CECT of a patient with a large Morgagni hernia shows herniation of mesenteric fat, vessels \triangleright , and transverse colon \blacksquare into the cardiophrenic angle hernia. Large Morgagni hernias may produce mass effect on adjacent structures, in this case the heart. (Right) Coronal CECT of the same patient shows the large anterior, right-sided diaphragmatic defect 🔁 associated with superiorly herniated abdominal fat, vessels, and transverse colon 🔁. Surgical reduction of the hernia was performed in this case.





Synonyms

• Anterior diaphragmatic hernia

Definitions

- Malunion of septum transversum (embryologic central tendon of diaphragm) to anterior body wall
- Centered in Morgagni foramen (diaphragmatic defect in sternocostal triangle)
- Intrathoracic migration of abdominal contents via retrosternal defect

IMAGING

General Features

- Best diagnostic clue
 - Retrosternal diaphragmatic defect with hernia sac containing omental fat ± bowel
- Location
 - Retrosternal diaphragm
 - o ~90% right-sided, 5% left-sided, 5% bilateral

Radiographic Findings

- Radiography
 - Right cardiophrenic angle mass ± air-filled bowel
 - Smooth margin with lung, obscures heart border
 - Lateral view confirms retrosternal location

CT Findings

- Defect in retrosternal diaphragm
- Hernia sac containing mesenteric vessels, fat ± bowel, viscera
 - Most contain only omental fat
 - Other contents: Transverse colon (most common), liver, small bowel, stomach, kidney
- Coronal and sagittal reformatted images for optimal visualization of diaphragmatic defect
 - Abdominal vessels, omental/mesenteric fat, and organs within hernia
- With associated pericardial defect, hernia sac may protrude into pericardial space
- CECT for assessment of complications (incarceration, strangulation, perforation)

MR Findings

- Direct multiplanar imaging
- Single-shot, fast spin-echo with respiratory triggering to eliminate motion
- Improved resolution of diaphragm and defect (compared to CT)
- Signal characteristics depend on content of hernia sac
 Hyperintense on T1WI and T2WI due to fat content

Imaging Recommendations

Best imaging tool
 CT with multiplanar reformatted images or MR

DIFFERENTIAL DIAGNOSIS

- Mediastinal Fat
- Intact diaphragm
- Homogeneous fat density; no bowel content or vessels

Cardiophrenic Mass

- Pericardial cyst, mediastinal lipoma/liposarcoma, localized pleural disease, thymoma, lymphadenopathy
- Intact diaphragm

PATHOLOGY

General Features

- Etiology
 - Natural weakness in anteromedial diaphragm related to passage of superior epigastric vessels
 - Congenital defect secondary to maldevelopment of septum transversum (precursor of diaphragm)
 - Post-traumatic (uncommon)
 - Positive intra-abdominal pressure may drive abdominal contents (including viscera) into hernia sac

Gross Pathologic & Surgical Features

- Hernia contained by pleuroperitoneal sac (> 90%)
- Usually small, containing only omental fat

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - ~ 50% of affected adults are asymptomatic
 - Epigastric or retrosternal discomfort, bloating, dyspnea
- Other signs/symptoms
 - Abdominal pain: Incarceration/strangulation, infarction of herniated fat or bowel (10% of cases)

Demographics

- Age
 - Most cases are diagnosed in adults
 - o > 50% of congenital form diagnosed > 5 years of age
- Epidemiology
 - o Rare (2-10% of all congenital diaphragmatic hernias)o 70% in women

Natural History & Prognosis

- Herniated bowel conveys increased risk of strangulation/ischemia/perforation
- Herniation may progress with high intra-abdominal pressure (obesity, pregnancy, chronic cough, blunt trauma)

Treatment

• Surgical repair recommended, especially if hernia contains bowel (risk of strangulation)

DIAGNOSTIC CHECKLIST

Consider

• Morgagni hernia in patient with cardiophrenic mass containing bowel on radiography &/or fat and mesenteric vessels on CT/MR

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Bochdalek Hernia

KEY FACTS

TERMINOLOGY

• Intrathoracic herniation of abdominal/retroperitoneal contents via posterior diaphragmatic defect

IMAGING

- Radiography
 - Well-defined posterior basilar mass; obscures hemidiaphragm
 - Left-sided in 80%
- CT
 - Posterior diaphragmatic defect
 - $\circ~$ Identification of herniated retroperitoneal fat \pm viscera
 - Assessment of unusual complications (incarceration, strangulation, perforation)

• MR

- Excellent discernment of diaphragm muscle and defect
- Retroperitoneal fat: High signal intensity on T1WI and T2WI
- Best imaging tools: Multiplanar CT or MR

TOP DIFFERENTIAL DIAGNOSES

- Diaphragmatic eventration
- Paravertebral mass
- Diaphragmatic rupture
- Congenital diaphragmatic hernia

PATHOLOGY

- Herniation through remnant of developmental pleuroperitoneal canal
- No peritoneal membrane encases hernia sac

CLINICAL ISSUES

- Typically incidental finding in asymptomatic adult
 - More common in older adult subjects with chronic obstructive lung disease

DIAGNOSTIC CHECKLIST

• Consider Bochdalek hernia in asymptomatic adult with posterior basilar opacity that obscures hemidiaphragm on radiography

(Left) PA chest radiograph of an asymptomatic 45- year-old woman shows a well-defined left basilar opacity \boxtimes that obscures a portion of the left hemidiaphraam. (Right) Composite image with lateral chest radiograph (left) and sagittal NECT (right) of the same patient shows the posterior location of the abnormality 🛃, which corresponds to retroperitoneal fat 🔁 herniating through a left Bochdalek hernia. Note superior migration of retroperitoneal vessels 🛃 and the left kidney \implies toward the diaphragmatic defect.





(Left) Axial NECT of a patient with a Bochdalek hernia shows the posterior location of the diaphragmatic defect \blacksquare and fine linear opacities within the herniated fat compatible with retroperitoneal vessels \rightarrow . (Right) Composite image with sagittal NECT (left) and T2WI MR (right) shows a left Bochdalek hernia that contains retroperitoneal fat ▷ (high signal intensity on T1WI and T2WI MR) and vessel flow voids 🔁. Note superior displacement of the left kidney \triangleright and spleen \triangleright . (Courtesy L. Chelala, MD.)





Bochdalek Hernia

TERMINOLOGY

Synonyms

• Posterior diaphragmatic hernia

Definitions

- Bochdalek foramen: Posterior diaphragmatic defect
 Between lateral arcuate ligament and posterolateral 12th rib attachment
- Intrathoracic herniation of abdominal contents
 - Age, chronic obstructive pulmonary disease, and obesity may promote herniation

IMAGING

General Features

- Best diagnostic clue
 - Herniation of retroperitoneal fat through posterior diaphragmatic defect
- Location
 - Posterior diaphragm; lateral or medial
 - o 80% left-sided, 15% bilateral
- Size
- Variable; typically small
- Morphology
 - Contents: Typically retroperitoneal fat; larger defects may contain adrenal gland, kidney, bowel, stomach, spleen, pancreatic tail, liver

Radiographic Findings

- Posterior mass; obscures portion of hemidiaphragm
- Well-defined margins

CT Findings

- Posterior diaphragmatic defect
- Identification of herniated retroperitoneal fat ± viscera
- Assessment of unusual complications: Incarceration, strangulation, perforation

MR Findings

- Excellent discernment of diaphragm muscle and defect
- Retroperitoneal fat: High signal intensity on T1WI and T2WI

Imaging Recommendations

- Best imaging tool
 - Multiplanar CT or MR for optimal evaluation of diaphragmatic defect and herniated contents
 - Single-shot, fast spin-echo MR with respiratory triggering to eliminate motion

DIFFERENTIAL DIAGNOSIS

Diaphragmatic Eventration

- Thin but intact hemidiaphragm
- Most common on left; "scalloped" diaphragmatic contour

Paravertebral Mass

 Neurogenic neoplasm, lymphadenopathy, vertebral discitis/osteomyelitis, aneurysm, extramedullary hematopoiesis

Diaphragmatic Rupture

• Traumatic rupture from penetrating or blunt injury

- Penetrating injuries affect either hemidiaphragm; blunt trauma affects left > right
- Latent complications: Visceral herniation and strangulation

Congenital Diaphragmatic Hernia

- Partial agenesis of hemidiaphragm; neonates and infants
- Associations: Pulmonary hypoplasia, congenital heart disease; may be surgical emergency

PATHOLOGY

General Features

- Etiology
 - Abdominal content herniation via diaphragmatic defect (remnant of developmental pleuroperitoneal canal) ± weak muscle fibers in posterior lumbar-costal triangle
 - Contributory factors: ↑ intra-abdominal pressure (e.g., obesity, pregnancy, trauma)
- Associated abnormalities
 - Chronic obstructive pulmonary disease

Gross Pathologic & Surgical Features

- No peritoneal membrane encasing hernia sac (> 90%)
- Adhesions to adjacent pleural surface

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Typically asymptomatic; incidental finding
 - o Nonspecific chest pain or GI symptoms reported

Demographics

- Epidemiology
 - o 90% of congenital diaphragmatic hernias
 - Prevalence 6% in adults overall
 - Prevalence up to 20% at age 70 years

Natural History & Prognosis

- Usually of no clinical significance
 - More common in older adult patients and in those with chronic obstructive pulmonary disease
- Surgical reduction considered if herniated abdominal viscera (even if asymptomatic)

DIAGNOSTIC CHECKLIST

Consider

 Bochdalek hernia in asymptomatic adult with posterior basilar opacity that obscures hemidiaphragm on radiography

Image Interpretation Pearls

- Identification of posterior diaphragmatic defect and herniated retroperitoneal fat are diagnostic
 - Viscera, vessels help identify content as retroperitoneal

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Introduction

The airways are tubular structures that conduct air through their lumina, represent twenty-four generations of dichotomous branching, and are divided into large airways (trachea, bronchi) and small airways (bronchioles, terminal bronchioles, respiratory bronchioles, and alveolar ducts). The airways can also be functionally divided into three zones: (1) **Conductive** (air conduction only) consisting of the trachea, bronchi, and membranous bronchioles, (2) **transitional** (conductive and respiratory) composed of respiratory bronchioles and alveolar ducts, and (3) **respiratory** (respiratory only) consisting of alveoli and alveolar sacs.

Congenital, neoplastic, infectious, and inflammatory processes may involve the airways and may be categorized based on whether they involve the large or the small airways. Large airway diseases may manifest with airway narrowing, dilatation, &/or mural thickening. Small airway diseases include emphysema characterized by destruction of structures within the secondary pulmonary lobule and cellular and constrictive bronchiolitis.

Neoplasms

Lung cancer (squamous cell carcinoma and small cell carcinoma) may manifest as central neoplasms that produce an endoluminal airway lesion or extrinsic airway encasement &/or narrowing. Uncommon malignant airway neoplasms include **bronchial carcinoid**, **adenoid cystic carcinoma**, and mucoepidermoid carcinoma. Airway metastases may be the first manifestation of occult malignancy. Airway neoplasms may produce postobstructive atelectasis or pneumonia. Airway neoplasms may directly invade adjacent structures, may manifest as an endoluminal nodule or mass or may circumferentially encase and narrow the airway lumen. CT is the imaging modality of choice for assessment of airway neoplasms and allows evaluation of adjacent structures for identification of local invasion &/or lymphadenopathy. Volume-rendered techniques and virtual bronchoscopy may provide valuable information for surgical planning.

Morphologic Alterations of the Airway Lumen

Airway Narrowing

Saber-sheath trachea is associated with chronic obstructive pulmonary disease (COPD) and characterized by a decrease in the coronal tracheal diameter and an increase in the sagittal tracheal diameter.

Tracheal stenosis is typically acquired as a complication of endotracheal intubation and may be focal or diffuse. Congenital tracheal stenosis is rare, may be associated with other anomalies, and is typically seen in neonates and infants.

Tracheomalacia and **tracheobronchomalacia** are characterized by expiratory airway lumen collapse due to weakness of tracheal &/or bronchial cartilages and can be assessed with dynamic CT obtained during expiration.

Inflammatory conditions, such as **polyangiitis and granulomatosis**, **amyloidosis**, and **relapsing polychondritis**, may produce focal or diffuse tracheal wall thickening and may also involve the central bronchi.

A well-recognized form of bronchial stenosis is the **middle lobe syndrome** characterized by chronic middle lobe atelectasis from a variety of etiologies, including neoplasms, broncholiths, and chronic infectious and noninfectious inflammatory conditions.

Airway Dilatation

Bronchiectasis refers to irreversible bronchial dilatation and may be categorized and graded as cylindrical, varicose, or cystic (in increasing order of severity). Although it may be identified on radiography, it is optimally assessed on CT. Normal bronchial diameter generally equals the diameter of its adjacent paired pulmonary artery branch. Bronchial diameters larger than those of adjacent pulmonary arteries are consistent with bronchiectasis. Bronchiectasis may result from infectious or inflammatory processes and may be seen in association with the retractile effects of fibrosis (i.e., traction bronchiectasis). Other etiologies include fungal hypersensitivity, mucociliary clearance disorders, structural airway abnormalities, systemic diseases, and primary and secondary immunodeficiencies.

Small Airways Disease

Emphysema may be classified as centrilobular, paraseptal, or panlobular types. Noninvasive quantification of emphysema may be performed using visual quantification of disease severity as well as computer-assisted quantification. Identification of emphysema usually confirms a history of cigarette smoking, and affected patients are at an increased risk of primary lung cancer.

Cellular bronchiolitis manifests on CT as centrilobular nodules of soft tissue or ground-glass attenuation. It may be associated with tree-in-bud opacities (resembling the morphology of a budding tree) in which the linear component corresponds to the dilated centrilobular bronchiole impacted with mucus, fluid, or pus, while the nodular component corresponds to peribronchiolar inflammation. It is frequently secondary to infection or aspiration. Other etiologies include **respiratory bronchiolitis (RB)**, **respiratory bronchiolitisassociated interstitial lung disease (RB-ILD)**, hypersensitivity pneumonitis, follicular bronchiolitis, and diffuse panbronchiolitis.

Constrictive bronchiolitis is characterized by mosaic lung attenuation that manifests with geographic areas of alternating decreased and increased lung attenuation, characteristically accentuated on expiratory HRCT (air-trapping), and may be associated with bronchial dilatation and bronchial wall thickening. Constrictive bronchiolitis may be a manifestation of infectious, connective tissue, or inhalational lung diseases or as a complication of transplantation.

Summary

Airways diseases may exhibit a variety of indirect and direct imaging manifestations. Imaging diagnosis requires a systematic assessment of the large and small airways and careful characterization of the specific airway abnormalities seen on imaging. CT and HRCT are valuable tools in the imaging assessment of affected patients.

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Approach to Airways Disease

Airway Neoplasm



Tracheal Narrowing



(Left) Coronal CECT MinIP reformatted image of a patient with tracheal adenoid cystic carcinoma shows an irregular lobulated endotracheal mass 🔁 with mediastinal invasion and severe left lung atelectasis. (Right) Composite image with axial (left) and coronal (right) NECT shows coronal narrowing of the intrathoracic tracheal lumen and normal caliber of the extrathoracic trachea and central bronchi characteristic of saber-sheath trachea, a common cause of tracheal narrowing in patients with COPD.

Bronchiectasis



Emphysema

(Left) Axial NECT of a young woman with recurrent respiratory infections since childhood shows severe bilateral bronchiectasis, bronchial wall thickening, mucus plugs, and pulmonary mosaic attenuation. The patient was evaluated and diagnosed with IgA deficiency. (Right) Axial NECT shows centrilobular emphysema manifesting as multifocal lucencies with imperceptible walls 🔁 within the lobular cores of secondary pulmonary lobules. Characteristic central dot-like structures 🔁 represent lobular arteries.

Bronchiectasis



Small Airways Disease



(Left) Axial NECT of a patient with nontuberculous mycobacterial infection shows multifocal centrilobular nodules and tree-in-bud opacities rightarrow associated withbronchial wall thickening and characteristic middle lobe volume loss and bronchiectasis Axial NECT of a patient with constrictive bronchiolitis secondary to graft-vs.-host disease shows mosaic lung attenuation with areas of abnormal hyperlucent lung ⊇ adjacent to normal higher attenuation parenchyma 🔁 accentuated on expiration.

TERMINOLOGY

• Benign neoplasm composed of mesenchymal tissues of varying proportions

IMAGING

- Radiography
 - Postobstructive findings (most common): Atelectasis, consolidation, bronchiectasis
 - Endoluminal nodule in central airway
 - Occasionally normal
- CT
 - Focal endoluminal lesion in central airway
 - o Internal fat &/or calcification suggest diagnosis
 - Fat in endoluminal nodule only seen in airway hamartoma or lipoma
 - Postobstructive findings: Atelectasis, consolidation, bronchiectasis
 - Little or no uptake on FDG PET

TOP DIFFERENTIAL DIAGNOSES

- Squamous cell carcinoma
- Metastasis
- Lipoma
- Chondroma
- Carcinoid

CLINICAL ISSUES

- Age: 50-70 years
- Signs/symptoms
 - Asthma-like symptoms
 - o Cough, dyspnea, stridor, pneumonia
- Treatment: Bronchoscopic or surgical resection

DIAGNOSTIC CHECKLIST

- Airway hamartomas account for approximately 1.4-13% of all pulmonary hamartomas
- Consider airway hamartoma in patient with endoluminal nodule with intrinsic fat &/or calcification

(Left) PA chest radiograph of a patient with an endobronchial hamartoma shows left lower lobe atelectasis 🔁. Note bronchiectatic airways in the atelectatic left lower lobe, suggestive of chronic volume loss. (Right) Axial CECT of the same patient shows a left lower lobe endobronchial nodule 🔁 with macroscopic fat, surgically proven to represent an endobronchial hamartoma. Endobronchial lipoma could also be considered in the differential diagnosis, but would exhibit only fat attenuation on CT.





(Left) Composite image with axial NECT (left) and FDG PET (right) of a 79-year-old man shows a partially calcified left upper lobe endobronchial nodule 🔁 with intrinsic fat attenuation that did not exhibit significant FDG avidity 🔁. Endobronchial hamartoma was confirmed following endoscopic resection. (Right) Composite image with axial CECT in lung (left) and soft tissue (right) window shows a right lower lobe endobronchial nodule 🔁 with suggestion of intrinsic fat 🔁. Hamartoma was confirmed following surgical excision.





Synonyms

• Endobronchial hamartoma

Definitions

• Benign neoplasm comprised of mesenchymal tissues in varying proportions

IMAGING

General Features

- Best diagnostic clue
 - Indolent or slowly-growing endobronchial lesion with internal fat &/or calcification
- Location
- Central bronchus > trachea
- Size
 - Usually < 2 cm; larger lesions may completely obstruct airway
- Morphology
 - Smooth or lobular, sharply-marginated

Radiographic Findings

- Radiography
 - **Postobstructive effects** (most common manifestation)
 - Atelectasis, often lobar
 - Consolidation from post-obstructive pneumonia
 - Distal bronchiectasis in chronic airway obstructionEndoluminal nodule in central airway uncommonly
 - visualizedOccasionally normal

CT Findings

- NECT
 - Focal endoluminal lesion in central airway; typically solitary
 - o Internal fat &/or calcification suggests diagnosis
 - Fat in endoluminal nodule: Airway hamartoma or lipoma
 - Endobronchial hamartomas tend to contain more macroscopic fat than pulmonary hamartomas
 - Postobstructive effects
 - Atelectasis, often lobar
 - Consolidation, bronchiolitis, ground-glass opacity
 - Distal bronchiectasis with parenchymal destruction and fibrosis in cases of chronic obstruction
- PET
 - Typically little or no FDG uptake
 - Rarely FDG uptake > mediastinal blood pool, likely from chronic inflammation

MR Findings

Identification of intralesional fat is diagnostic
 ± T1- and T2-hyperintense foci of fat

Imaging Recommendations

- Best imaging tool
 - CT is imaging study of choice for assessment of endoluminal lesions

DIFFERENTIAL DIAGNOSIS

Squamous Cell Carcinoma

- Middle-aged/older patient with smoking history
- Endoluminal lesion with extraluminal growth and circumferential airway involvement
- Metastatic lymphadenopathy

Metastasis

- Endoluminal lesion of variable size; often multiple
- Hematogenous spread: Breast, colon, renal, thyroid, melanoma

Lipoma

• Fat-containing endoluminal lesion without soft tissue component

Chondroma

- Endoluminal lesion with calcification
- Calcification may also occur in malignant lesions

Bronchial Carcinoid

• Calcification in 25-30%, contrast enhancement

PATHOLOGY

General Features

- Etiology
- Benign neoplasm

Microscopic Features

- Multiple tissue elements
 - o Cartilage (most profuse), fat, bone

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asthma-like symptoms
 - Cough, dyspnea, stridor, pneumonia
 - Uncommonly asymptomatic

Demographics

- Age
 - o 50-70 years
- Sex
 - Reported M:F prevalence 2-4:1
 - Epidemiology
 - o Rare benign airway neoplasm
 - o 1.4-13% of all pulmonary hamartomas

Treatment

- Bronchoscopic resection if small
- Surgical resection may be required for large lesions

DIAGNOSTIC CHECKLIST

Consider

• Airway hamartoma in patient with endoluminal nodule with intrinsic fat &/or calcification

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TERMINOLOGY

- Airway nodules (papillomas) due to human papilloma virus (HPV) infection
- Invasive papillomatosis: Dissemination to lungs

IMAGING

- Airway wall thickening or nodularity
- Multiple pulmonary nodules/masses
 - Larger nodules more likely to cavitate
 - Seeding of posterior dependent lungs
- Growth rate
 - Most nodules grow slowly
 - Rapid growth suspicious for squamous cell carcinoma
- Complications
 - Squamous cell carcinoma
 - Secondary infection
 - Airway obstruction: Atelectasis, postobstructive pneumonia

TOP DIFFERENTIAL DIAGNOSES

- Tracheobronchopathia osteochondroplastica
- Granulomatosis with polyangiitis
- Tracheobronchial amyloidosis
- Relapsing polychondritis

PATHOLOGY

- Infection with HPV; types 6 and 11 most common
- Larynx most commonly affected
- Diagnosis made by laryngoscopy and biopsy

CLINICAL ISSUES

- Mild involvement may be asymptomatic
- Hoarseness due to laryngeal involvement
- May be mistaken for asthma when symptomatic
- Treatment
 - o Self-limited disease usually requires no treatment
 - Surgical and medical therapies for lesions causing airway obstruction

(Left) Graphic shows the morphologic features of invasive tracheobronchial papillomatosis with characteristic central airway nodules \square , peribronchovascular cavitary lesions 🔁, and scattered small solid nodules 🔁. (Right) Coronal 3D reformatted image of a patient with tracheobronchial papillomatosis shows irregular airway wall contours due to tracheal 🛃 papillomas. Central airway wall nodularity is a characteristic imaging feature.





(Left) Coronal NECT of a patient with tracheobronchial papillomatosis shows mid tracheal papillomas \square , multiple solid \ge and cavitary *▶* nodules, and tree-in-bud opacities 🛃. (Right) Axial NECT of a patient with longstanding solid 🖂 and cavitary lung nodules ラ due to papillomatosis demonstrates a new spiculated left lower lobe nodule 🔁. Subsequent biopsy revealed squamous cell lung cancer. Most pulmonary nodules in papillomatosis exhibit slow growth. Rapid growth raises suspicion for squamous cell carcinoma.





Synonyms

• Recurrent respiratory papillomatosis (RRP)

Definitions

- Airway nodules (papillomas) secondary to human papilloma virus (HPV) infection
- Upper > lower airways Invasive papillomatosis
 - Dissemination to lungs

IMAGING

General Features

- Best diagnostic clue
 - Thickening or nodularity of airway walls
 - Multiple solid and cavitary pulmonary nodules &/or masses
- Location
 - Larynx is most commonly affected site
 - Variable involvement of lower airways
 - □ 5-29% of cases
 - Invasive papillomatosis
 - Perihilar and central location in coronal plane
 - Posterior distribution in axial plane
- Size
 - o Invasive papillomatosis
 - Variable size
 - Most nodules 1-3 cm in diameter
- Morphology
 - Invasive papillomatosis
 - Smaller nodules usually solid
 - Larger nodules more likely to cavitate

Radiographic Findings

- Radiography
 - o Airways
 - Thickening &/or nodularity of airway walls
 May not be visible on radiography
 - Multiple pulmonary nodules &/or masses
 - May exhibit cavitation

CT Findings

- NECT
 - o Airways
 - Thickening or nodularity of airway walls
 Upper > lower airways
 No calcification
 - Solitary papillomas
 - Less common than multiple papillomas
 Typically located in lobar or segmental bronchi
 - Tree-in-bud opacities
 - Bronchiectasis
 - Recurrent infection
 - Airway obstruction

• Multiple pulmonary nodules

- Larger nodules more likely to cavitate
 Thin or thick and irregular cavity walls
- Posterior lung involvement may be related to gravity
 Represents seeding of dependent lung

- Nodules may communicate with adjacent airways
- Nodule growth manifestations
 - □ Ground-glass opacity
 - □ Consolidation
- Growth rate
 - $\hfill\square$ Most pulmonary nodules demonstrate slow growth
 - Rapid growth should raise suspicion for squamous cell carcinoma
 - □ Growth rate may increase during pregnancy
- Complications
 - Squamous cell carcinoma
 - Secondary infection
 - □ Cavitation with air-fluid levels
 - Atelectasis
 - Usually secondary to intraluminal papillomas
 - □ ± postobstructive pneumonia

Imaging Recommendations

- Best imaging tool
 - CT is optimal imaging modality for identification of airway nodules, lung evaluation for invasive papillomatosis, and identification of development of squamous cell carcinoma

DIFFERENTIAL DIAGNOSIS

Tracheobronchopathia Osteochondroplastica

- Multiple small airway nodules; ± calcification
- Affects anterolateral tracheal and proximal bronchial walls
- Spares posterior membranous airway wall
- Asymmetric airway stenosis

Granulomatosis With Polyangiitis

- Multiple cavitary pulmonary nodules or masses
- Subglottic stenosis
- Airway wall thickening

Tracheobronchial Amyloidosis

- Calcified or noncalcified submucosal nodules with narrowing of tracheal lumen
- Posterior membrane not spared

Relapsing Polychondritis

- Noncalcified diffuse mural thickening and luminal narrowing of trachea and mainstem bronchi
- Anterior and lateral tracheal walls; tracheal cartilage

Sarcoidosis

- Airway distortion/stenosis
- May lead to atelectasis
- Nodular thickening of airway wall
- Mosaic attenuation, expiratory air-trapping

Squamous Cell Carcinoma

- Most common lung cancer to cavitate
 Cavitation in 15% of cases
- Strongly associated with cigarette smoking
- Increased risk with invasive papillomatosis

Pulmonary Metastases

- Multifocal pulmonary nodules &/or masses
- Squamous cell carcinomas and sarcomas may cavitate
- Airways not necessarily involved

Septic Emboli

- Poorly-defined pulmonary nodules or masses
- Varying degrees of cavitation

PATHOLOGY

General Features

- Etiology
 - HPV infection of respiratory tract
 - Peripartum sexual transmission of HPV
 Risk factors: Firstborn child, vaginal delivery, mother < 20 years of age
 - HPV types 6 and 11 are most common
 - Any portion of respiratory tract may be affected
 - □ 95% of cases involve larynx
 - Solitary papillomas more common in middle-aged male smokers
 - Airway dissemination (invasive papillomatosis)
 - □ < 1% seed lung
 - □ Surgical manipulation of laryngeal papillomas increases risk of dissemination
 - Lung seeding usually apparent in children or young adults
- HPV infection
 - Cutaneous and genital warts
 - Tropism for keratinizing epithelium
 - o Cervical cancer

Gross Pathologic & Surgical Features

- Sessile or papillary lesions with vascular core lined by squamous epithelium
- Airway papillomas may be exophytic or endophytic
- Cauliflower-like shape

Microscopic Features

- Laryngeal and pulmonary lesions composed of squamous cells
- Cavities lined with squamous epithelium
 - Squamous epithelium may spread across airspaces via pores of Kohn

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Mild involvement may be asymptomatic
 - Hoarseness most common symptom due to laryngeal involvement
 - Wheezing and stridor may be mistaken for asthma
 - Other symptoms depend on size, number, and location of papillomas
 - Dyspnea, hemoptysis
 - Postobstructive pneumonia
- Pulmonary function tests
 - Upper airway obstruction pattern
- Laryngoscopy
 - Direct visualization of papillomas
 - Biopsy necessary for typing of HPV

Demographics

- Age
 - o Adults: 2 cases/100,000 population

- Bimodal age distribution
 - Children: 18 months to 3 years of age
 - Adults: 4th decade of life
- Sex
 - Children: M = F
 Adults: M > F

Natural History & Prognosis

- Usually self-limited disease in young patients
- Pulmonary nodules typically grow very slowly
- Rapid growth suspicious for squamous cell carcinomaInvasive papillomatosis
 - Death from respiratory failure
 - o Mortality as high as 50%
 - o 2% incidence of squamous cell carcinoma
 - Usually > 15 years after development of papillomatosis
 - Carcinomas often multicentric

Treatment

- Self-limited disease usually requires no treatment
- Surgical and medical therapies for lesions causing airway obstruction
 - Laser ablation of airway lesions
 - Numerous procedures usually necessary
 - Technically difficult with involvement of lower airways
 - Viral respiratory precautions important for health care providers
 - Aerosolization of virus
 - o Tracheostomy
 - Treatment of airway obstruction
 - More commonly required in younger patients
 - Antiviral agents may slow growth
 - o Interferon may slow growth
 - Systemic or direct intralesional injection
- Smoking cessation
 - Decreases risk of squamous cell carcinoma
 - Tobacco carcinogen synergistic with papillomas

DIAGNOSTIC CHECKLIST

Consider

• Tracheobronchial papillomatosis in patients with multiple airway nodules

Image Interpretation Pearls

 Evaluation of lungs for evidence of invasive papillomatosis and lesions suspicious for squamous cell carcinoma

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(Left) Axial NECT of a patient previously treated for a solitary tracheal papilloma shows an irregular nodule 🖂 in the anterior aspect of the trachea that represented a recurrence. Solitary papillomas are less common than multiple papillomas and are typically located in lobar or segmental bronchi. (Right) Axial CECT of a patient with tracheobronchial papillomatosis shows multiple right lower lobe clustered solid nodules 🔁. Note adjacent patchy ground-glass opacities 🖻 representing aspiration pneumonitis.





(Left) Axial CECT demonstrates multiple mural nodules 🔁 in the anterolateral tracheal carina. Tracheobronchial papillomatosis manifests as thickening or nodularity of the airway walls without evidence of calcification. (Right) Sagittal CECT of the same patient shows numerous soft tissue nodules \supseteq along the anterior wall of the trachea. CT is the optimal imaging modality for visualization of airway nodules and identification of invasive papillomatosis and squamous cell carcinoma.





(Left) Axial NECT of a patient with tracheobronchial papillomatosis shows numerous lower lobe thickwalled cavitary \supseteq and solid nodules 🔁. Associated complications, such as secondary infection, atelectasis ± postobstructive pneumonia, and lung cancer, may also be identified. (Right) Axial NECT of the same patient shows a lobulated endoluminal carinal nodule \square that extends into the right upper lobe bronchus $\overline{\Rightarrow}$ and multiple right lung cysts with thin irregular walls 🛃

TERMINOLOGY

- Squamous cell carcinoma (SCC)
- Most common primary tracheal malignancy

IMAGING

- Distal 1/3 of trachea or mainstem bronchi
- Radiography
 - Often subtle; detection requires careful inspection on PA and lateral chest radiography
 - Focal endoluminal tracheal nodule or mass
 - Cross-sectional imaging indicated in smoker with hemoptysis despite of normal chest radiograph
- CT
 - Difficult differentiation from other malignancies
 - Nodular or lobular tracheal nodule or mass, narrowing of tracheal lumen
 - Extraluminal extension and circumferential involvement should suggest malignancy
- FDG PET/CT: Most demonstrate increased FDG uptake

TOP DIFFERENTIAL DIAGNOSES

- Adenoid cystic carcinoma
- Mucoepidermoid carcinoma
- Carcinoid
- Benign tracheal and bronchial neoplasms
- Airway metastases
- Sarcoma

CLINICAL ISSUES

- Nonspecific symptoms; may mimic asthma
- Dyspnea, cough, hemoptysis, wheezing, stridor
- Age: 6th-7th decades of life
- Males affected up to 4x as often as females
- Strong association with cigarette smoking
- Prognosis worse than that of adenoid cystic carcinoma

DIAGNOSTIC CHECKLIST

• Consider SCC in middle-aged or older man with smoking history and tracheal tumor

(Left) Axial CECT of 66-yearold woman with tracheal squamous cell carcinoma shows a mass 🔁 with an endoluminal component 🖂 that narrows the tracheal lumen. Tissue sampling demonstrated squamous cell carcinoma, the most common tracheal malignancy, which is strongly associated with cigarette smoking. (Right) Sagittal CECT of the same patient shows an elongate lobulated mass 🔁 that protrudes into the tracheal lumen. Reformatted images are very useful for assessment of tumor length.











Abbreviations

• Squamous cell carcinoma (SCC)

Definitions

- Most common primary malignant tracheal neoplasm
- Arises from surface airway epithelium

IMAGING

General Features

- Best diagnostic clue
 - Polypoid and frequently ulcerated mass or nodule that projects into tracheal lumen
 - o Infiltration/invasion of adjacent mediastinal structures
 - Frequent regional metastatic lymphadenopathy at presentation
- Location
 - $\circ~$ Distal 1/3 of trachea or proximal bronchi
- Size
 - Variable; usually < 2.5 cm in maximum diameter

Radiographic Findings

- Radiography
 - Trachea is classic blind spot for radiologists
 - $\circ~$ Focal endoluminal tracheal nodule or mass
 - Asymmetric tracheal wall thickening
 - May involve posterior tracheal wall
 - Exophytic growth
 May compress/invade esophagus &/or adjacent structures
 - Focal thickening of paratracheal &/or tracheoesophageal stripes
 - o Thickening of posterior wall of bronchus intermedius
 - Regional mediastinal &/or hilar metastatic lymphadenopathy
 - Atelectasis
 - Segmental, lobar
 - Postobstructive pneumonia
 - Recurrent pneumonia should raise suspicion for endobronchial lesion, particularly in smokers

CT Findings

- NECT
 - Difficult to differentiate from other tracheal neoplasms
 - Nodular or polypoid endoluminal tracheal nodule or mass
 - Frequently ulcerated lesion
 - Irregular surface contours
 - Asymmetric tracheal wall thickening
 - Irregular contours
 - Adjacent peritracheal fat stranding suggests local invasion
 - Extraluminal extension and circumferential involvement
 - Obliteration of tissue planes with adjacent mediastinal structures if locally invasive

• May be multifocal (10%)

- Severe airway luminal narrowing common at presentation
 - > 50% airway lumen obliteration in asymptomatic patients

- Postobstructive pneumonia
 - Involvement and occlusion of major bronchi
 - Consolidation and volume loss in distribution of occluded airway
 - Primary endobronchial lesion may be obscured by surrounding airspace disease
- o Regional metastatic lymphadenopathy
- Mediastinal and hilar lymph nodes frequently affected

• CECT

- IV contrast aids in assessment of local invasion
 - Facilitates assessment of vascular invasion
 Vessel wall irregularity &/or narrowing indicates invasion
 - Better delineation of tumor and adjacent mediastinal structures
- o Large lesions may show heterogeneous enhancement
- o Lymph node &/or distant metastases in 30% of cases
 - Intrinsic low attenuation in metastatic lymph nodes indicates necrosis, which is common
 - In addition to mediastinal lymph nodes, other lymph node stations may be involved, such as supraclavicular and axillary
- May invade recurrent laryngeal nerve
 - May cause vocal cord paralysis
- Infrequent systemic metastases other than pulmonary metastases
 - Metastatic pulmonary nodules commonly cavitate

Imaging Recommendations

- Best imaging tool
 - CT is optimal imaging modality for evaluation of tracheal and bronchial neoplasms
 - CT is imaging method of choice for evaluation and follow-up of palliative airway stents
 - Assessment of stent integrity, location, and patency
- Protocol advice
 - Thin-section CT aids in detection and characterization of small lesions
 - IV contrast for differentiation of lesion from adjacent vascular structures
 - Facilitates assessment of vascular invasion
 - Axial CT images may underestimate longitudinal extent of lesion
 - Multiplanar reformatted images for determination of length of involvement
 - Volume rendering techniques and virtual bronchoscopy
 Helpful for surgical planning

Nuclear Medicine Findings

- PET/CT
 - SCC typically demonstrates increased FDG uptake
 - Small lesions may demonstrate less FDG uptake than large lesions
 - Used for staging
 - Guides biopsy of FDG-avid lymph nodes and metastases
 - Detection of distant metastases may preclude surgery

DIFFERENTIAL DIAGNOSIS

Adenoid Cystic Carcinoma

• M = F (as opposed to SCC, in which M > F)

- Affects younger patient population (3rd-4th decades of life)
- Not associated with cigarette smoking
- Distal trachea and mainstem bronchi
- May affect long segments of trachea
- Growth along submucosa and perineural structures
- Variable FDG uptake on FDG PET/CT

Mucoepidermoid Carcinoma

- Children and young adults
- Primarily affects lobar and segmental bronchi
- Endoluminal polypoid lesions or mural nodules
- May adapt to branching airway morphology
- May show intrinsic foci of calcification
- No association with cigarette smoking
- Variable FDG uptake on FDG PET/CT

Carcinoid

- Commonly affects mainstem and lobar bronchi
- Well-defined endobronchial nodules
- Frequent intense contrast enhancement due to hypervascularity
- Postobstructive atelectasis/pneumonitis
- May demonstrate little to no FDG uptake on FDG PET/CT
 Abusical cascing idea many likely to show in second 500
- Atypical carcinoids more likely to show increased FDG uptake than typical carcinoids

Benign Neoplasms

- Hamartoma and lipoma
- Internal macroscopic fat is diagnostic Chondroma: Internal chondroid calcification
- Calcification not indicative of benignity
- Papilloma
 - Usually small and multiple
 - o Also involves larynx
 - Associated cavitary pulmonary nodules and cystic lung lesions

Airway Metastases

- Direct tracheal invasion from lung or esophageal cancer
- Lymphatic or hematogenous dissemination
- Hematogenous metastases from any primary malignancy, but most commonly
 - Renal cell carcinoma
 - o Melanoma
 - Colon cancer
 - Breast cancer

Sarcoma

- Rare, chondrosarcoma is most common tracheal sarcoma • Irregular calcification (chondroid matrix)
 - Spares posterior tracheal wall because of absence of cartilage

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonspecific symptoms; may mimic asthma
 - Dyspnea
 - Cough
 - Wheezing
 - Stridor

- New onset of hoarseness in smoker
- Hemoptysis in smoker should raise suspicion for malignancy
- Upper airway obstructive symptoms usually do not develop until > 50% tracheal narrowing

Demographics

- Age
- o 6th-7th decades of life
- Sex
 - Males affected up to 4x as often as females
- Epidemiology
 - Rare tumor of respiratory tract, but most common tracheal malignancy in adults
 - Association with cigarette smoking
 - Metachronous or synchronous tumors of oropharynx, larynx, and lungs

Natural History & Prognosis

- **Prognosis worse than that of adenoid cystic carcinoma** • Usually locally advanced at presentation
- 1/3 have pulmonary or mediastinal lymph node metastases at diagnosis
- 5-year survival rate: 39-73%
- 10-year survival rate: 18-53%

Treatment

- Surgery is only curative option
- Radiotherapy in cases in which surgery is not feasible or as adjuvant or palliative measure
- Laser, tracheal or bronchial stents as palliative measures
- Chemotherapy has no established role currently

DIAGNOSTIC CHECKLIST

Consider

- SCC in middle-aged or older man with smoking history and tracheal tumor
- SCC in smoker with new onset of asthma or hoarseness

Image Interpretation Pearls

- Hemoptysis in smoker with normal chest radiograph should raise suspicion for airway malignancy and prompt further assessment with CT
- Airways are common blind spot on radiography
- Suspect SCC in cases of
 - o Focal asymmetric tracheal wall thickening
 - Exophytic endoluminal tracheal nodule
 - o Severe airway narrowing even in absence of symptomso Assess patients with SCC for signs of local invasion
- Multifocal primary tracheal tumors are not uncommon in patients with SCC
- Metastatic lymphadenopathy is commonly necrotic

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(Left) Axial CECT of a 57-yearold woman with tracheal squamous cell carcinoma shows a large tracheal mass \supseteq that produces almost complete tracheal obstruction. (Right) Coronal CECT of the same patient shows a large mass \supseteq that obliterates the tracheal lumen. Given the degree of obstruction, an emergency tracheostomy was performed, followed by tumor debulking as a temporary measure to relieve the obstruction. Chemoradiation, laser therapy, and stents are palliative therapies reserved for unresectable tumors.





(Left) Axial CECT of a 65-yearold man shows a squamous cell carcinoma that produces circumferential mural thickening \supseteq and severe stenosis of the trachea and abuts the aorta \bowtie concerning for mediastinal invasion. (Right) Sagittal NECT of the same patient shows direct mediastinal invasion \supseteq by the tumor. While the treatment of choice for tracheal tumors is surgical resection, invasion of adjacent organs, extensive lymphadenopathy, and metastases are contraindications.





(Left) Axial CECT of a 41-yearold man with tracheal squamous cell carcinoma shows a small anterior tracheal nodule 2. (Right) Axial CECT of the same patient obtained 5 months later shows interval development of a tracheal mass with an endoluminal component 乏 and irregular thickening of the anterior tracheal wall 🔁. Soft tissue attenuation in the adjacent fat 🖂 is highly concerning for mediastinal invasion. Up to 30% of affected patients have lymph node or pulmonary metastases at initial staging.

Adenoid Cystic Carcinoma

KEY FACTS

TERMINOLOGY

- Adenoid cystic carcinoma (ACC)
- Rare primary malignant tracheal neoplasm arising from submucosal glands

IMAGING

- Radiography
 - Trachea is common "blind spot" for radiologists
 - Nodule or mass within tracheal/bronchial air column
 - o Tracheal/bronchial stenosis of variable length
 - Atelectasis, recurrent pneumonia
- CT
 - Circumferential mural airway thickening
 - Often affects long segments of distal trachea or mainstem bronchi
 - o Polypoid tracheal nodule or mass; may involve bronchi
 - Local invasion of adjacent mediastinal fat
 - Mediastinal lymphadenopathy

TOP DIFFERENTIAL DIAGNOSES

- Squamous cell carcinoma
- Mucoepidermoid carcinoma
- Metastases
- Sarcoma
- Benign neoplasms

PATHOLOGY

• Perineural extension is histologic hallmark of ACC

CLINICAL ISSUES

- Symptoms/signs: Dyspnea, cough, stridor, wheezing, hemoptysis
- Treatment: Surgical resection with end-to-end anastomosis of trachea ± adjuvant radiotherapy

DIAGNOSTIC CHECKLIST

• Consider ACC in differential diagnosis of tracheal tumors, especially those with long segment airway involvement

(Left) Coned-down PA chest radiograph of 62-year-old woman shows focal stenosis \supseteq of the proximal left main stem bronchus that was not identified initially. The central airways are a common "blind spot" for radiologists and should be evaluated carefully. (Right) Axial CECT of the same patient shows mural thickening of the left mainstem bronchus 🔁 with an associated endoluminal soft tissue nodule. Biopsy confirmed adenoid cystic carcinoma, which commonly affects the distal trachea and proximal mainstem bronchi.





(Left) Coronal CECT of the same patient shows the endoluminal tumor nodule 🖂 and long segment mural thickening of the left mainstem bronchus 🖂 Multiplanar reformatted images allow assessment of the length of airway involvement. (Right) Fused axial FDG PET/CT of the same patient shows metabolic activity \blacksquare similar to that of mediastinal background suggesting a low-grade neoplasm. FDG avidity in these lesions is associated with a high likelihood of lymph node and distant metastases.





Abbreviations

• Adenoid cystic carcinoma (ACC)

Synonyms

• Cylindroma; term no longer in use

Definitions

- Uncommon malignant central airway neoplasm that arises from submucosal (tracheobronchial) glands
- 2nd most common malignant tracheal neoplasm

IMAGING

General Features

- Best diagnostic clue
 - Diffuse smooth or nodular circumferential tracheal wall thickening
 - Longitudinal extent of tumor is typically greater than axial extent
 - Endoluminal polypoid or broad-based mass arising from central airway wall
- Location
 - More frequent in distal 2/3 of trachea
 - May involve mainstem bronchi
 - Frequent long segment involvement due to submucosal growth
- Morphology
 - Homogeneous soft tissue lesion
 - Well-defined or irregular margins
 - Ulceration is uncommon (unlike squamous cell carcinoma)
 - Circumferential tracheal wall thickening vs. polypoid endotracheal lesion
 - o Infiltration of adjacent mediastinal structures

Radiographic Findings

- Radiography
 - Trachea is frequent "blind spot" for radiologists
 - o Focal nodule or mass within tracheal air column
 - Segmental tracheal or mainstem bronchus luminal narrowing
 - o Atelectasis
 - Extent of volume loss depends on lesion location within airway
 - Lobar, multilobar, or whole lung
 - Hyperinflation due to distal air-trapping
 - Postobstructive pneumonitis/pneumonia
 - Recurrent or nonresolving pneumonia
 - o Mediastinal lymphadenopathy
 - Nodular thickening of paratracheal or tracheoesophageal stripes (> 4 mm)

CT Findings

- CECT
 - Circumferential or nodular soft tissue involving trachea/major bronchi
 - Frequent homogeneous soft tissue mural thickening
 Often affects long tracheal segments due to submucosal extension
 - May exhibit circumferential airway involvement

- Variable degrees of airway luminal narrowing
- Signs of local invasion
 - Stranding/obliteration of adjacent mediastinal fat
 Frank invasion of adjacent structures
- Metastatic mediastinal lymphadenopathy
- Pulmonary and pleural metastases less common than in salivary gland ACC
 - □ Lymph node or distant metastases in 10% of cases
 - Metastatic disease when present, typically involves lungs
- Longitudinal extend is optimally visualized on coronal reformatted images

$\circ~$ Polypoid or broad-based soft tissue nodule or mass

- Endoluminal involvement of distal trachea/central bronchi
- Infiltration of affected tracheal wall
- PET/CT
 - Heterogeneous FDG uptake within lesion
 - o SUV range: 1.5-17.6
 - Tumors with high SUV associated with lymph node and distant metastases
 - Detection of distant metastases
 - Useful for radiotherapy planning when tumor is adjacent to atelectasis

Imaging Recommendations

- Best imaging tool
 - CT is imaging modality of choice for assessment of tracheal neoplasms
- Protocol advice
 - o Thin-section imaging (< 2 mm)
 - Small field of view focused on large airways
 - Multiplanar reformatted images
 - Assessment of length of airway involvement and local invasion
 - Useful for surgical planning
 - Virtual bronchoscopy may help as guide for transbronchial biopsy

DIFFERENTIAL DIAGNOSIS

Squamous Cell Carcinoma

- Most common primary malignant tracheal neoplasm
- Average age: 60-70 years
- Men much more frequently affected than women
- Strong association with cigarette smoking
- Polypoid endoluminal mass with irregular &/or lobulated borders
 - Extraluminal tumor growth
- May be multifocal
- Metastatic lymphadenopathy &/or distant metastases at presentation
- ± synchronous head and neck malignancy

Mucoepidermoid Carcinoma

- Uncommon neoplasm
- Young adults, usually younger than 30 years
- Origin from submucosal glands in tracheobronchial tree
- More common in lobar and segmental bronchi
- Endoluminal nodule ± distal bronchial mucoid impaction

Bronchial Carcinoid Tumor

- Tracheobronchial carcinoids are most commonly typical carcinoids
- Young adults; men and women equally affected
- Affected patients frequently present with recurrent postobstructive atelectasis or pneumonia
- Carcinoid syndrome in 5% of cases (i.e., diarrhea, palpitations, abdominal pain, flushing)
- Mainstem, lobar, and segmental bronchus involvement more frequent than tracheal involvement
- Well-defined solid nodule with variable endoluminal component
- Intense contrast enhancement due to tumor vascularity
- Calcification in 26% of cases

Metastases

- Direct tracheal invasion by thyroid, lung, or esophageal cancer
- Hematogenous or lymphatic metastases to tracheal/bronchial walls
- Hematogenous metastases from any primary malignancy but most commonly
 - o Renal cell carcinoma
 - o Melanoma
 - o Colon cancer
 - Breast cancer
- Solid enhancing nodules/polyps projecting into lumina of major airways

Sarcomas

- Extremely rare
- Fibrosarcoma, synovial sarcoma, chondrosarcoma

Benign Neoplasms

- Hamartoma and lipoma: Internal macroscopic fat is diagnostic
 - Most common benign tracheal tumor
 - Affected patients usually present with recurrent infection or hemoptysis
 - May exhibit intrinsic fat, cartilage, fibrous tissue
 - Popcorn calcification and macroscopic fat are diagnostic
- Squamous papilloma and papillomatosis
 - Recurrent endoluminal lesions
 - Transmission of papilloma virus 6 and 11 during birth
 - Malignant transformation to squamous cell carcinoma in 10% of cases
 - Larynx is most frequently affected
 - Nodules may be sessile or pedunculated
 - Lung involvement: Cavitary pulmonary nodules
- Chondroma: Internal calcification (stippled or amorphous)
 Often indistinguishable from hamartoma
- Hemangioma: More frequent in childhood
- Other benign tumors: Leiomyoma, schwannoma, neurofibroma

PATHOLOGY

General Features

- Histologic subtypes: Cribriform (best prognosis), trabecular, and solid (worse prognosis)
- ACC is nonencapsulated and grows within submucosa toward mucosa

• Perineural extension is histologic hallmark of ACC

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Affected patients may be asymptomatic until tumor reaches advanced stage
 - Insidious onset of symptoms
 - Often misdiagnosed as adult asthma
 - Nonspecific respiratory symptoms
 - Dyspnea
 - Cough
 - Stridor
 - Wheezing
 - Hemoptysis
 - Recurrent pneumonia in same anatomic location
- Clinical profile
- Average age: 40-50 years
- \circ M=F
- No association with cigarette smoking or alcohol consumption

Natural History & Prognosis

- 5-year survival: 65-100%
- 10-year survival: 50-60%
- At risk for tracheoesophageal fistula, especially following radiation treatment.

Treatment

- Surgical resection with end-to-end tracheal anastomosis ± adjuvant radiotherapy
 - Recurrence reported even in cases with negative margins at time of resection
 - Tumor involvement of > half the trachea precludes surgical resection
- Palliative radiotherapy in nonsurgical cases
- Chemotherapy not generally indicated
- Tracheobronchial stents
- Palliative treatment

DIAGNOSTIC CHECKLIST

Consider

• ACC in differential diagnosis of solid tracheal tumors

Image Interpretation Pearls

• Diffuse smooth or nodular circumferential tracheal mural thickening (long segment)

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Adenoid Cystic Carcinoma





(Left) PA chest radiograph of 58-year-old woman with adenoid cystic carcinoma shows abrupt long segment tracheal stenosis 🖅. Adenoid cystic carcinoma is the second most common malignant tracheal neoplasm, and affected patients have an average age at presentation of 40-50 years. (Right) Axial CECT of the same patient shows marked circumferential nodular mural thickening \supseteq of the trachea due to submucosal growth of tumor and severe tracheal stenosis, a classic imaging finding of adenoid cystic carcinoma.





(Left) Axial CECT of a 62-yearold woman with adenoid cystic carcinoma shows focal nodular thickening \supseteq of the upper tracheal wall. (Right) Coronal CECT of the same patient confirms focal tracheal mural thickening with a nodular component \square that protrudes into the tracheal lumen, a frequent imaging finding of adenoid cystic carcinoma. Management consists of surgical resection with end-to-end tracheal anastomosis. Postoperative radiotherapy is recommended for patients with incomplete surgical excision.





(Left) PA chest radiograph of a 69-year-old woman with adenoid cystic carcinoma shows short segment tracheal stenosis \supseteq just above the carina. (Right) Axial CECT of the same patient shows asymmetric thickening of the tracheal wall secondary to submucosal tumor growth 🖂 Note mediastinal lymphadenopathy 🔁 reported in 10% of patients with adenoid cystic carcinoma at initial diagnosis. Palliative radiotherapy is recommended as a treatment option in cases with extensive unresectable neoplasm.

TERMINOLOGY

- Mucoepidermoid carcinoma (MEC)
- Primary pulmonary salivary gland-type tumor
- Origin in large airway bronchial glands: Functionally equivalent to oropharyngeal salivary glands

IMAGING

- Radiography
 - Postobstructive pneumonia/atelectasis
 - o Rarely, visualization of endoluminal nodule or mass
 - Well-defined pulmonary nodule or mass
- CT
 - Well-circumscribed endobronchial lesion
 - May conform to airway morphology
 - Ovoid or spherical shape, often lobulated
 - Segmental and lobar bronchi most commonly affected
 - Distal obstructive pneumonia or atelectasis
 - Punctate or coarse calcification in 25-50%
 - o Variable heterogeneous contrast enhancement

TOP DIFFERENTIAL DIAGNOSES

- Carcinoid tumor
- Squamous cell carcinoma
- Adenoid cystic carcinoma
- Airway metastasis
- Endobronchial hamartoma

CLINICAL ISSUES

- Obstructive airway symptoms
- ~ 50% of patients < 40 years
- TNM system used for staging MEC
- Treatment of choice is surgical resection
- Prognosis related to tumor grade and stage

DIAGNOSTIC CHECKLIST

- Consider MEC in young patient with endoluminal lesion in segmental airway
- Primary lung cancer is much more common than MEC and should be included in differential diagnosis

(Left) PA chest radiograph of an asymptomatic 62-year-old woman shows an incidentally discovered left midlung zone nodule \supseteq projecting over the left perihilar region. (Right) Axial CECT of the same patient shows a left upper lobe lobulated nodule that exhibits a bronchial relationship \square , the so-called bronchus sign, typically described with carcinoid tumor. Mucoepidermoid carcinoma, diagnosed at surgical excision, most commonly occurs in association with lobar or segmental bronchi.





(Left) Axial fused FDG PET/CT of the same patient shows a well-defined FDG-avid nodule \square . High SUV correlates with higher tumor grade, lymph node metastases, distant metastases, and worse longterm outcome. (Right) Coronal FDG PET of the same patient shows FDG avidity within the left upper lobe nodule 🔁. There is no evidence of lymph node or distant metastases. The treatment of choice for mucoepidermoid carcinoma is surgical resection. Adjuvant chemoradiation is the recommended treatment in advanced disease.





Abbreviations

Mucoepidermoid carcinoma (MEC)

Definitions

- Primary pulmonary salivary gland-type tumors: MEC and adenoid cystic carcinoma
 - Origin in large airway bronchial glands: Functionally equivalent to oropharyngeal salivary glands
 - Represent < 1% of all lung cancers
 - MEC and adenoid cystic carcinoma are most common salivary gland-type tumors

IMAGING

General Features

- Best diagnostic clue
 - Endoluminal, smooth or lobular, ovoid or spherical nodule or mass in segmental or lobar bronchus
- MEC is most common in lobar or segmental bronchiLocation
 - Central airway: ~ 45% (mainstem bronchus > trachea)
 - Peripheral lung: ~ 55% (segmental and lobar bronchi)
- Size
 - o Average: 3 cm
- Morphology
 - Well-defined endoluminal nodule
 - o Spherical or ovoid lesion with lobular borders
 - Longest diameter often conforms to airway shape

Radiographic Findings

- Postobstructive pneumonia/atelectasis common
- Well-defined pulmonary nodule or mass
- Rarely, visualization of endoluminal nodule or mass

CT Findings

- Well-circumscribed endobronchial lesion
 - May conform to airway morphology; longest dimension parallels airway lumen
 - Ovoid or spherical shape, often lobulated
- Distal obstructive pneumonia or atelectasis
- Distal bronchiectasis, endobronchial mucus plugs
- Punctate or coarse calcification in 25-50%
- Variable heterogeneous contrast enhancement
- Metastases usually only with high-grade MEC
 Lymph nodes (ipsilateral hilar > mediastinal)
 - o Distant metastases: Pleura, bones, liver

Nuclear Medicine Findings

• High SUV correlates with higher tumor grade, ↑ lymph node metastases, worse long-term outcome

Imaging Recommendations

Best imaging tool
 CT is modality of choice for airway assessment

DIFFERENTIAL DIAGNOSIS

Squamous Cell Carcinoma of Airways

- Most common primary malignant airway neoplasm
- Usually affects trachea: Irregular margins, frequent extraluminal extension

Carcinoid Tumor

- More common than MEC
- Typically affects lobar bronchi
- Marked contrast enhancement; calcification in 1/3

Adenoid Cystic Carcinoma

- More common in trachea, especially near carina
- Irregular margins, frequent extraluminal extension

Airway Metastasis

• Known primary malignancy elsewhere

Endobronchial Hamartoma

• Well-defined endobronchial nodule; may contain macroscopic fat or popcorn calcification

PATHOLOGY

General Features

• TNM system used for staging MEC

Staging, Grading, & Classification

- Histopathologically classified as low or high grade
- High-grade MEC: Propensity for mural invasion and lymph node metastases

Microscopic Features

- Indistinguishable from primary salivary gland MEC
- High-grade MEC mimics adenosquamous lung cancer
 Molecular techniques for diagnostic dilemmas
 - Gene MAML2 (translocation 11;19)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Obstructive airway symptoms: Cough, hemoptysis, wheezing, stridor, recurrent pneumonia
 - Minority of patients are asymptomatic

Demographics

• Age

- o ~ 50% of patients < 40 years
- Epidemiology
 - No significant association with cigarette smoking

Natural History & Prognosis

- Prognosis usually good; correlates with tumor grade
 Complete resection is usually curative in low-grade MEC
- Metastases in ~ 10%; usually high-grade MEC

Treatment

• Surgical resection

DIAGNOSTIC CHECKLIST

Consider

• Consider MEC in young patient with endobronchial lesion in segmental airway

SELECTED REFERENCES

 Han X et al: Radiological and clinical features and outcomes of patients with primary pulmonary salivary gland-type tumors. Can Respir J. 2019:1475024, 2019 (Left) PA chest radiograph of a 32-year-old man who presented with persistent cough and episodes of hemoptysis shows an irregular left infrahilar mass 🛃 that projects over the left retrocardiac region. Up to 50% of patients with mucoepidermoid carcinoma are younger than 40 years of age. (Right) Axial CECT of the same patient shows that the left lower lobe mass ᠫ exhibits a large endobronchial component that nearly occludes the airway with a crescentic air lucency \supseteq that partially outlines the mass.





(Left) Coronal CECT of the same patient shows the left lower lobe mass 🔁 and adjacent bronchiectasis 🖂 located inferior to the lesion and secondary to postobstructive effects of the central neoplasm. (Right) Axial fused FDG PET/CT of the same patient shows metabolic activity within the left lower lobe mass. Although, high SUV correlates with the presence of lymph node and distant metastases, less than 10% of patients with mucoepidermoid carcinoma have metastatic disease at the time of presentation.





(Left) Axial CECT of a 32-yearold woman with mucoepidermoid carcinoma shows a well-defined lobulated mass 🔁 in the middle lobe with a visible endobronchial component 🖂 (Right) Axial CECT of the same patient (soft tissue window) shows heterogenous contrast enhancement of the middle lobe mass. The majority of mucoepidermoid carcinomas show moderate to marked contrast enhancement and typically exhibit a spherical or ovoid morphology and lobulated borders.





Mucoepidermoid Carcinoma





(Left) Axial CECT of a 36-yearold patient with a central mucoepidermoid carcinoma who presented with an episode of hemoptysis shows a well-defined endoluminal nodule \supseteq within the left mainstem bronchus. (Right) Coronal CECT of the same patient confirms the presence of an endobronchial soft tissue nodule \supseteq with an eccentric punctate calcification 🔁 located inferiorly. Punctate or coarse calcifications are present in approximately 25-50% of cases of mucoepidermoid carcinoma.





(Left) PA chest radiograph of a 19-year-old patient with mucoepidermoid carcinoma and a history of persistent cough for 10 months shows complete right lower and middle lobe atelectasis \square . (Right) Axial CECT of the same patient shows an endobronchial nodule 🔁 located in the lumen of the bronchus intermedius, which produced middle and right lower lobe atelectasis (not shown). Postobstructive atelectasis &/or pneumonia are common imaging manifestations of central obstructing airway neoplasms.





(Left) Axial CECT of a 57-yearold patient with mucoepidermoid carcinoma shows a well-defined right lower lobe lobulated soft tissue mass \supseteq with adjacent subsegmental atelectasis 🖂 (**Right**) Axial CECT of the same patient (soft tissue window) shows a heterogeneously enhancing right lower lobe central mass 🔁. Biopsy demonstrated a low-grade mucoepidermoid carcinoma, which carries an excellent prognosis.

TERMINOLOGY

- Spread of malignancy to airway
 - Airway dissemination of tumor cells, lymphatic, or hematogeneous spread

IMAGING

- Radiography
 - Atelectasis: Lung, lobar, segmental
 - Obstructive pneumonitis
 - Endotracheal or endobronchial lesion rarely apparent
- CECT
 - Endoluminal soft tissue nodule or mass
 - Obstructive pneumonitis
 - Consolidation in distribution of affected airway
 - Fluid-filled bronchi distal to obstruction
 - Atelectasis distal to obstructing lesion
 - Atelectasis with associated shift of pulmonary fissures
 - Systemic metastases

TOP DIFFERENTIAL DIAGNOSES

- Non-small cell lung cancer
- Carcinoid
- Tracheal neoplasms
- Hamartoma

PATHOLOGY

• Renal cell and colon cancers most common

CLINICAL ISSUES

- Symptoms/signs: Cough, hemoptysis, wheezing, pneumonia, atelectasis
- Prognosis usually poor because of disseminated neoplasm elsewhere

DIAGNOSTIC CHECKLIST

• Consider airway metastasis in patients with malignancy and endobronchial lesion with obstructive pneumonia or atelectasis

(Left) Axial CECT of a 46-yearold woman with thyroid cancer shows a small endotracheal metastasis \supseteq as well as lung 🔁 and pleural metastases 🔁. Patients with airway metastases usually have extensive metastatic disease. (Right) Axial CECT of a 70-year-old man with renal cell carcinoma shows soft tissue filling and distending the lumen of the left upper lobe bronchus and its segmental branches 🖂 Biopsy showed metastasis. Renal and colon cancers are the most common sources of airway metastases.





(Left) Axial CECT of a 35-yearold man with persistent cough and metastatic synovial sarcoma shows a left mainstem bronchus mass 🔁 that extends into the left lower lobe bronchi with resultant atelectasis 🖂 Dyspnea, cough, and hemoptysis are the most common symptoms in affected patients. (Right) Coronal CECT of the same patient shows the endobronchial obstructing mass \implies that causes left lung atelectasis 🔁. Stents and laser ablation are used as palliation for severe airway obstruction.





Synonyms

- Endobronchial metastasis
- Endotracheal metastasis

Definitions

- Spread of malignancy to airway
- Most common in patients with renal, colon, breast, and endometrial cancers and melanoma

IMAGING

General Features

- Best diagnostic clue
 - Endobronchial or endotracheal nodule or mass on CT
 Usually associated with extensive systemic metastatic disease
- Location
 - Trachea and larger bronchi
- Size
 - Range from small mural nodule to large obstructing mass
- Morphology
 - Smooth or polypoid endoluminal lesion

Radiographic Findings

- Atelectasis: Lung, lobar, segmental
- Endotracheal or endobronchial lesion rarely apparent

CT Findings

- CECT
 - Endoluminal soft tissue nodule or mass, may obstruct airway: Fluid-filled bronchi distal to obstruction (finger-inglove sign)
 - Obstructive pneumonitis
 - Consolidation in distribution of affected airway
 - Atelectasis distal to obstructing lesion
 Volume loss, shift of fissures
 - Systemic metastases
- FDG-PET/CT
 - Identification of endoluminal lesion associated with postobstructive atelectasis or pneumonia

Imaging Recommendations

- Best imaging tool
 - CECT: Superior to radiography
 - Optimal imaging modality for evaluation of airway neoplasia
- Protocol advice
 - Thin-section CECT: Multiplanar reformatted images for delineation of tumor extent
 - 3D imaging (virtual bronchoscopy) may help for surgical planning

DIFFERENTIAL DIAGNOSIS

Non-Small Cell Lung Cancer

- No known extrathoracic primary malignancy
- Usually affects current or former cigarette smokers

Carcinoid

• Often hypervascular

• No known extrathoracic primary malignancy

Tracheal Neoplasms

- Primary tracheal neoplasms more common than metastases
- Most common primaries: Squamous cell carcinoma and adenoid cystic carcinoma

Hamartoma

- No known extrathoracic primary malignancy
- Heterogeneous with dystrophic calcification
- Macroscopic fat usually diagnostic

PATHOLOGY

General Features

- Renal cell and colon carcinoma most common
- Possible routes include bronchial dissemination of tumor cells, lymphatic or hematogeneous spread

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Cough
 - Hemoptysis: Hypervascular tumors, such as renal cell carcinoma melanoma
 - o Wheezing
 - o Pneumonia
 - Atelectasis
- Other signs/symptoms
- Rarely, patients may expectorate tissue fragments

Demographics

- Epidemiology
 - Present in 4% of patients with extrapulmonary malignancies

Natural History & Prognosis

- Prognosis usually poor due to disseminated disease
- Chronic obstruction may lead to recurrent pneumonia

Treatment

- Dependent on site and status of primary neoplasm
- Endobronchial cryoablation or laser therapy for palliation
- Chemotherapy and palliative radiation therapy
- Surgery may be considered if no active malignancy elsewhere

DIAGNOSTIC CHECKLIST

Consider

• Primary airway neoplasm in differential diagnosis of endoluminal obstructing airway lesions

Image Interpretation Pearls

• Endobronchial lesion with obstructive pneumonia or atelectasis in patient with known malignancy

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Saber-Sheath Trachea

KEY FACTS

TERMINOLOGY

• Abnormal configuration of intrathoracic trachea: Coronal dimension is ≤ 2/3 of sagittal dimension

IMAGING

• Best diagnostic clue: Side-to-side narrowing of intrathoracic trachea

• Radiography

- Lateral chest radiograph: Widening of sagittal diameter of intrathoracic trachea
- Frontal chest radiograph: Narrowing of coronal diameter of intrathoracic trachea
- Frontal tracheal diameter (FTD)/lateral tracheal diameter (LTD) < 2/3
 - Specificity: 95%; sensitivity: < 10%
- CT
 - o Side-to-side narrowing of intrathoracic trachea
 - Inward bowing of lateral tracheal walls during expiration or Valsalva maneuver

TOP DIFFERENTIAL DIAGNOSES

- Tracheal stenosis
- Tracheobronchomalacia
- Tracheobronchomegaly
- Diffuse tracheal narrowing

PATHOLOGY

 Most commonly associated with emphysema, chronic obstructive pulmonary disease

CLINICAL ISSUES

- Prognosis depends on severity of narrowing and tracheomalacia
- Treatment directed at emphysema
- Tracheal stenting and surgery uncommon

DIAGNOSTIC CHECKLIST

• Consider saber-sheath trachea in smokers with characteristic tracheal deformity on imaging

(Left) Graphic shows an abnormal configuration of the intrathoracic trachea, with narrowing of its coronal diameter and widening of its sagittal diameter. The shape and configuration are characteristic findings of saber-sheath trachea. (Right) Axial CECT demonstrates a narrow coronal tracheal diameter \supseteq with resultant saber-sheath configuration. Note bilateral lung lucencies with imperceptible borders 🖂, consistent with centrilobular emphysema. Saber-sheath trachea is most commonly associated with emphysema.





(Left) PA chest radiograph of a patient with chronic obstructive pulmonary disease demonstrates side-to-side narrowing of the intrathoracic trachea \supseteq , consistent with saber-sheath trachea. (Right) Axial CECT of the same patient shows side-to-side narrowing of the intrathoracic trachea \supseteq , consistent with saber sheath trachea. Other findings that may be *identifiable on CT include* inward bowing of the lateral tracheal walls during expiration or Valsalva maneuver.





Definitions

• Abnormal configuration of intrathoracic trachea: Coronal dimension is ≤ 2/3 of sagittal dimension

IMAGING

General Features

- Best diagnostic clue
 - Side-to-side narrowing of intrathoracic trachea that occurs abruptly at thoracic inlet
- Location
 - o Intrathoracic trachea
 - Early: Trachea at thoracic inlet
 - Late: Entire intrathoracic trachea
 - Mainstem bronchi and extrathoracic trachea are normal
- Size
 - Normal tracheal dimensions
 - Sagittal diameter: 13-27 mm in males; 10-23 mm in females
 - Coronal diameter: 13-25 mm in males; 10-21 mm in females

• Saber-sheath trachea

- Coronal diameters < 13 mm in males; < 10 mm in females
- Frontal tracheal diameter (FTD)/lateral tracheal diameter (LTD) < 2/3

Radiographic Findings

- Frontal chest radiograph: Narrowing of coronal diameter of intrathoracic trachea
- Lateral chest radiograph: Widening of sagittal diameter of intrathoracic trachea
- FTD/LTD < 2/3
 - Specificity for emphysema: 95%
 - Sensitivity for emphysema: < 10%

CT Findings

- Side-to-side narrowing of intrathoracic trachea
- Inward bowing of lateral tracheal walls during expiration or Valsalva maneuver

Imaging Recommendations

- Best imaging tool
 CT with multiplanar reformatted images
- Protocol advice
 - CT during forced expiration or Valsalva maneuver

DIFFERENTIAL DIAGNOSIS

Tracheal Stenosis

• Segmental narrowing of intrathoracic trachea on expiratory CT

Tracheobronchomalacia

- Weakness of central airway walls
- At least 70% tracheal collapse on expiratory CT

Tracheobronchomegaly

- a.k.a. Mounier-Kuhn syndrome
- Marked dilatation of trachea and mainstem bronchi

Diffuse Tracheal Narrowing

- Infection: Bacterial, fungal, and viral organisms
- Tracheobronchopathia osteochondroplastica
 - Osteocartilaginous lesions in anterior and lateral tracheal walls; posterior wall spared
- Granulomatosis with polyangiitis
- Involves upper and lower respiratory tracts
- Amyloidosis
 - Submucosal nodules or masses involving any portion of tracheal wall
- Relapsing polychondritis
- Rare autoimmune connective tissue disorder
 Inflammation and destruction of cartilaginous tissue
- Sarcoidosis
 - Intraluminal granulomatous lesions
 - Extrinsic compression from lymph nodes or fibrosis

PATHOLOGY

General Features

- Etiology
 - Restricted dimensions of paratracheal mediastinum due to retained air in upper lobes
 - Calcification of cartilaginous rings secondary to injury from chronic coughing
- Associated abnormalities
 - Most commonly associated with emphysema, chronic obstructive pulmonary disease
 - Tracheobronchopathia osteochondroplastica less commonly

Gross Pathologic & Surgical Features

- Deformity of tracheal cartilage results in narrowing
- Calcification of cartilaginous rings

CLINICAL ISSUES

Presentation

Most common signs/symptoms
 Dyspnea, shortness of breath, chronic cough

Demographics

- Age
 - o Older patients (> 50 years) with emphysema

Natural History & Prognosis

• Depends on severity of narrowing and presence or absence of tracheomalacia

Treatment

- Directed at emphysema
- Tracheal stenting and surgery uncommon

DIAGNOSTIC CHECKLIST

Consider

• Saber-sheath trachea in smokers with characteristic tracheal deformity on imaging

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TERMINOLOGY

• Focal or diffuse tracheal narrowing

IMAGING

- Radiography
 - Focal or diffuse tracheal narrowing
 - Tracheal cartilage rings may be visible if calcified
- CT
 - Stenosis involving tracheal cartilage ± membranous posterior wall
 - Multiplanar reformations, volume rendering, and virtual bronchoscopy enhance evaluation
 - Assessment for any source of extrinsic compression
 - Expiratory imaging may show associated malacia
- MR
 - Greatest utility in pediatric patients
 - Identification and characterization of adjacent soft tissue masses and vasculature

TOP DIFFERENTIAL DIAGNOSES

- Post-intubation stenosis
- Tracheal neoplasia
- Saber-sheath trachea
- Infectious/inflammatory-related stenosis

CLINICAL ISSUES

- May mimic chronic obstructive physiology
- Congenital forms are rare; affected patients present early

DIAGNOSTIC CHECKLIST

- Evaluate location, extent, severity, and morphology of stenosis
- Search for evidence of associated soft tissue component, lymphadenopathy, vascular anomaly, mediastinal mass
- Include larynx in evaluation to check for subglottic stenosis
- Classification systems
 - Location, degree of narrowing, and transition zone of stenosis

(Left) Graphic shows features of acquired focal tracheal stenosis 🔁 secondary to prior prolonged intubation. (Right) Composite image with coronal NECT (left) and volumerendered CT reformation (right) of a patient with postintubation tracheal stenosis shows focal hourglass-shaped tracheal narrowing 🔁. Location, severity, and transition margins are important descriptors for classification and clinical management. (Used with permission from AIRP.)





(Left) Composite image with axial NECT in lung (left) and soft tissue (right) window of a patient with tracheal stenosis due to tracheobronchopathia osteochondroplastica shows anterolateral mural thickening \blacksquare and nodular calcifications that spare the posterior membranous trachea. (Used with permission from AIRP.) (Right) Composite image with axial NECT in lung (left) and soft tissue (right) window of the same patient shows a lesser degree of airway stenosis just above the tracheal bifurcation. (Used with permission from AIRP.)





Definitions

• Focal or diffuse tracheal narrowing

IMAGING

General Features

- Best diagnostic clue
 - o Tracheal narrowing relative to proximal/distal segment
- Location
- May occur in upper, mid, &/or lower third of tracheaMorphology
 - ~ 30% diffuse; 20% funnel-shaped; 50% segmental Post-intubation stenosis often hourglass-shaped

Radiographic Findings

- Focal or diffuse narrowing of tracheal air column
- Tracheal cartilage rings may be visible if calcified

CT Findings

- Multiplanar reformations, 3D-volume rendering, and virtual bronchoscopy; depict location, length, contour, patency
- Involvement of tracheal cartilage ± posterior membrane
- Evaluation for potential source of extrinsic compression
- Inspiratory and expiratory imaging helps discern stenosis (fixed defect) from tracheomalacia (dynamic)

MR Findings

- Static and dynamic MR useful in pediatric patients
- Identification and characterization of adjacent soft tissue masses and vasculature

Imaging Recommendations

- Best imaging tool
 - CT with multiplanar and 3D reformations: Anatomic detail and assessment of disease extent
- Protocol advice
 - o Expiratory imaging may show associated malacia
 - Inclusion of larynx to exclude subglottic stenosis
 - o CECT for identification of vascular compression

DIFFERENTIAL DIAGNOSIS

Post-Intubation or Tracheostomy Stenosis

- Typically 1.5- to 2.5-cm segment
- Subglottic; eccentric or concentric
- Fibrosis with fixed deformity or webs

Infectious/Inflammatory Tracheal Stenosis

- Viral, fungal, bacterial, tuberculous etiologies
- Sarcoidosis, IgG4-related disease

Systemic Autoimmune Diseases

• Granulomatosis with polyangiitis, relapsing polychondritis, ulcerative colitis, Crohn disease

Tracheal Neoplasms

- Respiratory squamous papillomatosis (benign)
- Squamous cell carcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, carcinoid tumor
- Contiguous invasion by malignancy, airway metastases

Tracheobronchopathia Osteochondroplastica

- Submucosal osteocartilaginous nodules
- Posterior tracheal membrane spared
- Idiopathic, older patients ± cough

Tracheobronchial Amyloidosis

- Submucosal nodular amyloid deposition ± calcifications
- Usually diffuse; posterior tracheal membrane **not** spared
- Rare; ~ 1% of patients with amyloidosis

Congenital Tracheal Stenosis

- Rare, almost always symptomatic
- > 50% have "napkin ring" stenosis
- May be secondary to extrinsic compression by bronchopulmonary or vascular malformations

Saber Sheath Trachea

- Associated with chronic obstructive pulmonary disease; almost exclusively males
- Fixed intrathoracic tracheal narrowing (coronal diameter)

PATHOLOGY

Staging, Grading, & Classification

- Trachea divided into upper, mid, and lower 1/3
- Degree of cross-sectional narrowing reported
 o ≤ 25%, 26-50%, 51-75%, 76-90%, > 90%
- Transition (abrupt or tapered) clinically relevant

Gross Pathologic & Surgical Features

- Tracheal wall thickening: Concentric vs. eccentric, nodular vs. smooth, focal vs. diffuse
- Mucosa, submucosa, cartilage ± membranous portions variably involved by spectrum of pathologies

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Progressive dyspnea, cough
- Wheezing, stridor, hoarseness
- Other signs/symptoms
 - May mimic chronic obstructive physiology

Treatment

- Dilatation ± stenting for unresectable disease
- Resection and end-to-end anastomosis in surgical cases

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Look for associated soft tissue component, lymphadenopathy, extrinsic compression by vessel or mass
- Include larynx in evaluation for assessment of subglottic stenosis

Reporting Tips

• Classification systems: Location, degree of airway narrowing, and transition zone of stenosis

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TERMINOLOGY

• Increased compliance and excessive collapsibility of trachea &/or bronchi

IMAGING

- Fluoroscopy
 - Diagnosis based upon > 50% decrease in airway lumen during expiration or coughing
- CT
 - Paired end-inspiratory/dynamic expiratory CT
 - Malacia defined as > 70% decrease in cross-sectional area with expiration
 - Most common finding during dynamic expiration: Tracheal collapse with anterior crescentic bowing of posterior membranous trachea (frown sign)
 - Coughing is most sensitive method for eliciting tracheal collapse on CT
 - May reveal source of chronic extrinsic tracheal compression (e.g., thyroid goiter, anomalous vessel)

TOP DIFFERENTIAL DIAGNOSES

- Chronic obstructive pulmonary disease
- Tracheal stenosis
- Relapsing polychondritis
- Chronic tracheal inflammation/infection
- Longstanding extrinsic compression
- Radiation

PATHOLOGY

 Weakening of cartilage ± hypotonia of posterior membranous trachea with degeneration and atrophy of longitudinal elastic fibers

CLINICAL ISSUES

- Intractable cough, dyspnea, wheezing, recurrent respiratory infections
- Currently regarded as underdiagnosed condition
- Acquired form relatively common in adults, incidence increases with advancing age

(Left) Frontal chest radiograph of a 57-year-old man with Mounier-Kuhn disease (tracheobronchomegaly) shows remarkable dilatation of the trachea \implies . Although considered a congenital lesion, patients with Mounier-Kuhn often present in the 4th-5th decades of life. (Right) Composite inspiratory (left) and expiratory (right) sagittal NECT of the same patient shows a diffusely dilated trachea $\stackrel{\sim}{\longrightarrow}$ that exhibits dramatic loss of luminal patency (collapse) during forced expiration \boxtimes , findings diagnostic of tracheomalacia.











Synonyms

• Tracheomalacia, bronchomalacia

Definitions

• Increased compliance and excessive collapsibility of trachea &/or bronchi

IMAGING

General Features

- Best diagnostic clue
 - Frown sign on expiration: Crescentic "lunate" anteroposterior narrowing of tracheal lumen that resembles facial frown
- Location
 - o Diffuse: May involve entire trachea ± bronchi
 - Focal: Post-intubation, focal stenosis, chronic
 - compression
- Size
 - End-inspiration tracheal lumen may be normal, widened in coronal (lunate trachea) or sagittal (saber sheath trachea) diameter, or focally narrowed (malacia may accompany focal stenosis)
 - > 70% reduction in airway lumen at expiration on CT is diagnostic
- Morphology
 - Intrathoracic trachea: Collapse with expiration due to positive extratracheal pressures
 - Extrathoracic trachea: Collapse with inspiration due to negative intratracheal pressures

Radiographic Findings

- Radiography
 - Often not evident on end-inspiratory radiography

Fluoroscopic Findings

- Chest fluoroscopy
 - Cine airway fluoroscopy historically used to evaluate tracheal wall mobility between inspiration and forced expiration or during coughing
 - Diagnosis based upon > 50% decrease in airway lumen during expiration or coughing
 - Limitations: Subjective interpretation, operatordependent, inability to simultaneously evaluate anteroposterior and lateral tracheal walls, limited visualization of tracheal anatomy and adjacent mediastinal structures

CT Findings

- NECT
 - Paired inspiratory-dynamic expiratory CT
 - Inspiratory CT: Comprehensive assessment of airway anatomy, including size, shape, wall thickness, and relationship to adjacent structures
 - Dynamic expiratory CT: Assessment of central airway collapse during 1 helical acquisition
 - Malacia: > 70% decrease in cross-sectional area with expiration
 - Most common finding during dynamic expiration: Tracheal collapse + anterior crescentic bowing of posterior membranous trachea (frown sign)

- Multiplanar and 3D reformations (including virtual bronchoscopy) not required for diagnosis
 - May reveal craniocaudad extent and morphology of tracheal abnormality
- Cine mode CT during repeated coughing maneuvers
 - Coughing: Most sensitive method for eliciting tracheal collapse
 - Can be performed with electron beam or multidetector CT
 - Requires multiple acquisitions to cover central airways

MR Findings

- 50- to 100-ms imaging time allows cine evaluation of tracheal collapse during coughing
- Dynamic ultrashort echo-time MR (UTE MR) recently used in infants
 - Computational fluid dynamics used to assess tracheal resistance and work of breathing
- Only limited published data regarding these techniques

Imaging Recommendations

- Best imaging tool
- Paired inspiratory-dynamic expiratory helical CT imaging
 Protocol advice
 - o Helical CT with 2.5- or 3.0-mm collimation
 - 50% overlapping reconstruction intervals for multiplanar reformations and 3D reconstructions
 - Perform at suspended inspiration and during dynamic, forced exhalation
 - Forced exhalation or coughing maneuver elicits greater collapse than end-expiration
 - Low-dose (40-mAs) technique recommended for dynamic expiration phase and cine imaging acquisition to limit radiation exposure

DIFFERENTIAL DIAGNOSIS

Chronic Obstructive Pulmonary Disease (COPD)

- Emphysema
 - Saber-sheath trachea

Tracheal Stenosis

• Post-intubation tracheal stenosis

Relapsing Polychondritis

- Wall thickening ± calcification that spares posterior membranous wall
- Recurrent chondritis in respiratory tract (~ 50%), ears, nose, and joints
- May induce tracheomalacia ± tracheal stenosis

Longstanding Extrinsic Compression

- Mass adjacent to trachea
 - Thyroid goiter
 - Ectatic/anomalous vasculature
 - Esophageal achalasia or stenting

Radiation

• Geographically marginated paramediastinal fibrosis with traction bronchiectasis

Mounier-Kuhn Syndrome

• Congenital tracheobronchomegaly
PATHOLOGY

General Features

- Etiology
 - Increased compliance and excessive collapsibility of airways due to weak cartilaginous rings
 - o Primary tracheomalacia: Congenital weakness
 - Abnormal cartilaginous matrix (chondromalacia, mucopolysaccharidoses, such as Hurler syndrome)
 - Inadequate maturity of cartilage (e.g., premature infants)
 - Congenital tracheoesophageal fistula or esophageal atresia
 - Mounier-Kuhn syndrome (congenital tracheobronchomegaly)
 - Secondary (acquired) tracheobronchomalacia
 - COPD (often correlates with severity of emphysema)
 - Prior (often prolonged) intubation with endotracheal or tracheostomy tube
 - Prior surgery (e.g., lung resection, lung transplantation)
 - Chronic inflammation (e.g., relapsing polychondritis, cystic fibrosis, chronic vaping)
 - Chronic extrinsic compression (e.g., thyroid mass, vascular ring, aneurysm)
 - Radiation therapy
 - Tracheoesophageal fistula
 - Idiopathic
- Associated abnormalities
 - Congenital form: ± associated cardiovascular abnormalities, polychondritis, bronchopulmonary dysplasia, gastroesophageal reflux
 - o Chondrodystrophies; Larsen syndrome; Trisomy 21
- Weakening of cartilage &/or hypotonia of posterior membranous trachea with degeneration and atrophy of longitudinal elastic fibers

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Intractable cough, dyspnea, wheezing, croup, recurrent respiratory infections
 - Congenital form usually manifests in first weeks to months of life: Expiratory stridor, cough, difficulty feeding
- Sudden exacerbation possible with anesthesia induction
- Widely regarded as underdiagnosed condition
- Patients often misdiagnosed as having asthma
- If imaging requisition states asthma, always look for tracheal stenosis, tracheal mass, or malacia
- Inspiratory wheeze if lesion extrathoracic; expiratory wheeze if lesion intrathoracic
- Post-intubation: Symptoms may appear several weeks to years after intubation
- Flexible bronchoscopic findings in tracheomalacia
 - > 50% narrowing of lumen in AP diameter
 Normal: < 40%
 - In children, expiratory-inspiratory cross-sectional area ratio < 0.35 (normal: 0.82)

Demographics

- Age
 - Neonates to older adults
- Sex
 - Acquired form has male predominance
- Epidemiology
 - Congenital form more common in premature infants
 - Acquired form relatively common in adults, incidence increases with advancing age
 - o 7-53% of patients with COPD
 - 15% of children and up to 70% of adults with cystic fibrosis
 - 5-23% of patients undergoing bronchoscopy for respiratory symptoms
 - 5-10% of patients referred to pulmonologists for chronic cough
 - 10% of patients referred for CTA for suspected pulmonary embolism

Natural History & Prognosis

- Acquired form usually progressive over time without therapy
- Congenital form sometimes self-limited (especially in premature infants with malacia due to immature cartilage)

Treatment

- Conservative therapy for mildly symptomatic patients
- Nasal continuous positive airway pressure can help relieve nocturnal symptoms
- Silicone stents for severely symptomatic patients who are poor surgical candidates
- Surgical repair with tracheoplasty procedure for severely symptomatic patients with diffuse malacia
- Surgical repair with aortopexy procedure when due to longstanding extrinsic compression by vascular lesion

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Recognize characteristics of expiratory CT to ensure that expiratory imaging is diagnostic
 - Increased lung attenuation
 - Decreased anteroposterior dimension of thorax
 - Posterior wall of trachea should be flat or bowed forward
- Malacia defined on basis of percentage change in tracheal lumen between inspiration and expiration
 - If either component of CT is not acquired during correct phase of respiration, diagnostic errors may occur
 - Coaching patient with careful breathing instructions necessary to ensure diagnostic study

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Tracheobronchomalacia





(Left) Axial NECT obtained during full inspiration shows a normal tracheal diameter. The posterior wall of the trachea (composed mainly of the trachealis muscle) bows outward \square , which indicates that this is an inspiratory image. (Right) Axial NECT of the same patient obtained during full expiration shows severe tracheal narrowing 🔁 in a frown sign configuration, which is highly suggestive of tracheomalacia. Inspiratory CT is insensitive for the detection of tracheomalacia.





(Left) NECT virtual bronchoscopy image obtained at end-inspiration shows a normal appearance of the tracheal lumen at level of carina. (Right) NECT virtual bronchoscopy image obtained during dynamic expiration at level of carina shows excessive anterior bowing of the posterior tracheal wall ➡, consistent with tracheomalacia.





(Left) Axial NECT of a patient with a history of symptomatic tracheobronchomalacia shows a stent \supseteq placed for treatment of a lunate-shaped trachea. (Right) Coronal NECT of the same patient shows stents 🛃 in the trachea and in the left mainstem bronchus ₽ placed endoscopically for . treatment of tracheobronchomalacia. Stents are most useful for symptomatic treatment of patients with tracheobronchomalacia when surgery is either contraindicated &/or refused by the patient.

Middle Lobe Syndrome

KEY FACTS

TERMINOLOGY

- Middle lobe syndrome (MLS)
- Right middle lobe (RML)
- Chronic/recurrent nonobstructive middle lobe atelectasis or consolidation on serial imaging

IMAGING

- Radiography
 - Persistent or recurrent RML opacification
 - Obscuration of right heart border; atelectasis, consolidation
- CT
 - Endoluminal, extrinsic or mixed etiologies
 - Obstruction (atelectasis)
 - Endoluminal neoplastic (e.g., carcinoid)
 - Endoluminal nonneoplastic (e.g., bronchial stenosis)
 - Extrinsic (e.g., lymphadenopathy)
 - o Non-obstructive: Indolent infection, asthma
 - o Mixed obstructive and nonobstructive (e.g., sarcoidosis

TOP DIFFERENTIAL DIAGNOSES

- Bacterial pneumonia
- Pectus excavatum deformity

PATHOLOGY

• Bronchiectasis, bronchitis, bronchiolitis, and organizing pneumonia

CLINICAL ISSUES

- Frequent incidental finding in asymptomatic patient imaged for other reasons
- Any age depending on etiology; F > M
- Symptoms and signs
 - Chronic cough, hemoptysis
 - Recurrent pulmonary infection
- Bronchoscopy is best option to determine etiology when not evident on CT
- Treatment
- Largely depending on etiology

(Left) Lateral chest radiograph of a patient with right middle lobe syndrome shows complete middle lobe opacification with approximation of the fissures \square indicative of atelectasis. (Right) Lateral chest radiograph of a patient with middle lobe pneumonia shows a similar middle lobe opacity \square . However, in this case, there is little displacement of the minor fissure. Middle lobe syndrome refers to chronic or recurrent middle lobe opacification due to volume loss or airspace disease.





(Left) Lateral chest radiograph of a patient with a right middle lobe bronchial carcinoid shows middle lobe linear opacities and volume loss 🔁. (Right) Composite image with axial NECT of the same patient at different contiguous levels shows obliteration \supseteq of the middle lobe bronchus and complete middle lobe postobstructive atelectasis 🔁. Note that the cause of the obstruction is not always evident on imaging, and bronchoscopy is often required to exclude malignancy.





Abbreviations

- Middle lobe syndrome (MLS)
- Right middle lobe (RML)

Synonyms

• Right MLS

Definitions

- Chronic or recurrent nonobstructive middle lobe atelectasis or consolidation
 - Identified on serial imaging
 - RML prone to atelectasis and airspace disease
 - Longer, narrower bronchus
 - Acute take-off from bronchus intermedius
 - RML bronchus surrounded by lymph nodes;
 - convergence of upper and lower lobe lymphatics
 - Minor fissure prevents collateral ventilation

IMAGING

General Features

- Best diagnostic clue
 - Chronic middle lobe atelectasis or opacification
- Location
 - Most commonly middle lobe followed by lingula

Radiographic Findings

- Radiography
 - MLS diagnosis implies serial chest radiography that shows persistent or recurrent RML involvement
 - Focal opacity obscuring right heart border
 - Wedge-shaped opacity on lateral chest radiography; sharply marginated by major and minor fissures
 - ± air bronchograms
 - Shifting of fissure(s) related to atelectasis
 - Rare identification of etiology

CT Findings

- Obstruction (atelectasis)
 - o Endoluminal, extrinsic, or mixed
 - Endoluminal neoplastic
 - □ Carcinoid: Peribronchovascular nodule with endoluminal component
 - □ Lung cancer: Nodule or mass; may be obscured by postobstructive pneumonitis
 - Endobronchial metastasis: Colon, renal, breast, melanoma, etc.
 - Endoluminal nonneoplastic
 - Broncholith
 - Airway erosion by adjacent lymph node; endoluminal calcification; difficult differentiation from extrinsic calcified peribronchovascular lymph node producing mass effect on airway (common in pneumoconiosis)
 - Foreign body
 - Common in older patients; radiopaque foreign body easily identified; nonradiopaque foreign body may be impossible to identify; common associated postobstructive pneumonitis typically without associated volume loss

- o Extrinsic
 - Lymphadenopathy of any etiology; difficult identification on NECT
 - Enlarged right atrium may compress RML bronchus; resultant chronic middle lobe atelectasis
- o Stenosis
 - Sequela of inflammatory or infections process; commonly associated with postradiation changes
- Non-obstructive
 - Indolent infection
 - Nontuberculous mycobacterial infection: Lady Windermere syndrome (bronchiectatic); often both RML and lingula involved; cellular bronchiolitis and bronchiectasis in other pulmonary lobes but to lesser extent
 - Chronic *Pseudomonas* infection: Indistinguishable from nontuberculous mycobacterial infection
 - o Asthma
 - Pure atelectasis
 - Smaller, less mature airways more prone to collapse with greater peripheral airway resistance, increased chest wall compliance, and incomplete development of collateral ventilation pathways
- Mixed
 - o Inflammatory
 - Sarcoidosis
 - Bilateral hilar and mediastinal lymphadenopathy ± intrinsic calcification
 - Coexisting endoluminal component (bronchial stenosis and micronodularity)
 - o Pneumoconiosis
 - Similar to sarcoidosis; coexisting lymphadenopathy (often calcified), bronchial stenosis, and micronodularity
 - Other findings of silicosis or coal worker's pneumoconiosis: Solid or calcified perilymphatic nodules, lymph nodes with eggshell calcification

Atelectatic middle lobe

- Triangular opacity bound by major fissure posteriorly and minor fissure anteriorly
- Shifting of fissures essential for differentiation from consolidation

Bronchiectasis

- Hypodense branching opacities: Mucus plugs or air within bronchiectatic airways
- Pleural thickening
- ± surrounding calcified lymph nodes or lung nodules related to prior granulomatous infection

Imaging Recommendations

- Best imaging tool
 - CT is optimal imaging modality for evaluation of bronchiectasis and endobronchial obstruction

DIFFERENTIAL DIAGNOSIS

Bacterial Pneumonia

• Acute illness; resolves in 4-6 weeks

Pectus Excavatum Deformity

• Vague middle lobe opacity on frontal radiography

Middle Lobe Syndrome

Etiology of Right Middle Lobe Syndrome		
Mechanism	Etiology	Disease Process
Obstructive		
Endoluminal	Neoplastic	Carcinoid Lung cancer Endobronchial metastasis
	Non-neoplastic	Broncholith Foreign body
Extrinsic	Lymphadenopathy	Benign Lymph node metastasis
	Anatomic	Enlarged right atrium
Stenosis	Bronchial stenosis	Post-inflammatory Post-infectious
	latrogenic	Radiation-induced
Non-Obstructive		
Infectious	Indolent infection	Nontuberculous mycobacteria Pseudomonas
Immature airways	Childhood asthma	
Post-inflammatory	Bronchiectasis	Ciliary dyskinesia Cystic fibrosis Allergic bronchopulmonary aspergillosis
Mixed		
Inflammatory	Sarcoidosis	
Pneumoconiosis	Pneumoconiosis	Silicosis and coal worker's pneumoconiosis
Infectious	Tuberculosis	Tuberculous lymphadenitis ± bronchial involvement

• Lateral radiograph shows characteristic sternal depression and no middle lobe airspace disease

PATHOLOGY

General Features

- Etiology
 - Chronic inflammatory process with lung destruction and fibrosis
 - Complete fissures prevent collateral ventilation; impaired clearing of secretions
 - ± bronchial compression by adjacent enlarged lymph nodes
 - Reported associations
 - Tuberculosis and atypical mycobacterial infection
 - Fungal infection
 - Sarcoidosis
 - Cystic fibrosis
 - Asthma; allergic bronchopulmonary aspergillosis

Gross Pathologic & Surgical Features

• Bronchiectasis, bronchitis, bronchiolitis, and organizing pneumonia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Frequent incidental finding in asymptomatic patient imaged for other reasons
 - Chronic cough, hemoptysis

- Recurrent pulmonary infection
- Other signs/symptoms
 - Dyspnea, chest pain, wheezing

Demographics

- Age
 - Any age depending on etiology
- Sex
 - o F>M

Diagnosis

- CT may allow determination of etiology, but often not possible
- Bronchoscopy is best option to determine etiology when not evident on CT
 - Bronchoscopy often required to exclude malignancy

Treatment

- Dependent on etiology
- Long-term antibiotics
- Balloon dilatation, stent placement, or laser therapy for focal stenosis
- Surgical lobectomy for recurrent pneumonia and failed medical management

- Rashid A et al: Infectious causes of right middle lobe syndrome. Cancer Control. 24(1):60-5, 2017
- Romagnoli V et al: Middle lobe syndrome in children today. Paediatr Respir Rev. 15(2):188-93, 2014

Middle Lobe Syndrome





(Left) PA chest radiograph of a patient with right middle lobe cancer shows an ill-defined opacity ⇒ that obscures the right cardiac border. (Right) Sagittal CECT of the same patient shows stenosis ⇒ at the origin of the right middle lobe bronchus and

postobstructive volume loss Description: While a definite mass is not evident, bronchoscopic biopsy demonstrated lung cancer. Bronchoscopy is critical for exclusion of malignancy in the context of right middle lobe syndrome.





(Left) Composite image with axial NECT of a patient with right middle lobe syndrome due to broncholithiasis shows an endobronchial broncholith rightarrow at the origin of the rightmiddle lobe bronchus and complete atelectasis of the right middle lobe 🔁 Broncholiths result from erosion of granulomatous lymph nodes (often from histoplasmosis) into the adjacent airway. (Right) Bronchoscopic photograph of the same patient shows the irregular obstructing endobronchial broncholith.





(Left) Lateral chest radiograph of a patient with silicosis and right middle lobe syndrome shows atelectasis \supseteq of the right middle lobe, which persisted on serial imaging. (Right) Axial CECT of the same patient shows extensive bilateral perilymphatic micronodularity, right middle lobe atelectasis $\overline{\mathbb{Z}}$, and nonspecific nodular stenosis of the right middle lobe bronchus \square . In silicosis and sarcoidosis, the mechanism of atelectasis can be mixed due to extrinsic compression by lymph nodes and endoluminal involvement by granulomas.

(Left) PA chest radiograph of a patient with sarcoidosis shows subtle reticulation \square in the region of the right middle lobe and to a lesser extent the lingula (note obscuration of the left heart border 🖂. (Right) Composite image with axial NECT (left) and NECT MIP reformatted image (right) of the same patient shows middle lobe volume loss \supseteq and extensive intrinsic bronchiectasis 🔁. Note irregular and nodular stenosis *I* at the origin of the right *i* at the origin of the right middle lobe bronchus due to endoluminal granulomas.





(Left) PA chest radiograph of a patient with indolent nontuberculous mycobacterial infection shows ill-defined right middle lobe 🔁 and lingular 🖂 opacities. (Right) Composite image with axial CECT (left) and CECT minIP reformatted image of the same patient shows middle lobe volume loss and extensive bronchiectasis. Note extensive mosaic attenuation elsewhere. The constellation of findings is virtually diagnostic of nontuberculous mycobacterial infection in an older white woman.





(Left) PA chest radiograph of a young woman with asthma shows hazy opacities 🔁 in the region of the middle lobe. This finding is subtle and can be easily overlooked. (Right) Composite image with axial NECT of the same patient at contiguous levels shows complete right middle lobe atelectasis ⊇. Asthma is a common cause of middle lobe syndrome in young individuals. Postulated hypotheses include smaller and less mature airways and incomplete development of collateral ventilation pathways.





Middle Lobe Syndrome





(Left) Lateral chest radiograph of a patient with a history of histoplasmosis shows complete right middle atelectasis ⊇. (Right) Axial NECT of the same patient shows complete atelectasis of the right middle lobe. Bronchoscopic assessment demonstrated benignappearing stenosis at the origin of the right middle lobe bronchus. Similar findings could be seen in the context of remote treated tuberculosis.





(Left) PA chest radiograph of a patient who underwent mediastinal radiation therapy demonstrates post radiation changes in the region of the right middle lobe \supseteq and the left mid lung zone 🔁 with resultant obscuration of the cardiac borders. (Right) Composite image with axial NECT minIP reformatted image (left) and axial NECT (right) of the same patient shows complete right middle lobe atelectasis \supseteq with scattered intrinsic foci of bronchostenosis.





(Left) PA chest radiography of a patient with severe cardiomegaly shows persistent right middle lobe opacity 🔁 on serial imaging (not shown). (Right) Axial NECT of the same patient shows right middle lobe atelectasis 🔁 and nonvisualization of the right middle lobe bronchus. The patient underwent bronchoscopy which revealed extrinsic compression secondary to the adjacent markedly enlarged right atrium. Bronchoscopy is critical for exclusion of endobronchial malignancy.

KEY FACTS

TERMINOLOGY

- Granulomatosis with polyangiitis (GPA)
- ANCA-associated vasculitis (AAV)
- Multisystem disease characterized by small to medium vessel necrotizing vasculitis with granulomatous inflammation

IMAGING

- Tracheal wall thickening
- Smooth or nodular
- Circumferential (involvement of posterior membranous trachea)
- Tracheal stenosis
 - Subglottic strictures more frequent than distal involvement
- Tracheomalacia
- Associated with stenosis or cartilage injury
- Bronchiectasis, atelectasis, &/or pneumonia
 - Associated with distal airway involvement

TOP DIFFERENTIAL DIAGNOSES

- Postintubation/post-tracheostomy stenosis
- Tracheobronchial amyloidosis
- Relapsing polychondritis
- Tracheobronchopathia osteochondroplastica

PATHOLOGY

• GPA is clinical phenotype of AAV

CLINICAL ISSUES

- Dyspnea, hoarseness, and stridor
- Tracheobronchial involvement is frequent in GPA (15-55%)
- Tracheal involvement typically occurs in setting of multisystem disease

DIAGNOSTIC CHECKLIST

 Consider airway-PGA in differential diagnosis of circumferential tracheal wall thickening &/or subglottic stenosis

(Left) Coronal NECT of a patient with granulomatosis with polyangiitis and airway involvement shows mild diffuse mucosal nodularity with segmental tracheal narrowing 🖂. (Right) Coronal CECT minIP reformatted image of a patient with granulomatosis with polyangiitis and airway involvement shows focal severe stenosis of the subglottic trachea 🔁, a common manifestation of airway involvement.





(Left) Coronal NECT of a patient with granulomatosis with polyangiitis and airway involvement shows longsegment mural thickening of the trachea with secondary tracheal stenosis ▷. (Right) Axial NECT of a patient with granulomatosis with polyangiitis and airway involvement shows eccentric asymmetric soft tissue thickening of the right greater than left tracheal wall ▷.





Abbreviations

- Granulomatosis with polyangiitis (GPA)
- ANCA-associated vasculitis (AAV)

Synonyms

• Wegener granulomatosis (WG)

Definitions

• Multisystem disease characterized by small to medium vessel necrotizing vasculitis with granulomatous inflammation

IMAGING

Radiographic Findings

• Segmental or lobar atelectasis due to airway involvement

CT Findings

- Tracheal wall thickening
 - Smooth or nodular
 - Segmental and focal (2- to 4-cm length)
 - Circumferential (involvement of posterior membranous trachea)
- Tracheal stenosis
 - Subglottic strictures more frequent than distal or bronchial involvement
- Tracheomalacia
 - Associated with stenosis or cartilage injury
- Bronchiectasis, atelectasis, &/or pneumonia
 Associated with distal airway involvement

Imaging Recommendations

- Protocol advice
 - Dynamic NECT (inspiratory and expiratory)
 - Multiplanar reformations
 - Imaging should include chest and neck (from level of glottis)

DIFFERENTIAL DIAGNOSIS

Postintubation/Post-Tracheostomy Stenosis

- At tracheal stoma or at site of endotracheal tube balloon
- Symmetric narrowing < 2 cm in length
- Hourglass shape

Tracheobronchial Amyloidosis

- Focal or diffuse nodular soft tissue mural thickening
 Mural calcification/ossification may be present
- Involvement of posterior membranous airway wall

Relapsing Polychondritis

- Long-segment tracheobronchial strictures
- Spares posterior membranous trachea
- Involvement of extrathoracic cartilages

Tracheobronchopathia Osteochondroplastica

- Focal or diffuse soft tissue &/or calcified mural nodules
- Spares posterior tracheal wall

PATHOLOGY

General Features

• Etiology

- GPA is clinical phenotype of AAV
- Immunoassay techniques define two major ANCA serotypes: Proteinase 3 (PR3)-ANCA and myeloperoxidase (MPO)-ANCA
- Pathogenesis of AAV involves genetic and epigenetic factors (low DNA methylation in regulating MPO and PR3 transcription)
- Inflammatory mucosal erosions (mucosal ulcers)
- Genetics
 - PR3-ANCA vasculitis is associated with genes SERPINA1 (encoding alpha-1 antitrypsin), PRTN (encoding PR3), and human leukocyte antigen (HLA) loci (HLA-DP4)
 - MPO-ANCA vasculitis has been reported to be associated with HLA-DQ

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dyspnea, hoarseness, and stridor
- Other signs/symptoms
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- Pulmonary and kidney disease manifestations
- Frequent tracheobronchial involvement (15-55%)
- Tracheal involvement typically occurs in setting of multisystem disease
- Cases of isolated large airway involvement have been described

Demographics

- Age
 - o Any age; mean age at diagnosis: 40-55 years
- Sex
- Airway involvement much more common in women
- Epidemiology
 - o Prevalence: 21.8 cases per 100,000 persons

Natural History & Prognosis

• Airway stenosis should be considered severe manifestation of GPA

Treatment

• Tracheal stenosis requires treatment with high-dose systemic glucocorticoids and cyclophosphamide or rituximab

DIAGNOSTIC CHECKLIST

Consider

• Airway-GPA in differential diagnosis of circumferential tracheal mural thickening or subglottic stenosis

SELECTED REFERENCES

1. Kitching AR et al: ANCA-associated vasculitis. Nat Rev Dis Primers. 6(1):71, 2020

KEY FACTS

TERMINOLOGY

- Focal or diffuse submucosal deposition of amyloid in tracheobronchial tree
 - Characterized by amyloid light chain (AL) protein

IMAGING

- Nodular soft tissue thickening of airway wall
 - o Multifocal submucosal plaques (most common)
 - May involve posterior tracheal wall
 - Focal airway nodules
 - May exhibit calcification
- May affect larynx, trachea, central and segmental bronchi
- Obstructive effects
 - Bronchiectasis
 - Atelectasis
 - o Consolidation
 - Hyperinflation

TOP DIFFERENTIAL DIAGNOSES

- Acquired tracheal stenosis
- Tracheobronchopathia osteochondroplastica
- Granulomatosis with polyangiitis
- Relapsing polychondritis
- Tracheal neoplasms

PATHOLOGY

 Abnormal protein deposition in submucosal aspects of airway walls

CLINICAL ISSUES

- Symptoms/signs (gradual onset over several years)
 Chronic cough, dyspnea, wheezing, hemoptysis
- Wide age range: 16-85 years (mean: 53 years)
- 5-year survival rates: Range of 30-50%
- Treatment: Bronchoscopic/surgical resection, radiation therapy for progressive disease

(Left) PA chest radiograph (coned-down to the trachea) shows smooth bilateral paratracheal stripe thickening \square , suggestive of tracheal wall thickening. (Right) Coronal CECT shows diffuse tracheobronchial wall thickening \blacksquare with areas of significant luminal narrowing and scattered amorphous calcifications 🛃 in areas of airway wall thickening. Diffuse, undulating circumferential airway wall thickening with or without calcification is typical of tracheobronchial amyloidosis.





(Left) Axial CECT of a patient with focal tracheal amyloidosis shows thickening of the anterolateral upper tracheal walls 🔁. This disease may be asymmetric or circumferential, and most commonly affects the cervical trachea. (Right) Axial CECT shows amyloidosis manifesting as smooth, circumferential mural thickening 🛃 of the right upper lobe and bilateral mainstem bronchi with smooth luminal narrowing. Calcification may or may not be present.





Synonyms

• Airway amyloidosis

Definitions

- Focal or diffuse submucosal deposition of amyloid in tracheobronchial tree
 - Characterized by amyloid light chain (AL) protein

IMAGING

General Features

- Best diagnostic clue
 - Focal or diffuse nodular soft tissue thickening of airway walls ± calcification

Radiographic Findings

- Chest radiography is often normal
- Atelectasis &/or consolidation from airway obstruction

CT Findings

- Nodular soft tissue thickening of airway wall
 - Multifocal submucosal plaques: Most common in cervical trachea, eccentric or circumferential, may involve posterior tracheal wall
 - Focal airway nodule(s)
 - May exhibit calcification
 - May produce luminal narrowing and obstruction
- May affect larynx, trachea, and central to segmental bronchi
 - Associated postobstructive effects: Atelectasis, consolidation, bronchiectasis, hyperinflation

MR Findings

- Focal or diffuse airway wall thickening
- ± luminal narrowing and obstruction
- Low signal intensity relative to skeletal muscle on T2WI
- ± contrast enhancement

Nuclear Medicine Findings

- Bone scintigraphy may show uptake of Tc-99m diphosphonate in amyloid deposits
- Reports of uptake of technetium pyrophosphate in amyloid deposits

Imaging Recommendations

- Best imaging tool
 - Volumetric thin-section CT: Identification of submucosal abnormalities, determination of extent of involvement, assessment of secondary effects of airway obstruction
- Protocol advice
 - Multiplanar reformatted images to assess longitudinal extent of airway involvement

DIFFERENTIAL DIAGNOSIS

Acquired Tracheal Stenosis

- History of prolonged intubation
- Focal, circumferential, or eccentric soft tissue thickening of airway wall
- Located at tracheal stoma or level of tube balloon cuff

Tracheobronchopathia Osteochondroplastica

- Nodular mural tracheobronchial osseous/chondroid lesions
 Typically calcified
 - Anterolateral tracheal walls; spares posterior trachea

Granulomatosis With Polyangiitis

- Subglottic involvement: Soft tissue thickening of tracheal wall and luminal stenosis
- Posterior tracheobronchial walls may be involved
- May affect distal tracheobronchial tree

Relapsing Polychondritis

• Soft tissue thickening of airway wall: Spares posterior trachea, ± calcification, typically limited to airway cartilages

Tracheal Neoplasms

- Typically focal airway soft tissue nodule
- May exhibit local invasion or mediastinal lymphadenopathy

PATHOLOGY

General Features

- Etiology
- o Unknown
- Extracellular deposition of abnormal eosinophilic proteins

Gross Pathologic & Surgical Features

• Thick irregular airway wall with waxy or firm deposits

Microscopic Features

- Abnormal protein deposition in submucosal aspects of airway walls
- Stains with Congo red
 - Characteristic apple-green birefringence on polarized microscopy

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Symptoms (gradual onset over several years): Chronic cough, dyspnea, wheezing, hemoptysis
 May be misdiagnosed as asthma

Demographics

- Age
- Wide range: 16-85 years (mean: 53 years)
- Sex

o M:F = 2:1

Natural History & Prognosis

• 5-year survival rates: Range of 30-50%

Treatment

- Bronchoscopic treatment of obstructing airway lesions
- Surgical resection; usually for extensive involvement
- Medical therapy; limited success
- Radiation therapy for progressive disease

- 1. Bedayat A et al: Tracheobronchial tumors: radiologic-pathologic correlation of tumors and mimics. Curr Probl Diagn Radiol. 49(4):275-84, 2020
- 2. Shepard JO et al: Imaging of the trachea. Ann Cardiothorac Surg. 7(2):197-209, 2018

KEY FACTS

TERMINOLOGY

- Tracheobronchopathia osteochondroplastica (TO)
- Rare idiopathic benign condition characterized by multiple submucosal osteocartilaginous nodules in central airway walls (trachea and proximal bronchi)

IMAGING

- Radiography
 - Chest radiograph may be normal
 - Nodular irregularity of tracheal wall
 - Asymmetric tracheal stenosis
 - Central bronchial narrowing/obstruction
- CT
 - Multiple small mural nodules ± calcification
 - Involvement of anterolateral tracheal and proximal bronchial walls
 - Sparing of posterior membranous trachea
 - Postobstructive atelectasis/consolidation

TOP DIFFERENTIAL DIAGNOSES

- Tracheobronchial amyloidosis
- Relapsing polychondritis
- Granulomatosis with polyangiitis
- Tracheolaryngeal papillomatosis

PATHOLOGY

- Multifocal submucosal tracheal and bronchial nodules
- Intact mucosa
- Hyalinized fibrocollagenous tissue with fibrosis, calcification

CLINICAL ISSUES

- Usually asymptomatic
- Dyspnea, cough, wheezing, hemoptysis, recurrent pneumonia
- Treatment
 - Endoscopic/surgical resection or stent placement for obstructing lesions

(Left) Axial CECT of a 57-yearold woman with tracheobronchopathia osteochondroplastica shows calcified plaque-like nodules \square along the anterolateral tracheal walls and characteristic sparing of the posterior membranous trachea. (Right) Axial NECT of a 67-year-old man with tracheobronchopathia osteochondroplastica shows anterior tracheal mural calcified nodules 🔁. This is an idiopathic benian condition that typically affects the trachea and the mainstem bronchi.





(Left) Axial NECT of a 61-yearold woman with tracheobronchopathia osteochondroplastica shows submucosal calcified and noncalcified anterolateral tracheal nodules 🔁. Most patients are asymptomatic, and the diagnosis is made incidentally. (Right) Axial NECT of a 63-year-old woman shows nodularity of the left anterolateral tracheal wall *⊡*, consistent with tracheobronchopathia osteochondroplastica, which may manifest with calcified or noncalcified rounded or plaque-like mural nodules.





Abbreviations

• Tracheobronchopathia osteochondroplastica (TO)

Synonyms

- Tracheopathia osteoplastica
- Tracheopathia osteochondroplastica

Definitions

• Rare idiopathic benign condition: Multiple submucosal osteocartilaginous nodules in central airway walls (trachea and proximal bronchi)

IMAGING

General Features

- Best diagnostic clue
 - o Nodular anterolateral tracheal wall
 - Sparing of posterior membranous tracheal wall
- Location
 - o Anterolateral tracheal walls; typically distal 2/3 of tracheao Proximal bronchial walls
- Size
 - o Small uniform nodules; 1-5 mm
- Morphology
- Round, plaque-like, polypoid; may coalesce

Radiographic Findings

- Radiography
 - Chest radiograph usually **normal**
 - Nodular irregularity of tracheal wall
 - Asymmetric tracheal stenosis
 - Central bronchial stenosis/obstruction: Lobar collapse, postobstructive pneumonia

CT Findings

- Multiple small mural nodules; protrude into airway lumen • Calcified or noncalcified
- Involvement of anterolateral tracheal and proximal bronchial walls
- Spares posterior membranous airway wall (where there is no cartilage)
- Variable degree of airway stenosis
- Saber-sheath appearance of trachea in some patients
- Direct visualization and assessment of postobstructive effects
 - o Atelectasis
 - Postobstructive pneumonia
- Occasional involvement of larynx and subglottic trachea

Imaging Recommendations

- Best imaging tool
 - CT is imaging modality of choice for identification and characterization of TO
- Protocol advice
 - o Intravenous contrast administration is not required

DIFFERENTIAL DIAGNOSIS

Tracheobronchial Amyloidosis

• Circumferential tracheal/bronchial wall thickening, calcified or noncalcified submucosal nodules

- Involvement of posterior membranous trachea
- Narrowing of airway lumen

Relapsing Polychondritis

- Thickening of tracheal and mainstem bronchial cartilages
- Anterolateral tracheal walls; membranous trachea spared
- Affects other cartilaginous structures: Ear and joints

Granulomatosis and Polyangiitis

- Noncalcified, diffuse, nodular or smooth circumferential tracheal mural thickening
- Segmental and subsegmental bronchial wall thickening
- Association with multiple pulmonary nodules, masses, or consolidations with frequent cavitation

Tracheolaryngeal Papillomatosis

- Noncalcified mucosal nodules; also affects larynx
- Childhood or young adulthood presentation
- Distal dissemination may lead to cavitary pulmonary nodules

PATHOLOGY

Gross Pathologic & Surgical Features

 Multifocal submucosal tracheal and bronchial nodules; intact mucosa

Microscopic Features

- Hyalinized fibrocollagenous tissue with fibrosis, calcification, necrosis
- Cartilaginous, osseous, and hematopoietic tissues
- Squamous metaplasia of overlying mucosa

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Usually asymptomatic
 - Dyspnea, cough, wheezing, hemoptysis, recurrent pneumonia
 - o May be discovered during intubation or bronchoscopy

Demographics

- Age
- Usually > 50 years of age
- Sex
- Male > female
- Epidemiology
 Idiopathic
 - 0.5% prevalence at autopsy

Natural History & Prognosis

- Slow progression
- Usually incidental diagnosis

Treatment

• Endoscopic/surgical resection or stent placement for obstructing lesions

- Cho HK et al: Clinical course of tracheobronchopathia osteochondroplastica. J Thorac Dis. 12(10):5571-5579, 2020
- Kamangar N: Tracheobronchopathia osteochondroplastica. Mayo Clin Proc. 94(6):949-50, 2019

Relapsing Polychondritis

KEY FACTS

TERMINOLOGY

- Relapsing polychondritis (RPC)
- Autoimmune disease characterized by recurrent inflammation of cartilaginous structures

IMAGING

- Tracheal wall thickening
 - Wall thickness > 2 mm ± calcification
- Spared posterior membrane
- Increased airway wall attenuation
- Destruction of cartilaginous rings
- Tracheal or tracheobronchial narrowing (late finding)
- Mosaic attenuation
- Air trapping (expiratory CT)

TOP DIFFERENTIAL DIAGNOSES

- Granulomatosis with polyangiitis
- Tracheopathia osteochondroplastica
- Amyloidosis

PATHOLOGY

- Unknown etiology of RPC
- Postulated autoimmune reaction to type II collagen (abundant in cartilage and sclera)

CLINICAL ISSUES

- Auricular chondritis
- Ocular manifestations (scleritis, episcleritis, or conjunctivitis)
- Nasal chondritis (painful inflammation of nasal cartilage)
- Costochondritis (retrosternal chest pain)
- Laryngotracheal and pulmonary involvement (50% during disease course)
- Respiratory complications and lower respiratory tract infections represent most common causes of death

DIAGNOSTIC CHECKLIST

• Consider RPC in patients with tracheal wall thickening (> 2 mm) that spares posterior membrane

(Left) Axial NECT of the head of a patient with relapsing polychondritis shows extensive calcification of the cartilages of the external ear ⊇. Besides the auricular cartilages, many other cartilages can be involved, including nasal, costochondral, and laryngeal. (Right) Axial NECT of the same patient shows marked smooth tracheal wall thickening ⊇ that spares the posterior membranous trachea.





(Left) Coronal NECT minIP reformatted image of a patient with relapsing polychondritis shows narrowing of the distal trachea and the right mainstem bronchus a. (Right) Axial expiratory NECT of the same patient shows expiratory collapse of the distal trachea and areas of pulmonary air trapping 2.

Tracheobronchomalacia is a common sequela related to recurrent inflammation of the tracheal cartilages and is often associated with mosaic attenuation and air-trapping.





Abbreviations

• Relapsing polychondritis (RPC)

Definitions

• Autoimmune disease characterized by recurrent inflammation of cartilaginous structures

IMAGING

General Features

- Best diagnostic clue
 - o Tracheal wall thickening, spares posterior membrane

Radiographic Findings

- Radiography
 - Trachea and mainstem bronchi
 - Diffuse mural thickening
 - Spared posterior tracheal stripe on lateral radiography
 - Fixed or variable stenosis
 - o Lung
 - Obstructive atelectasis or pneumonia
 - Bronchiectasis (25%)
 - Air-trapping (50%)
 - o Cardiovascular
 - Aneurysm, especially involving ascending aorta
 - Cardiac enlargement from aortic or mitral valve regurgitation or pericarditis

CT Findings

- NECT
 - o Tracheal wall thickening
 - Wall thickness > 2 mm ± calcification
 - Spared posterior membrane
 - o Increased airway wall attenuation
 - Destruction of cartilaginous rings
 - o Tracheal or tracheobronchial stenosis (late finding)
 - o Mosaic attenuation
 - o Bronchiectasis
- Expiratory CT
 - Tracheobronchomalacia: Tracheobronchial expiratory collapse
 - o Air-trapping
 - Hypoattenuation foci on background of hyperattenuating normal lung (expiratory CT)
 - Malacia or fixed tracheobronchial stenoses

Imaging Recommendations

- Best imaging tool
 - Dynamic NECT (inspiratory and expiratory)

DIFFERENTIAL DIAGNOSIS

Granulomatosis With polyangiitis

- Concentric irregular tracheal wall thickening
- Cavitary nodules/consolidations and ground-glass opacities
- Smooth subglottic narrowing
- c-ANCA(+)

Tracheobronchopathia Osteochondroplastica

• Tracheal wall thickening, spares posterior membrane

- Nodules that protrude into tracheal lumen
- Older age group

Amyloidosis

- Concentric and irregular tracheal wall thickening with secondary narrowing
- Occasional calcification

PATHOLOGY

General Features

- Etiology
 - Unknown etiology of RPC
 - Postulated autoimmune reaction to type II collagen (abundant in cartilage and sclera)
 - Three separate phenotypes: Hematological form (10%), respiratory form (25%), mild form (65%)
- Associated abnormalities
 - Other autoimmune disorders

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Auricular chondritis (most common manifestation)
 - Ocular manifestations (scleritis, episcleritis, conjunctivitis)
 - Nasal chondritis (painful inflammation of nasal cartilage)
 - Costochondritis (retrosternal chest pain)
 - Laryngotracheal and pulmonary involvement (50% during disease course)
 - Laryngeal chondritis (hoarseness, stridor)
- Other signs/symptoms
 - Cardiovascular involvement (aortic regurgitation, aneurysms)
 - Skin manifestations (purpura, papules, nodules)
- Glomerulonephritis from circulating immune complexes

Demographics

- Age
 - Middle-aged adults
- Sex
 - Slight female predominance
- Epidemiology
 - o Incidence: 3.5 individuals/million persons/year
 - Prevalence of respiratory impairment (20-50%)

Natural History & Prognosis

- 5-year survival: 75%
- Respiratory complications and lower respiratory tract infections are most common causes of death
- Cardiovascular involvement is second most common cause of death

DIAGNOSTIC CHECKLIST

Consider

• RPC in patients with tracheal wall thickening (> 2 mm) that spares posterior membrane

- 1. Chauhan K et al: Relapsing Polychondritis 2021
- 2. de Montmollin N et al: Tracheobronchial involvement of relapsing polychondritis. Autoimmun Rev. 18(9):102353, 2019

Rhinoscleroma

KEY FACTS

TERMINOLOGY

- Scleroma
- Upper respiratory tract granulomatous infection caused by *Klebsiella rhinoscleromatis*

IMAGING

- Best diagnostic clue: Irregular subglottic mucosal thickening with crypt-like spaces
- Tracheal wall thickening
 - Concentric, symmetric or asymmetric, no calcification Crypt-like spaces
- Tracheal stenosis
- Subglottic with distal tracheobronchial involvement
- Nodularity of tracheal mucosa
- Thickening of epiglottis, aryepiglottic folds, and vocal cords
- Symmetric or asymmetric bilateral nasal masses
- Nasal polyps and enlarged turbinates

TOP DIFFERENTIAL DIAGNOSES

- Laryngotracheal papillomatosis
- Granulomatosis with polyangiitis
- Relapsing polychondritis
- Amyloidosis

PATHOLOGY

- Mikulicz cells (proliferative/granulomatous stage)
 - Large, foamy, mononuclear cells that contain numerous gram-negative bacilli

CLINICAL ISSUES

- Nasal obstruction, rhinorrhea, epistaxis, and stridor
- Endemic in Central America, Egypt, tropical Africa, and India
- Females more commonly affected
- Risk factors: Poor hygiene, nutritional deficiencies, living in crowded and rural areas

(Left) Axial CECT shows circumferential subglottic narrowing and mucosal thickening \blacksquare that exhibits crypt-like airspaces \mathbf{E} , which are characteristic findings of rhinoscleroma and are not associated with other etiologies of subglottic tracheal narrowing. The cryptlike spaces represent dilated orifices of the goblet cells that line the fibrotic tracheal wall. (Right) Coronal NECT minIP reformatted image shows focal subglottic stenosis 乏 and air-filled submucosal crypts ⊇, characteristic of rhinoscleroma.





(Left) Axial CECT of a patient with rhinoscleroma shows diffuse smooth circumferential mural thickening 🔁 that involves the mid tracheal wall. (Right) Axial CECT of the same patient obtained 6 months after antibiotic treatment shows marked interval reduction of the tracheal wall thickening *⊡*. Overall, longterm antibiotic therapy (i.e., 3 months) is associated with good response, although recurrences may occur in short or prematurely interrupted treatments.





Synonyms

• Scleroma

Definitions

• Upper respiratory tract granulomatous infection caused by *Klebsiella rhinoscleromatis*

IMAGING

General Features

- Best diagnostic clue
 - Irregular subglottic mucosal thickening with crypt-like spaces

CT Findings

- Tracheal wall thickening
 - Concentric, symmetric or asymmetric
 - No calcification
 - Crypt-like spaces represent dilated orifices of goblet cells that line fibrotic tracheal wall
- Tracheal stenosis
 - Subglottic with distal tracheobronchial involvementFocal or diffuse
- Nodularity of tracheal mucosa
- Thickening of epiglottis, aryepiglottic folds, and vocal cords
- Symmetric or asymmetric bilateral nasal masses
- Nasal polyps and enlarged turbinates

MR Findings

- Granulomatous stage
 High or mixed signal intensity on T2WI; homogenous or heterogeneous contrast enhancement
- Fibrotic stage
 - Low signal intensity on T2WI; slight contrast enhancement

DIFFERENTIAL DIAGNOSIS

Laryngotracheal Papillomatosis

- Laryngotracheal mucous nodules with intraluminal extension
- Solid &/or cavitary pulmonary nodules

Granulomatosis With Polyangiitis

- Concentric and irregular tracheal wall thickening
- Subglottic stenosis
- Cavitary nodules &/or consolidations, ground-glass opacities

Relapsing Polychondritis

- Recurrent cartilaginous inflammation (ear, nose, joints, larynx, tracheobronchial tree)
- Tracheal wall thickening, spared posterior membrane

Amyloidosis

- Concentric irregular tracheal wall thickening with secondary stenosis
- Occasional calcification

PATHOLOGY

General Features

• Etiology

- o K. rhinoscleromatis: Gram-negative diplobacillus
- Infection acquired by inhalation of contaminated droplets; begins in nasopharynx; spread to adjacent structures
- o Positive cultures in 50% of cases

Staging, Grading, & Classification

- Stage I: Atrophic/catarrhal
- Persistent fetid purulent nasal discharge
- Stage II: Proliferative/granulomatous
 Mass formation with tissue destruction
- Stage III: Sclerotic
 - Extensive scarring, fibrosis, and chronic inflammatory cells

Microscopic Features

Mikulicz cells (proliferative/granulomatous stage)
 Large, foamy, mononuclear cells; contain numerous gram-negative bacilli

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nasal obstruction (100%)
 - o Rhinorrhea (46%)
 - o Epistaxis (29%)
 - o Anosmia or cacosmia (32%)
 - o Stridor (15%)
 - o Duration of symptoms 1.5-8 years

Demographics

- Age
 - o 10-57 years of age (average: 35 years)
- Sex
- Females more commonly affected
- Epidemiology
 - Endemic in Central America, Egypt, tropical Africa, India, and Indonesia
 - Risk factors
 - Poor hygiene, nutritional deficiencies, living in crowded and rural areas

Natural History & Prognosis

- Relapse (27%)
 - Related to short course of therapy or suspension of treatment

Treatment

- Antibiotics (rifampicin, sulfamethoxazole-trimethoprim, and quinolones) for at least 2-3 months
- Surgery and laser procedures in selected patients

- Mariz BALA et al: Respiratory scleroma: a clinicopathologic study of 51 cases from Guatemala. Oral Dis. 26(3):670-6, 2020
- Umphress B et al: Rhinoscleroma. Arch Pathol Lab Med. 142(12):1533-6, 2018

Bronchitis

KEY FACTS

TERMINOLOGY

- Chronic bronchitis (CB)
- Chronic obstructive pulmonary disease (COPD)
- Productive cough on most days for ≥ 3 months in each of 2 consecutive years without other causes

IMAGING

• Radiography

- Normal chest radiograph in most
- Bronchial wall thickening: Tram-track opacities, peribronchial cuffing, increased interstitial markings
- Hyperinflation
- CT
 - o Bronchial wall thickening
 - Mosaic attenuation, expiratory air-trapping
 - Mucus in tracheobronchial tree
 - Bronchial diverticula
 - Cor pulmonale: Enlarged central pulmonary arteries and right heart chambers

TOP DIFFERENTIAL DIAGNOSES

- Centrilobular emphysema
- Asthma
- Acute bronchitis
- COPD exacerbation

PATHOLOGY

• Mucous gland hypertrophy and hyperplasia

CLINICAL ISSUES

- Etiologies: Smoking, occupational exposure, air pollution
- Symptoms: Productive cough, dyspnea, wheezing
- 4% of USA adults > 18 years have diagnosis of CB
- Treatment: Bronchodilators, steroids

DIAGNOSTIC CHECKLIST

• Clinical criteria must be fulfilled for diagnosis; therefore, imaging findings are only supportive

(Left) Graphic shows morphologic features of chronic bronchitis that include generalized thickening of the trachea and central bronchi and coating of central airway walls with a thick layer of mucus. Inset depicts a thickened bronchiole in cross section with thick endoluminal mucus. (Right) PA chest radiograph of a heavy smoker shows tram-track opacities 🔁 and peribronchial cuffing \square , consistent with the thickened airway walls characteristic of chronic bronchitis.





(Left) Coronal CECT of a smoker with productive cough shows diffuse mild to moderate bronchial wall thickening \blacksquare and an incidentally discovered left upper lobe ground-glass nodule 🛃 Patients with chronic bronchitis due to smoking are also at risk for lung cancer. (Right) Axial CECT of a smoker with a clinical diagnosis of chronic obstructive pulmonary disease shows severe bilateral centrilobular emphysema and central bronchial wall thickening \blacksquare , findings that often coexist.





Abbreviations

- Chronic bronchitis (CB)
- Chronic obstructive pulmonary disease (COPD)

Definitions

- CB defined clinically, not anatomically
 - Productive cough on most days for ≥ 3 months in each of 2 consecutive years without other causes
- COPD encompasses patients with CB, emphysema, and both

IMAGING

Radiographic Findings

- Radiography
 - Most patients with isolated CB have normal chest radiographs
 - Bronchial wall thickening
 - Tram-track or tramline opacities
 - Longitudinally oriented bronchi with thickened walls
 - Peribronchial cuffing, ring shadows
 Thickened bronchi seen on end, adjacent to pulmonary arteries
 - Increased interstitial lung markings; "dirty lungs"
 - **Hyperinflation**; may be related to coexisting emphysema
 - Cor pulmonale
 - Enlarged right ventricle, dilated central pulmonary arteries, peripheral arterial pruning

CT Findings

- Bronchial wall thickening
 - Bronchi have higher thickness:diameter ratio
 - Bronchial wall thickening more common in heavy cigarette smokers
 - Correlation between bronchial wall thickening and airway obstruction
- Mucus in tracheobronchial tree
- Mosaic attenuation, expiratory air-trapping
- Bronchial diverticula
- Cor pulmonale
 - Enlarged central pulmonary arteries and right heart chambers

DIFFERENTIAL DIAGNOSIS

Centrilobular Emphysema

- Commonly coexists with CB
- Also found in smokers
- Hyperinflated lungs on radiography
 - Relative upper lung lucency characteristic of emphysema not seen in isolated CB
- Reliably diagnosed on HRCT

Asthma

- May coexist with CB
- May exhibit bronchial wall thickening and hyperinflation
- Airflow obstruction reversible with bronchodilator treatment

Acute Bronchitis and COPD Exacerbation

- Often superimposed on CB
- Acute onset, often after viral upper respiratory infection

PATHOLOGY

General Features

- Etiology
 - Cigarette smoking
 Occupational exposure: Mining, textile industry
 - Occupational exposure: Mining, textile industry
 - Air pollution
 Genetics: Linkage to chromosomes 22 and 12p
- Gross Pathologic & Surgical Features
- Inflamed, erythematous bronchial mucosa with increased mucus on bronchial surfaces

Microscopic Features

- Mucous gland hypertrophy and hyperplasia
- Goblet cell hyperplasia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Productive cough
- Other signs/symptoms
- Dyspnea, wheezing, chest tightness, hemoptysis
- Cor pulmonale: Peripheral edema
- "Blue bloater"
 - Cyanosis related to hypoxemia
 - Peripheral edema from right heart failure
- Pulmonary function tests often normal in pure CB

Demographics

- Sex
 - o Male > female
- Epidemiology
 - 4% of USA adults > 18 years have diagnosis of CB
 - CB frequency proportional to cigarette smoking

Natural History & Prognosis

• Acute exacerbation due to lower respiratory tract infection

Treatment

- Smoking cessation
- Bronchodilators, steroids
- Pulmonary rehabilitation, supplemental oxygen
- Immunizations against influenza and pneumococcus

DIAGNOSTIC CHECKLIST

Consider

• Clinical criteria must be fulfilled for diagnosis; therefore, imaging findings are only supportive

- Bhatt SP et al: Imaging advances in chronic obstructive pulmonary disease. insights from the genetic epidemiology of chronic obstructive pulmonary disease (COPDGene) study. Am J Respir Crit Care Med. 199(3):286-301, 2019
- Lynch DA et al: CT-definable subtypes of chronic obstructive pulmonary disease: a statement of the Fleischner Society. Radiology. 277(1):192-205, 2015

Bronchiectasis

KEY FACTS

TERMINOLOGY

• Irreversible bronchial dilatation usually associated with inflammation of bronchial wall

IMAGING

- Radiography
 - Linear opacities that correspond to dilated airways and thickened airway walls; tram-track opacities
 - Rounded or branching tubular lucencies and cystic spaces that represent dilated airways; ± air-fluid levels
- HRCT/thin-section CT
 - ↑ bronchoarterial ratio (B/A); signet ring sign
 B/A > 1.5: Indicative of bronchiectasis
 - Lack of bronchial tapering: Earliest and most sensitive sign of bronchiectasis
 - Bronchiolectasis: Visualization of airway within 1 cm of costal pleura or abutting mediastinal pleura
- **MR**: Increasingly used for serial imaging of young patients given no ionizing radiation

TOP DIFFERENTIAL DIAGNOSES

- Bronchitis
- Bronchial atresia
- Cystic lung disease

PATHOLOGY

• Etiologies: Infection (most common), cystic fibrosis, allergic bronchopulmonary aspergillosis, chronic aspiration, central airway obstruction

CLINICAL ISSUES

- Estimated prevalence of 139 cases/100,000 persons in USA, ↑ incidence with ↑ age
- Signs and symptoms: Chronic cough, mucopurulent sputum production, dyspnea, ± hemoptysis, may be asymptomatic

DIAGNOSTIC CHECKLIST

• Distribution of bronchiectasis and ancillary findings help narrow differential diagnosis

(Left) Graphic shows degrees of severity of bronchiectasis. Cylindrical 🗁 bronchiectasis, the mildest form, manifests with uniform bronchial dilatation and absence of airway tapering. Varicoid 🔁 bronchiectasis manifests as beaded bronchi. Saccular 🔁 bronchiectasis results when dilated bronchi exhibit a rounded cystic morphology. (Right) Axial NECT of a patient with cystic fibrosis shows bronchiectasis manifesting with the signet ring sign; the dilated airway \supseteq represents the "ring" and the adjacent artery the stone \square .





(Left) Axial NECT of the same patient shows varicoid bronchiectasis 🔁 characterized by a beaded morphology of the dilated airway. Note airway wall thickening, clustered centrilobular nodules 🖂, and mosaic attenuation (from associated constrictive bronchiolitis). (Right) Axial NECT of a patient with a history of chronic aspiration shows severe right lower lobe cystic bronchiectasis with intrinsic air-fluid levels 🔁 within dilated airways. Note adjacent centrilobular nodules \bowtie and tree-in-bud opacities.





Definitions

• Irreversible dilatation of cartilage-containing bronchi

IMAGING

General Features

- Best diagnostic clue
 - Bronchial dilatation; lack of bronchial lumen tapering
- Location
 - o Focal
 - Confined to 1 lobe or segment, often postinfectious or secondary to aspiration
 - Postobstructive bronchiectasis from endobronchial lesion (slow-growing tumor, broncholith, foreign body)
 - Extrinsic compression by mass or lymphadenopathy, proximal bronchial stenosis, distal post-stenotic dilatation
 - o Diffuse
 - Central
 - Allergic bronchopulmonary aspergillosis (ABPA), Mounier-Kuhn, Williams-Campbell
 - Peripheral: Upper lobe predominant
 - Cystic fibrosis (CF), mycobacterial infection, sarcoidosis
 - Peripheral: Lower lobe predominant
 - Pulmonary fibrosis (usual interstitial pneumonia, nonspecific interstitial pneumonia), chronic aspiration, immunodeficiency, autoimmune/collagen vascular disease, α-1 antitrypsin deficiency
 - Peripheral: Middle lobe/lingular predominant
 - Atypical mycobacterial infection, primary ciliary dyskinesia (PCD), acute respiratory distress syndrome (ARDS)
 - Peripheral: Diffuse involvement
 Bronchiolitis obliterans syndrome (post-transplant)
- Spectrum of severity/of bronchiectasis (1950 Reid Classification)
 - Cylindrical: Mild; uniformly increased bronchial diameter
 - **Varicose**: Moderate; serpiginous or string of pearls appearance; alternating dilatation and stenoses
 - **Saccular**/cystic: Severe; cluster of grapes appearance; rounded, spherical dilatation ± intrinsic fluid or air-fluid levels

Radiographic Findings

- Linear opacities that correspond to dilated airways and thickened airway walls; tram-track opacities
- Rounded or branching tubular lucencies and cystic spaces that represent dilated airways; ± air-fluid levels

CT Findings

- Direct signs
 - Bronchial dilatation

 - B/A > 1.5: Indicative of bronchiectasis

- Signet ring sign: Dilated airway represents "ring" and adjacent artery represents "stone"
- Absence of bronchial tapering: Earliest and most sensitive sign of bronchiectasis
- Bronchiolectasis: Visualization of airway within 1 cm of costal pleura or abutting mediastinal pleura
- Indirect signs (may or may not be present)
 - Bronchial wall thickening ± mucoid impaction, fluid-filled bronchi
 - o Centrilobular nodules (tree-in-bud opacities)
 - Mosaic attenuation (inspiratory) and air-trapping (expiratory) due to constrictive bronchiolitis

MR Findings

- Increasingly used for serial imaging of young patients given no ionizing radiation
- T1-weighted and T2-weighted fast/turbo spin-echo sequences provide anatomic imaging of large airways: Bronchial dilatation, mural thickening, mucus plugs
- Hyperpolarized gas (typically helium, occasionally xenon) provides functional evaluation of air-trapping

Imaging Recommendations

- Best imaging tool
 - HRCT/thin-section CT
- Protocol advice
 - Inspiratory and expiratory CT for assessment of severity of bronchiectasis and concurrent air-trapping
 - Minimum-intensity projection images may enhance detection of bronchiectasis and air-trapping

DIFFERENTIAL DIAGNOSIS

Chronic Bronchitis

• Bronchial wall thickening, normal diameter and morphology

Bronchial Atresia

- Dilated mucus-filled bronchi distal to atretic bronchial segment
- Associated hyperlucency and hypoperfusion of involved pulmonary segment

Cystic Lung Disease

- Saccular bronchiectasis may mimic cystic lung disease
- Bronchiectasis characterized by continuity of cystic lucencies with airways; no connection between cystic lucencies and airways in cystic lung disease

Cavitary Lung Disease

- Cavitary metastases
- Laryngeal papillomatosis: Pulmonary cystic lesions often associated with endobronchial/tracheal soft tissue nodules

PATHOLOGY

General Features

- Etiology
 - Cole's vicious cycle hypothesis
 - Airway injury \rightarrow inflammatory response \rightarrow bronchial wall damage
 - Tissue damage → impaired mucociliary clearance → further inflammation → progressive airway wall destruction

- Infection
 - Majority of bronchiectasis is postinfectious &/or due to chronic/recurrent infection
 - Tuberculosis and non-tuberculous mycobacterial infection (classic form): Fibrocavitary disease and bronchiectasis; asymmetric upper lobe involvement
 - Non-tuberculous mycobacterial infection (bronchiectatic form): Bronchiectasis, volume loss, middle lobe/lingular bronchiolitis; older women (Lady Windermere syndrome)
- o Congenital
 - CF
 - Congenital mutation in CFTR gene with resultant thick endobronchial secretions and impaired clearance
 - Common colonization/recurrent infection with Staphylococcus aureus, Haemophilus influenzae, Pseudomonas aeruginosa, progressive airway destruction
 - PCD
 - Autosomal recessive defect of ciliary structure/function; impaired mucociliary clearance
 - Kartagener syndrome: Bronchiectasis, situs inversus, chronic sinusitis
 - Tracheobronchomegaly (Mounier-Kuhn syndrome)
 - □ Thinning of tracheal and 1st- to 4th-order bronchial wall elastic fibers, cartilage, smooth muscle
 - Williams-Campbell syndrome
 - Cartilage deficiency involving mid-order (4th-6th generations) bronchi; sparing of trachea and central bronchi
 - Yellow Nail syndrome (lymphatic hypoplasia): Yellow nails, chronic pleural effusions, bronchiectasis
 - α-1 antitrypsin deficiency: Elastase abnormality produces panlobular emphysema, bronchitis, bronchiectasis
- Immunologic or inflammatory
 - ABPA
 - Hypersensitivity to Aspergillus antigens; chronic inflammation, airway damage
 - High attenuation or calcified inspissated debris in dilated bronchi
 - Chronic aspiration
 - □ Progressive bronchiectasis in dependent lung
 - Toxic fume inhalation/inhalational lung injury (such as ammonia)
 - Autoimmunity/collagen vascular disease
 Hyperimmune response results in chronic airway inflammation
 - Immunodeficiency: Congenital and acquired
 - Immune-related airway damage vs. airway damage from recurrent infection
 - ARDS
 - Anterior nondependent fibrosis and bronchiectasis; consolidated dependent lung relatively spared from barotrauma
- Proximal bronchial obstruction
 - Post-inflammatory stenosis or extrinsic compression by mass or lymphadenopathy with proximal bronchial stenosis and post-stenotic dilation

- Endoluminal obstruction by slow growing tumor, foreign body, or broncholith
- Traction from adjacent fibrosis
 - Idiopathic interstitial pneumonias, sarcoidosis, fibrotic hypersensitivity pneumonitis, radiation fibrosis
- Epidemiology
 - Estimated prevalence of 139 cases/100,000 persons in USA, increased incidence with increased age

Gross Pathologic & Surgical Features

- Irreversible dilatation due to loss of cartilage and elastic fibers
 - Most commonly involves medium-sized bronchi of 4th-9th generations
 - Bronchial artery hypertrophy in response to chronic inflammation
- Bronchiectatic airways often colonized with 1 or more organisms

Microscopic Features

• No specific histologic features, bronchial wall acute and chronic inflammation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chronic cough, mucopurulent sputum production, dyspnea, ± hemoptysis
 - Mild bronchiectasis often asymptomatic

Demographics

- Age
 - Prevalence (exclusive of CF) increases with age
 - Sex • More common and severe in women

Natural History & Prognosis

 Variable prognosis; outcome depends on treatment of underlying cause

Treatment

- Nonoperative: Smoking cessation, vaccination, postural drainage, antibiotics, bronchodilators
- Operative/interventional: Bronchial artery embolization (severe hemoptysis), surgical resection of localized disease, lung transplantation for selected cases

DIAGNOSTIC CHECKLIST

Consider

• Central bronchial obstruction by neoplasm or lymphadenopathy in patients with focal bronchiectasis

Image Interpretation Pearls

• Distribution of bronchiectasis and ancillary findings help narrow differential diagnosis

- 1. Tiddens HAWM et al: The radiological diagnosis of bronchiectasis: what's in a name? Eur Respir Rev. 29(156), 2020
- Juliusson G et al: Diagnostic imaging in adult non-cystic fibrosis bronchiectasis. Breathe (Sheff). 15(3):190-7, 2019

Bronchiectasis





(Left) PA chest radiograph of a patient with bronchiectasis secondary to nontuberculous mycobacterial infection shows tram-track \blacksquare and tubular \bowtie opacities that correlate with airway wall thickening and dilated mucus-filled airways, respectively. (Right) Coronal CECT of a patient with previous tuberculosis shows left upper lobe volume loss and architectural distortion with intrinsic cylindrical bronchiectasis 🔁. Most cases of bronchiectasis are secondary to chronic or recurrent pulmonary infection.





(Left) Composite image with coronal NECT in lung (left) and soft tissue (right) window of a patient with allergic bronchopulmonary aspergillosis shows highattenuation debris 🔁 within right upper lobe bronchiectasis, a characteristic finding. (Right) Axial NECT of a patient with idiopathic pulmonary fibrosis shows basilar varicoid traction bronchiectasis 🔁 on a background of honeycombing. Fibrotic interstitial lung diseases are usually associated with traction bronchiectasis and bronchiolectasis.





(Left) Axial NECT of a patient with Williams-Campbell syndrome shows bilateral central cystic bronchiectasis \square that characteristically affects 4th- to 6th-generation bronchi. (Right) Axial CECT of a patient with Kartagener syndrome shows typical findings of situs inversus and bronchiectasis. Bronchiectasis affects the left middle and bilateral lower lobe bronchi ➡ with associated bronchial wall thickening, mucus plugs, surrounding cellular $bronchiolitis \overline{\mathbb{Z}}$, and mosaic attenuation.

Cystic Fibrosis

KEY FACTS

TERMINOLOGY

- Cystic fibrosis (CF): Autosomal recessive disorder that affects regulation of chloride transport
- Increased mucus viscosity impairs pulmonary mucociliary clearance, promotes microbial colonization, and leads to chronic, destructive airway-centered infections
- Accounts for up to 25% of all adult cases of bronchiectasis

IMAGING

- Bronchial wall thickening is earliest finding
- Diffuse bronchiectasis with greatest severity in upper lobes
- Mucous plugs, centrilobular nodules, tree-in-bud and branching opacities
- Atelectasis (subsegmental to lobar) due to bronchial obstruction
- Air-trapping
- Recurrent multifocal consolidations
- Role of CT tempered by large life-time radiation dose

TOP DIFFERENTIAL DIAGNOSES

- Allergic bronchopulmonary aspergillosis
- Primary ciliary dyskinesia
- Tuberculosis

CLINICAL ISSUES

- Demographics
 - o Most patients diagnosed by 3 years; M < F
 - Milder forms may be detected in adulthood
 - Chiefly affects Caucasians
- Symptoms and signs
 - Patients with mild disease may be asymptomatic
 - o Recurrent pneumonia, cough, dyspnea, wheezing
 - Hemoptysis, may be massive
- Sweat chloride test positive in 98% of patients with CF

DIAGNOSTIC CHECKLIST

• Consider CF in any adult with unexplained bronchiectasis, particularly when upper lobe predominant

(Left) Coronal CECT of a patient with cystic fibrosis shows bilateral upper lobe predominant peripheral cystic bronchiectasis 🖾, upper lobe cylindrical bronchiectasis \square , and tree-in-bud opacities 🖂, compatible with small airways mucoid impaction &/or infection. (Right) Composite axial CECT of the same patient confirms upper lobe cystic bronchiectasis 🔁 with adjacent consolidations \square , consistent with pneumonia. Note cylindrical bronchiectasis ➡ and centrilobular nodules \blacksquare in the mid and lower lung zones.





(Left) Coronal CECT of a patient with cystic fibrosis shows upper lobe cylindrical and saccular bronchiectasis with extensive mucus plugs 📨 due to thick airway secretions, which form a nidus for microbial colonization and infection. (Right) Composite axial CECT of the same patient confirms multilobar severe bronchiectasis with mucoid impaction. Ill-defined multilobar ground-glass opacities 🔁 suggest superimposed active lung inflammation or infection. Note mosaic attenuation \supseteq from small airways disease.





- Abbreviations
- Cystic fibrosis (CF)

Synonyms

• Mucoviscidosis

Definitions

- Autosomal recessive disorder; mutations of CF transmembrane conductance regulator (*CFTR*) gene; regulates chloride transport
 - Abnormally viscous secretions from exocrine glands (salivary and sweat glands, pancreas, large bowel, tracheobronchial tree)
 - o Multiorgan involvement; primarily lungs and pancreas
- Most common fatal hereditary disease in Caucasians
- Accounts for up to 25% of adult cases of bronchiectasis
- Variable severity attributed to spectrum of *CFTR* mutations

IMAGING

General Features

- Best diagnostic clue
 - o Diffuse bronchiectasis; severe upper lobe involvement
- Location
 - Upper lobe predominant abnormalities: Right upper lobe often initially and most severely affected

Radiographic Findings

- Radiography
 - o Less sensitive for earliest abnormalities
 - o Upper lobe bronchiectasis
 - Evaluation of acute complications (i.e., pneumonia, pneumothorax) and long-term surveillance

CT Findings

- Airways: Primary site of involvement
 - Bronchial wall thickening is earliest finding
 - Bronchiectasis: Most common finding
 - Most severe in upper lobes, right > left
 - Central and peripheral airways
 - Cylindrical, varicoid, saccular, cystic
 - Mucous plugs, centrilobular nodules, tree-in-bud and branching opacities
 - Atelectasis (subsegmental to lobar) due to bronchial obstruction
- Lung
 - o Air-trapping
 - Hyperinflation is early finding; initially reversible, then permanent (100%)
 - Mosaic lung attenuation from small airways disease is common
 - Recurrent multifocal consolidations
 - Pneumonia, atelectasis, retained secretions, hemorrhage
 - o Cystic or bullous changes, typically in upper lobes
 - Evolution of pulmonary abnormalities
 - Early disease
 - Mild bronchial wall thickening
 - Regional (lobular) air-trapping
 - □ Centrilobular nodules

- Moderate disease
 - Increased bronchial wall thickening
 - Cylindrical bronchiectasis
 - Increased air-trapping (segmental to lobar)
- End-stage disease
 - □ Progression to varicoid or saccular bronchiectasis
 - Proximal mucus plugs
 - □ Chronic/recurrent lobar collapse
- CT correlates more strongly with clinical status than spirometry
- o Multiple visual scoring systems on HRCT
- Radiomics-based CT scoring algorithms: Potential future role
- Cardiovascular: Pulmonary hypertension, cor pulmonale
- Associated findings
 - o Lymphadenopathy (reactive) is common
 - Pneumothorax from rupture of subpleural bullae
 - Pancreas: Homogeneous fat attenuation (not in milder forms)

MR Findings

- MR increasingly used for serial imaging of young patients to minimize ionizing radiation
- Structural assessment (reversible and irreversible changes)
 - o Bronchial wall edema, lung inflammation, mucus plugs: High signal on T2WI
 - o Inflamed airway walls may exhibit contrast enhancement
 - T2WI: Potential tool for monitoring acute respiratory exacerbations
- Functional imaging
 - Evaluation of regional ventilation defects and relative perfusion impairment
 - Chiefly applicable to children > 5 years of age
 - Dynamic fluorine-19, inhaled hyperpolarized gas: Promising techniques

Angiographic Findings

• Bronchial artery embolization for hemoptysis

Imaging Recommendations

- Best imaging tool
 - Chest radiography every 2-4 years recommended by CF Foundation
 - CT provides more information regarding structural lung disease but increases radiation exposure
- Protocol advice
 - Role of CT tempered by large lifetime radiation dose
 - Radiation dose reduction
 - Incremental CT (8x dose reduction) preferable to volumetric CT
 - Lower mAs

DIFFERENTIAL DIAGNOSIS

Allergic Bronchopulmonary Aspergillosis (ABPA)

- Central upper lobe predominant bronchiectasis
- Mucoid impaction; may exhibit high attenuation
- History of asthma, often with eosinophilia
- 2-25% of CF patients develop ABPA (likely underdiagnosed)

Primary Ciliary Dyskinesia

• Basilar predominant bronchiectasis

• Situs inversus in 50% cases; sinusitis is common

Tuberculosis

- Upper lobe volume loss; bronchiectasis in 50%
- Active infection: Cavitation + centrilobular nodules

Postinfectious Bronchiectasis

• Unilateral, lobar/sublobar; often lower lobe predominant

PATHOLOGY

General Features

- Etiology
 - Abnormal chloride transport
 - Impaired chloride ion and water exchange (hyperactivation of epithelial sodium channels)
 - Dehydrated viscous mucus inhibits cilial movement
 - Thick mucus: Barrier to treatment, substrate for
 - polymicrobial ecosystems; impairs expectoration • Pathophysiology
 - Upper lobes less effective than lower lobes in removing tenacious secretions
 - Infections often polymicrobial involving "ESKAPE" pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species), Haemophilus influenzae, Aspergillus fumigatus
 - Eradication of bacteria and fungi challenged by antimicrobial resistance and biofilm-forming bacteria
 - Chronic inflammation \rightarrow irreversible airway damage
- Genetics
 - o Autosomal recessive trait
 - Mutation of *CFTR* gene on long arm of chromosome 7
 - Abnormal chloride transport across cell membrane
 - Phenotypic variation in age of onset, severity of lung disease, magnitude of sweat chloride elevation, presence/severity of pancreatic regurgitation
- Associated abnormalities
 - Pancreatic regurgitation
 - CF-related diabetes (CFRD) in 2% children, 20% teens, 40-50% adults
 - Pansinusitis: Hypodeveloped, opacified paranasal sinuses, nasal polyps
 - Biliary cirrhosis
 - Bone demineralization: Osteoporosis (~ 24%), osteopenia (~ 38%); vertebral compression and rib fractures common
 - Infertility: Absent vas deferens in 98% of males; thick cervical mucus in females.
 - Meconium ileus in infants; distal intestinal obstructive syndrome (DIOS) in adults

Microscopic Features

- Early: Neutrophilic bronchitis/bronchiolitis, hyperplasia of smooth muscle cells and submucosal glands
- Progression to intense neutrophilic-dominant inflammation, mucoid impaction, polymicrobial growth
- Structural changes: Bronchiectasis, fibrosis, bronchial artery hypertrophy, pus-filled cysts
- Biofilm elaborated by microbes encases bacterial colonies, forms barrier to neutrophils and antibiotics

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Patients with mild disease may be asymptomatic; diagnosed in adulthood
 - Recurrent pneumonia; atypical asthma; productive cough, dyspnea, wheezing, pleuritic pain
 - Hemoptysis, may be massive
- Diagnosis
 - Newborn screening with heel stick: Assessment of levels of pancreatic enzyme immunoreactive trypsinogen
 - o Sweat chloride test positive in 98% patients with CF

Demographics

- Age
 - Most diagnosed by age 3 years; mild cases diagnosed in adulthood
- Sex
 - o M<F
- Ethnicity
- Common in Caucasians, rare in African Americans/AsiansEpidemiology
 - 3,200 new cases each year in USA
 - Currently 30,000 cases in USA, 70,000 worldwide
 - 80% prevalence of *P. aeruginosa* infection (adults)
 - 58% sputum samples positive for Aspergillus (adults)

Natural History & Prognosis

- Today, more patients survive into 5th decade of life and beyond
- Pulmonary exacerbations usually multifactorial, more prevalent in adults
- Accelerate lung functional decline, decrease survival
- Death: Respiratory failure, cor pulmonale, hemoptysis

Treatment

- Airway clearance therapies (ACTs): Postural drainage, oscillation devices, positive expiratory pressure, mucolytics, bronchodilators, prophylactic antibiotics
- Targeted gene therapy in active development
 CFTR modulators aim to correct gene malfunction
- Pancreatic enzyme replacement
- Segmental lung resection with video-assisted thoracoscopy for severe dependent bronchiectasis or infections resistant to antimicrobial therapy
- Lung transplantation
 - Bilateral prevents reinfection of transplanted lung (significant risk of bacterial and fungal recolonization)
 - o Median survival: ~ 8 years

DIAGNOSTIC CHECKLIST

Consider

 CF in any adult with unexplained bronchiectasis, particularly when upper lobe predominant

- 1. Chassagnon G et al: Quantification of cystic fibrosis lung disease with radiomics-based CT scores. Radiol Cardiothorac Imaging. 2(6):e200022, 2020
- 2. Milliron B et al: Bronchiectasis: mechanisms and imaging clues of associated common and uncommon diseases. Radiographics. 35(4):1011-30, 2015

Cystic Fibrosis





(Left) PA chest radiograph of a patient with cystic fibrosis shows right basilar airspace disease $\overline{\geq}$, consistent with combined right lower lobe and middle lobe atelectasis. Note bronchial wall thickening \boxtimes , cystic lucencies 🖂, consistent with saccular bronchiectasis, and multifocal consolidations. (Right) Contrast-enhanced axial ultrafast gradient-echo MR of a patient with cystic fibrosis shows left lower lobe bronchiectasis 🔁 with highsignal mucus. MR may be used for imaging follow-up of young patients to reduce radiation dose.





(Left) Coronal NECT of a patient with cystic fibrosis shows bronchiectasis 🖂, left lower lobe consolidation \supseteq , and a left upper lobe multicystic lesion 🔁 with adjacent pleural thickening. Left upper lobe bronchial lavage revealed Aspergillus species. (Right) Axial NECT of a patient with cystic fibrosis shows bronchiectasis 乏. Note mosaic perfusion with differential vessel diameters \bowtie in regions of higher versus lower pulmonary attenuation, consistent with small airways disease and resultant vasoconstriction.





(Left) Coronal NECT of a patient with cystic fibrosis shows subcarinal $lymphadenopathy \supseteq$ and leftupper lobe bronchiectasis 🖂 *Lymphadenopathy is very* common in affected patients and is often reactive. (Right) Axial NECT through the upper abdomen of the same patient shows fatty replacement \supseteq of the pancreas. This is a . common ancillary finding in patients with cystic fibrosis resulting from fatty replacement of the normal glandular parenchyma.

KEY FACTS

TERMINOLOGY

• Allergic bronchopulmonary aspergillosis (ABPA): Chronic airway inflammation and injury in patients with hypersensitivity to *Aspergillus* antigens

IMAGING

- Radiography
 - Migratory upper lung zone pulmonary opacities
 Bronchiectasis
 - BIOLICIIIECLASIS
 - Tram-track parallel linear opacities
 Mucoid impaction: May exhibit finger-in-glove sign
- CT/HRCT
 - Central upper lobe bronchiectasis
 - Bronchial wall thickening
 - Mucoid impaction
 - Soft tissue-attenuation branching opacities
 - High-attenuation or calcified mucus (30%)
 - o Centrilobular nodules, tree-in-bud opacities
 - o Mosaic attenuation, expiratory air-trapping

TOP DIFFERENTIAL DIAGNOSES

- Cystic fibrosis
- Primary ciliary dyskinesia
- Postinfectious bronchiectasis
- Congenital bronchial atresia

PATHOLOGY

• Inspissated mucus plugs contain Aspergillus and eosinophils

CLINICAL ISSUES

- 7-14% of corticosteroid dependent asthmatics have ABPA
- 6-15% of patients with cystic fibrosis have ABPA
- Signs and symptoms: Cough, dyspnea, expectoration of golden-brown mucus plugs, wheezing, hemoptysis
- Treatment: Oral corticosteroids, antifungals

DIAGNOSTIC CHECKLIST

• Consider ABPA in patients with asthma and central bronchiectasis with high-attenuation mucus plugs

(Left) PA chest radiograph of a 20-year-old woman with chronic asthma from allergic bronchopulmonary aspergillosis (ABPA) shows an ovoid left upper lobe opacity *▶*, lung hyperinflation, and no appreciable bronchiectasis. (Right) Composite image with axial NECT in lung (left) and soft tissue (right) window of the same patient shows a multinodular bronchocentric lingular consolidation with intrinsic tubular branching high-attenuation mucus 🔁 in left upper lobe segmental bronchi without significant bronchiectasis (ABPA-S).





(Left) PA chest radiograph of a 53-year-old-man with chronic asthma and ABPA shows bilateral upper lobe parallel linear tram-track opacities 🔁 *⊠*, consistent with upper lung bronchiectasis. (Right) Coronal NECT of the same patient shows upper lobe predominant central varicoid bronchiectasis 🔁 with bronchial wall thickening that corresponds to the tram-track radiographic abnormality. Note associated faint centrilobular nodules 🔁 and subtle constrictive bronchiolitis.





Abbreviations

• Allergic bronchopulmonary aspergillosis (ABPA)

Definitions

- ABPA: Chronic airway inflammation and injury in patients with hypersensitivity to *Aspergillus* antigens
 Allergic response to inhaled *Aspergillus* spores
 - Typically affects patients with **asthma** and **cystic fibrosis**
- Allergic bronchopulmonary mycoses: Chronic airway
 inflammation/injury due to hypersensitivity to other fungi
- Serological ABPA (ABPA-S): Mild form of disease with positive serology and other criteria, but without bronchiectasis

IMAGING

General Features

- Best diagnostic clue
 - Central bronchiectasis and mucoid impaction in asthmatic patient
- Location
 - o Central bronchiectasis, normal peripheral airways
 - Upper lobe predominance

Radiographic Findings

- Radiography
 - May be normal (ABPA-S)
 - Migratory upper lung zone pulmonary opacities
 - Consolidations, perihilar opacities, postobstructive pneumonia
 - Atelectasis
 - Reticular opacities and volume loss related to fibrosis
 - Bronchiectasis
 - Tram-track parallel linear opacities
 - Mucoid impaction demonstrating finger-in-glove sign
 May resolve post coughing or with treatment
 - May exhibit intrinsic air-fluid levels and mycetoma formation

CT Findings

- Bronchiectasis (95%)
 - Upper lobe involvement
 - Central bronchiectasis is typical
 - Peripheral airways may also be involved
 - o Multilobar, bilateral, asymmetric
 - o Cylindrical (early), varicose, cystic
 - May be air-filled or filled with soft tissue
 - May exhibit mycetoma formation
- Bronchial wall thickening
- Mucoid impaction (70%)
 - Homogeneous tubular &/or branching opacities
 - Soft tissue-attenuation mucus
 - High-attenuation or calcified mucus (30%)
- Centrilobular nodules, tree-in-bud opacities
- Mosaic attenuation, expiratory air-trapping
- Associated findings
 - Consolidation, atelectasis
 - Reticulation, architectural distortion, bullae
 - Pleural effusion

Imaging Recommendations

- Best imaging tool
 - CT/HRCT: Imaging modality of choice

MR Findings

- Noninvasive, radiation-free disease monitoring, evaluation of response to antifungal treatment
 - o Increasing use in pediatric population with cystic fibrosis
- Inverted mucoid impaction sign
 MR correlate of high-attenuating mucus on CT
 T1-hyperintense/T2-hypointense endobronchial mucus

DIFFERENTIAL DIAGNOSIS

Cystic Fibrosis

- ABPA in up to 15% of patients with cystic fibrosis
- Positive sweat chloride skin test
- Similar distribution of bronchiectasis

Primary Ciliary Dyskinesia

- Poor mucociliary clearing predisposes to recurrent infection and bronchiectasis
- ~ 50% have Kartagener syndrome
- Basilar predominant bronchiectasis

Postinfectious Bronchiectasis

- Recurrent pulmonary infection
 Bacteria, mycobacteria, viruses
- Transient ciliary dysfunction and poor mucus clearance with resultant airway damage

Congenital Bronchial Atresia

- Vascular insult to airway in early fetal development
- Focal short-segment airway atresia
- Mucocele distal to atresia
 - Round, ovoid, or tubular branching opacities
- Surrounding pulmonary hyperlucency

Immune Deficiency Disorders

- Human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS)
- Common variable immunodeficiency (CVID)
- Recurrent pulmonary infection with resultant bronchiectasis

Williams-Campbell Syndrome

- Rare congenital cartilage deficiency in subsegmental bronchi
- Bronchiectasis limited to 4th-, 5th-, and 6th-generation bronchi

Bronchocentric Granulomatosis

- Inflammatory response characterized by necrotizing granulomas along bronchi and bronchioles
- May be seen in ABPA or as response to infection
- Mimics ABPA, but may predominantly affect distal airways
- May manifest with mass, consolidation, or atelectasis

Asthma

- Bronchial wall thickening ± mild cylindrical bronchiectasis
- Atelectasis, consolidation, air-trapping
- Mucoid impaction may be seen without ABPA

Endobronchial Neoplasm

- Mucoid impaction distal to slow-growing neoplasm
 Carcinoid, hamartoma, lung cancer
- Usually unilateral; single lobar or segmental distribution

PATHOLOGY

General Features

- Etiology
 - Aspergillus fumigatus antigen stimulation
 - Type I IgE-mediated hypersensitivity reaction
 - □ ↑ levels of IgE and ↑ *A. fumigatus*-IgE and *A. fumigatus*-IgE and *A. fumigatus*-IgC antibodies
 - Type III (IgG-mediated) and type IV (cell-mediated) reactions
 - Other fungi: Allergic bronchopulmonary mycosis
- Genetics
 - Higher frequency of HLA-DR2 and HLA-DR5 genotypes
- Epidemiology
 - Estimated 7-14% of corticosteroid dependent asthmatics have ABPA
 - 6-15% of patients with cystic fibrosis have ABPA

Staging, Grading, & Classification

- Several and evolving diagnostic criteria
- Rosenberg-Patterson: Most well-acknowledged criteria
 - o Major criteria
 - Asthma
 - Immediate cutaneous reactivity to A. fumigatus
 - Elevated total serum IgE
 - Precipitating antibodies against A. fumigatus
 - Peripheral blood eosinophilia
 - Elevated serum IgE and IgG specific for A. fumigatus
 - Central bronchiectasis
 - Migratory pulmonary opacities
 - o Minor criteria
 - Expectorated golden-brown mucus plugs
 - Positive sputum culture for Aspergillus spp.
 - Late skin reactivity to A. fumigatus
- International Society for Human and Animal Mycology
 - Obligatory: Both must be present for diagnosis
 - + immediate cutaneous hypersensitivity to Aspergillus antigen or ↑ IgE levels against A. fumigatus
 - − ↑ total IgE levels > 1,000 IU/mL
 - Other: At least 2 must be present
 - + precipitating or IgG antibodies against A. fumigatus in serum
 - Radiological findings/changes typical of ABPA
 - Total eosinophil count > 500 cells/µL
- Clinical staging
 - Stage I: Acute
 - Stage II: Remission
 - Stage III: Exacerbation
 - o Stage IV: Corticosteroid dependent asthma
 - o Stage V: End-stage (fibrotic) lung disease
- Radiologic staging
 - Stage I: ABPA-S
 - Stage II: ABPA with bronchiectasis
 - Stage III: ABPA with high-attenuation mucus
 - Stage IV: ABPA with chronic pleuropulmonary fibrosis

Microscopic Features

- Inspissated mucus plugs contain *Aspergillus* and eosinophils • *Aspergillus*: Septate hyphae with 45° angle branching
- No invasion of bronchial epithelium
- Eosinophilic pneumonia
- Bronchocentric granulomatosis: Necrotizing granulomatous inflammation destroys walls of small bronchi and bronchioles

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough, dyspnea, expectoration, wheezing, hemoptysis
 Expectoration of thick, golden-brown mucus plugs
 - Cyanosis, digital clubbing, cor pulmonale in severe cases
 - Pleuritic chest pain and fever
- Other signs/symptoms
 - May occur in association with allergic Aspergillus sinusitis
 Immunologic reaction to Aspergillus antigens in paranasal sinuses
- Laboratory abnormalities
 - Peripheral eosinophilia: Usually > 1,000/µL; commonly > 3,000/µL
 - Elevated IgE: Usually > 1,000 ng/mL

Natural History & Prognosis

- Early diagnosis and treatment may delay (or even prevent) onset of bronchiectasis
 - All patients with bronchial asthma should be screened
- Recurrent ABPA may result in widespread bronchiectasis and fibrosis
 - 35% of exacerbations are asymptomatic but may result in lung damage
- ABPA may recur in patients with cystic fibrosis treated with lung transplantation

Treatment

- Oral corticosteroids are mainstay of therapy: Long-term therapy may be required
- Antifungal agents: Reduction of fungal load and antigenic stimuli to decrease inflammatory response
- Potential benefit of monoclonal antibody (against IgE) therapy
- Allergic fungal sinusitis: Initial surgical debridement, postoperative oral corticosteroids, supportive measures

DIAGNOSTIC CHECKLIST

Consider

• ABPA in patients with asthma and central upper lobe bronchiectasis, particularly when associated with soft tissue or high-attenuation mucus plugs

- Agarwal R et al: Allergic bronchopulmonary aspergillosis. Indian J Med Res. 151(6):529-49, 2020
- Asano K et al: New clinical diagnostic criteria for allergic bronchopulmonary aspergillosis/mycosis and its validation. J Allergy Clin Immunol. 147(4):1261-8.e5, 2020
- Dournes G et al: Allergic bronchopulmonary aspergillosis in cystic fibrosis: MR imaging of airway mucus contrasts as a tool for diagnosis. Radiology. 285(1):261-9, 2017





(Left) Axial NECT of a patient with ABPA shows upper lobe cystic and varicoid bronchiectasis with intrinsic bilateral partially calcified mycetomas within these preexisting "cavities." (Right) Coronal NECT of the same patient shows the central and upper lung predominance of varicoid and cystic bronchiectasis. Patients with bronchial asthma should be screened for ABPA, as early diagnosis and treatment has the potential to prevent progression of bronchiectasis.





(Left) Axial NECT of a patient with chronic asthma and ABPA shows characteristic mucoid impaction \blacksquare within bronchiectatic central airways. Such high-attenuation mucoid impaction is attributed to fungal material and mineral content and correlates with radiographic finger-in-glove tubular opacities. (Right) Axial NECT of a 44-year-old man with chronic asthma and ABPA shows mild bilateral upper lobe bronchiectasis 🖂, without endobronchial mucus or mucoid impaction.





(Left) High-power photomicrograph (GMS stain) shows septated hyphae with 45° angle branching ≥. Aspergillus organisms are often found in expectorated mucus of patients with ABPA. (From: DP Thoracic.) (Right) Axial HRCT of a 38-year-old woman with ABPA shows severe right lower lobe central bronchiectasis ≥ and right upper lobe consolidation and atelectasis ≥.

Primary Ciliary Dyskinesia

KEY FACTS

TERMINOLOGY

- Primary ciliary dyskinesia (PCD)
- Abnormal ciliary ultrastructure with resultant mucociliary dysfunction and otosinopulmonary disease
 - Kartagener syndrome: 50% of patients with PCD

IMAGING

- Radiography
 - Hyperinflation
 - o Bronchial wall thickening and bronchiectasis
 - Atelectasis, consolidation
- CT/HRCT
 - Bronchial wall thickening, mucus plugging
 - Bronchiectasis with predilection for lingula and middle and lower lobes
 - Centrilobular nodules, tree-in-bud opacities, consolidation
 - Mosaic attenuation, expiratory air-trapping
 - o Situs abnormalities

TOP DIFFERENTIAL DIAGNOSES

- Cystic fibrosis
- Allergic bronchopulmonary aspergillosis
- Postinfectious bronchiectasis
- Immune deficiency disorders

CLINICAL ISSUES

- Symptoms/signs
 - Neonatal respiratory distress
 - Chronic/recurrent rhinitis, secretory otitis media, sinusitis
 - Recurrent lower respiratory infection
 - Infertility in men, lowered fertility and ectopic pregnancy in women
 - o Situs abnormalities with Kartagener syndrome

DIAGNOSTIC CHECKLIST

• Consider PCD in patients with chronic rhinitis, otitis, and bronchial/pulmonary infection since infancy and in patients with abnormal situs and bronchiectasis

(Left) PA chest radiograph of a 44-year-old woman with Kartagener syndrome and primary ciliary dyskinesia who presented with productive cough shows dextrocardia \supseteq , a right aortic arch 🔁, and a right gastric bubble 🔁. The right upper lobe bronchus is hyparterial, and the left upper lobe bronchus is eparterial, consistent with situs inversus. (Right) Lateral chest radiograph of the same patient shows subtle lower lobe linear opacities that exhibit the tram-track sign 🖂, consistent with basilar bronchiectasis.





(Left) Axial CECT of the same patient shows basilar bronchiectasis 🖂, bronchial wall thickening \supseteq , mucus plugs 🖾, and mosaic attenuation/perfusion with areas of decreased lung attenuation \supseteq and vascularity. (Right) Axial NECT of the same patient obtained 3 months later because of recurrent pulmonary infection shows new left middle lobe pneumonia 🖂, bilateral lower lobe bronchiectasis, and mucus plugs. The middle lobe, lingula, and lower lobes are preferentially affected in primary ciliary dyskinesia.





Synonyms

- Dyskinetic cilia syndrome
- Immotile cilia syndrome: Misnomer as ciliary motion is present but abnormal

Definitions

• Primary ciliary dyskinesia (PCD)

- Genetic disorder causing ciliary defects and impaired mucociliary clearance
- Mucociliary dysfunction and chronic otosinopulmonary disease
- Abnormalities of situs in > 50% of cases; congenital heart disease in 25%

• Kartagener syndrome

- Triad of situs inversus, sinusitis &/or nasal polyposis, and bronchiectasis
- 50% of patients with PCD
- Kartagener-Afzelius syndrome
 - Kartagener described sinusitis, bronchiectasis, and situs inversus
 - Afzelius described associated infertility; structural abnormalities of motile cilia and sperm

IMAGING

General Features

- Best diagnostic clue
- Triad of abnormal situs, bronchiectasis, and sinusitis
 Location
 - Bronchiectasis with predilection for lingula and middle and lower lobes

Radiographic Findings

- Hyperinflation
- Bronchial wall thickening, bronchiectasis (tram-track sign)
- Atelectasis, consolidation
- Dextrocardia and situs abnormalities

CT Findings

- Bronchial wall thickening
- Mucus plugs
- Bronchiectasis with predilection for lingula and middle and basilar lower lobes
 - o Variable severity: Cylindrical, varicose, and cystic
 - Signet ring sign: Bronchial diameter > adjacent pulmonary artery diameter
 - CT section perpendicular to bronchial long axis
 - "Ring" correlates with dilated bronchus
 - "Stone" correlates with adjacent pulmonary artery
- Mosaic attenuation, expiratory air-trapping
- Centrilobular nodules, tree-in-bud and ground-glass opacities, consolidation
- Atelectasis, typically subsegmental
- Associated abnormalities
 - Abnormal situs: Situs inversus (50%), situs ambiguous (12%)
 - Congenital heart disease (25%)
 - o Sinusitis
 - Pectus excavatum and scoliosis

Imaging Recommendations

- Best imaging tool
 - HRCT is imaging study of choice for diagnosis and assessment of bronchiectasis
 - Chest radiographic abnormalities may suggest diagnosis in cases of Kartagener syndrome
- Protocol advice
 - Thin-slice multidetector CT with multiplanar reformatted images

DIFFERENTIAL DIAGNOSIS

Cystic Fibrosis

- Autosomal recessive condition; abnormal exocrine gland secretions
- Caucasian patient; typically diagnosed in childhood
- Recurrent infections, wheezing, dyspnea
- Severe upper lobe predominant bronchiectasis, mucus plugging, bronchial wall thickening, mosaic attenuation

Allergic Bronchopulmonary Aspergillosis

- Patient with asthma or cystic fibrosis
 Worsening asthma, cough, wheezing
- Reactivity to Aspergillus
- Central upper lobe predominant bronchiectasis
- Central mucoid impaction
 - May exhibit high attenuation on CT

Postinfectious Bronchiectasis

- Recurrent pulmonary infection
 Bacteria, mycobacteria, viruses
- Pulmonary infection may result in transient ciliary dysfunction and poor clearance of airway mucus
 - Subsequent bacterial colonization and host effects may lead to irreversible airway damage

Immune Deficiency Disorders

- Human immunodeficiency virus/acquired immune deficiency
- Common variable immunodeficiency
- Recurrent pulmonary infection
 Resultant bronchiectasis

Young Syndrome

- Abnormal viscosity of airway mucus
- Bronchiectasis, rhinosinusitis
- Infertility
 - Due to functional genital tract obstruction and abnormal sperm transport

PATHOLOGY

General Features

- Etiology
 - Compromised mucociliary clearance secondary to structural and functional ciliary abnormalities
 - Cycle of pulmonary infection \rightarrow airway destruction \rightarrow pulmonary infection
 - Airway abnormalities predispose to recurrent pulmonary infection
- Genetics
 - o Autosomal recessive disorder; genetic heterogeneity

- o 35 genetic mutations account for ~ 70% of cases of PCD
 - DNAI1 and DNAH5 encode components of outer dynein arms, account for > 30% of cases
 - Biallelic mutations linked to ~ 70% of known cases
- Associated abnormalities
 - Situs abnormalities
 - Situs inversus in ~ 66% of pediatric patients and ~ 50% of adults in one series
 - Congenital heart disease
 - o Infertility
 - Abnormal ciliary ultrastructure with abnormal ciliary beat frequency or abnormal ciliary orientation
 - May exhibit normal ultrastructure and beat frequency
 - Transient abnormalities of ciliary orientation may occur with airway infection/inflammation

Gross Pathologic & Surgical Features

- Diffuse bronchiectasis resulting from recurrent infection
- Pulmonary infection
- Dextrocardia, abnormal situs

Microscopic Features

- Bronchial inflammation, squamous metaplasia, ulceration
- Bronchial wall fibrosis and destruction
- Acute and chronic pneumonia, organizing pneumonia
- Electron microscopy: Ultrastructural ciliary defect
 - Most common: Absence or shortening of outer dynein arms or combined outer and inner dynein arm defects
 - $\circ~\sim$ 30% of patients with PCD have normal ciliary structure

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Neonates: Respiratory distress requiring ventilatory support (> 80%), rhinitis, atelectasis, pneumonia
 - Infants and children: Chronic/acute otitis media, rhinitis, sinusitis, chronic wet cough, recurrent pneumonia
 - Older patients: Recurrent sinus, ear, and pulmonary infections, male infertility
 - Recurrent lower respiratory tract infection
 - Haemophilus influenzae, Staphylococcus aureus, Streptococcus pneumoniae
 - S. aureus and nontuberculous mycobacteria are more common in adults
 - Productive cough, wheezing, coarse crackles, exertional dyspnea
 - Pulmonary function test: Obstructive or mixed obstructive-restrictive abnormalities
 - Infertility in men, lowered fertility and ectopic pregnancy in women
- Other signs/symptoms
 - Situs abnormalities in patients with PCD
 - Up to 50% of patients with PCD have situs inversus;
 12% have heterotaxy
 - Congenital heart disease (~ 25% of patients with PCD); often associated with situs abnormalities (heterotaxy)
 - o Aplasia/hypoplasia of paranasal sinuses
 - Chronic rhinosinusitis, nasal polyposis
 - o Other
 - Hydrocephalus, retinitis pigmentosa (rare)

Demographics

- Age
 - Typically diagnosed in childhood, adolescence, or adulthood: Median age at diagnosis: ~ 5.3 years
- Sex
 - No predilection; M = F
- Epidemiology
 - o Prevalence
 - Range: 1/10,000-20,000 population

Diagnosis

- Nasal biopsy or ciliary culture
 - Functional studies
 - Measurement of ciliary beat frequency, beat pattern, and coordination of ciliary motion
 - Ultrastructural studies
 - Evaluation of ciliary orientation and ultrastructure on electron microscopy
- Genetic testing

Screening

- Measurement of nasal nitric oxide
 - Low levels of exhaled nitric oxide in patients with PCD

Natural History & Prognosis

- Affected patients often present as newborns
- Delayed diagnosis; typically in late childhood and adolescence
- Good prognosis with early diagnosis and aggressive treatment
- Progressive decline in lung function reported

Treatment

- Close clinical follow-up
- Aggressive airway clearance and lung physiotherapy
- Antibiotics: Lung infection treatment and bronchiectasis prevention
- Immunization for influenza and pneumococcus
- Smoking cessation, removal from exposure to secondhand smoke
- Nasal lavage with saline, intranasal steroids for chronic rhinitis and polyposis
- Sinus surgery in selected cases
- Advanced pulmonary disease
 - Surgical intervention for severe bronchiectasis in selected patients
 - Lung transplantation for end-stage lung disease

DIAGNOSTIC CHECKLIST

Consider

• PCD in young patients with chronic rhinitis, otitis, and bronchial/pulmonary infection since infancy and in patients with abnormal situs and bronchiectasis

Image Interpretation Pearls

• Basilar bronchiectasis in young patient ± situs abnormality

- 1. Best S et al: Risk factors for situs defects and congenital heart disease in primary ciliary dyskinesia. Thorax. 74(2):203-5, 2019
- Dettmer S et al: Computed tomography in adult patients with primary ciliary dyskinesia: typical imaging findings. PLoS One. 13(2):e0191457, 2018

Primary Ciliary Dyskinesia





(Left) Coronal NECT of a 63year-old man with primary ciliary dyskinesia and life-long recurrent pulmonary infections shows bilateral bronchiectasis 🖂, bronchial wall thickening \supseteq , mucus plugs, and mosaic attenuation. (Right) Coronal NECT of the paranasal sinuses of the same , patient shows extensive . mucosal thickening and evidence of prior surgical intervention for treatment of recurrent sinusitis and polyposis. Abnormal ciliary function may affect the sinuses, middle ear, airways, and reproductive system.





(Left) Axial NECT of a 44-yearold man with primary ciliary dyskinesia shows basilar bronchiectasis, bronchial wall thickening, and mosaic attenuation. The paired dilated bronchi and adjacent pulmonary arteries demonstrate the signet ring sign 🔁. (Right) Axial CECT of a patient with situs inversus and primary ciliary dyskinesia shows mild left middle lobe bronchiectasis 🔁 Appropriate antibiotic treatment and aggressive lung physiotherapy may help ameliorate or prevent bronchiectasis in affected patients.





(Left) PA chest radiograph of a young woman with Kartagener syndrome shows situs inversus totalis, dense right lower lobe retrocardiac $consolidation \implies$ with intrinsic bronchiectasis, and multifocal bilateral pulmonary nodules. (Right) Axial HRCT of the same patient shows persistent right lower lobe consolidation 🖻 with volume loss, bronchiectasis and cavitation 🔁, and left middle lobe bronchiectasis 🖂, mucus plugging, and bronchiolitis. The findings are related to chronic infection secondary to primary ciliary dyskinesia.
KEY FACTS

TERMINOLOGY

• Mounier-Kuhn syndrome (MKS): Rare disorder characterized by atrophy of tracheal and mainstem bronchial elastic tissue and smooth muscle leading to significant central airway dilatation

IMAGING

- Radiography
 - o Tracheal diameter > than width of adjacent vertebrae
 - Increased lung volume (from obstructive physiology)
- HRCT/CT
 - Consider MKS if
 - Trachea > 30 mm
 - Left mainstem bronchus > 23 mm
 - Right mainstem bronchus > 24 mm
 - HRCT: Expiratory tracheal collapse due to tracheobronchomalacia
 - o Bronchiectasis (30-45%)
 - o Tracheobronchial diverticulosis (50%)

TOP DIFFERENTIAL DIAGNOSES

- Williams-Campbell syndrome
- Secondary tracheobronchomegaly

PATHOLOGY

- Unknown etiology, most likely congenital
- Numerous saccular diverticula between cartilages; bulging dilatation along posterior wall
- Thinning of muscularis mucosa and atrophy of longitudinal muscle and elastic fibers

CLINICAL ISSUES

- Cough (> 70%), recurrent infection (50%), dyspnea (> 40%)
- Diagnosis of chronic obstructive pulmonary disease (> 25%)
- Male predominance; M:F = 8:1
- Most cases diagnosed in 5th and 6th decades
- Obstructive physiology on pulmonary function tests
- Treatment: Mucolytic therapy, physical therapy, postural drainage

(Left) Coronal CECT of a patient with Mounier-Kuhn syndrome shows abnormal tracheobronchial dilatation and diverticulosis 🔁. This syndrome is characterized by deficiency of elastic and smooth muscle in the trachea and mainstem bronchi. Diverticula result from herniation of mucosa between adjacent airway cartilages. (Right) Sagittal CECT of the same patient confirms multiple tracheal diverticula ➡. Mounier-Kuhn syndrome is clinically characterized by cough, dyspnea, and recurrent pulmonary infections.





(Left) Axial NECT of a patient with Mounier-Kuhn syndrome shows dilatation of mainstem bronchi 🔁 and cystic bronchiectasis 🔁 Development of bronchiectasis has been attributed to recurrent infections resulting from abnormal mechanisms of mucus clearance. (Right) Coronal NECT of the same patient shows abnormal bronchial dilation, multiple diverticula \square , and bilateral central bronchiectasis 🖂 Bronchiectasis is present in up to 45% of patients with Mounier-Kuhn syndrome.





Abbreviations

• Mounier-Kuhn syndrome (MKS)

Synonyms

- Tracheobronchomegaly
- Congenital tracheobronchomegaly

Definitions

• Defect or atrophy of elastic and smooth muscle components of trachea and mainstem bronchi with resultant significant central airway dilatation

IMAGING

General Features

- Best diagnostic clue
 - Abnormal dilatation of central airways + multiple saccular diverticula
 - Scalloped or lobulated appearance of air column along tracheal and central bronchial walls
 - Narrowing or collapse of of trachea and mainstem bronchi on expiration

Radiographic Findings

- Consider diagnosis when tracheal diameter exceeds that of adjacent vertebral bodies
- Increased lung volume (from obstructive physiology)

CT Findings

- Maximum normal tracheal diameters (mean + 3 standard deviations); measured 20 mm cephalad to aortic arch
 Men: 27 mm (sagittal) and 25 mm (coronal)
 - o Women: 23 mm (sagittal) and 21 mm (coronal)
- Consider MKS if
 - o Trachea > 30 mm
 - Left mainstem bronchus > 23 mm
 - Right mainstem bronchus > 24 mm
 - Measurements > 3 standard deviations above normal are diagnostic of tracheobronchomegaly
- Tracheobronchial diverticulosis (50%)
 - Optimally visualized on sagittal images
- Bronchiectasis (30-45%)
- Tracheobronchomalacia (28%)
 - Significant tracheal luminal collapse (> 75% of inspiratory diameter)
- Expiratory air-trapping

Imaging Recommendations

- Best imaging tool
 - HRCT: Expiratory imaging critical for identification of tracheobronchomalacia
- Protocol advice
 - Multiplanar reformatted and minIP images may be useful for central airway evaluation

DIFFERENTIAL DIAGNOSIS

Williams-Campbell Syndrome

• Bilateral subsegmental bronchiectasis with normal trachea, mainstem bronchi, and segmental bronchi

Secondary Tracheobronchomegaly

- Associated with some chronic pulmonary conditions (e.g., pulmonary fibrosis, chronic infection, emphysema)
- Difficult differentiation from MKS; ancillary findings, such as interstitial lung disease, are helpful

PATHOLOGY

General Features

- Unknown etiology, most likely congenital
- Sporadic association of MKS with Ehlers-Danlos, Marfan, and cutis laxa syndromes suggests smooth muscle and connective tissue disorder
- Mostly affects males
- History of cigarette smoking is common

Staging, Grading, & Classification

- Type 1: Symmetric diffuse dilatation of trachea and mainstem bronchi
- Type 2: Distinct tracheal dilatation and diverticula
- Type 3: Mural diverticula that also involve distal bronchi

Gross Pathologic & Surgical Features

- Numerous saccular diverticula between cartilages; bulging dilatation along posterior tracheal wall
- Tracheobronchomegaly

Microscopic Features

- Thinning of muscularis mucosa and atrophy of longitudinal muscle and elastic fibers
- Loss of respiratory tract elastic fibers may be partial or complete and may exhibit patchy distribution
- Absence of tracheal wall myenteric plexus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough (> 70%), recurrent respiratory infection (50%), dyspnea (> 40%)
 - Common diagnosis of chronic obstructive pulmonary disease (> 25%)
- Other signs/symptoms
 - o Bronchial rales and wheezing on auscultation
 - Finger clubbing (common)
 - Obstructive physiology on pulmonary function tests

Demographics

- Male predominance; M:F ratio = 8:1
- Most cases diagnosed in 5th and 6th decades

Natural History & Prognosis

- No definitive data available regarding disease progression
- Anecdotal data suggests that once certain degree of airway dilatation has occurred, anatomic changes do not progress

Treatment

• Mucolytic therapy, physical therapy, and postural drainage to facilitate expectoration

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KEY FACTS

TERMINOLOGY

- Williams-Campbell syndrome (WCS)
 - Rare congenital syndrome
 - Partial or complete absence of cartilage in subsegmental bronchi

IMAGING

- Diffuse bilateral cylindrical/cystic bronchiectasis
- Normal trachea and mainstem/segmental bronchi
- Bronchial air-fluid levels may be associated with infection
- Dynamic CT
 - Inspiratory phase: "Ballooning" of bronchiectasis
 - Expiratory phase: Collapse of bronchiectatic airways
- Virtual bronchoscopy
 - Useful for clinicians; visualization of extent of involvement
 - Highlights absence of cartilage ring impressions along bronchial walls

TOP DIFFERENTIAL DIAGNOSES

- Cystic fibrosis
- Primary ciliary dyskinesia
- Allergic bronchopulmonary aspergillosis

PATHOLOGY

- Congenital syndrome
- Defective or completely absent bronchial wall cartilages of 4th- to 6th-generation bronchi
- Acquired hypothesis: Adenovirus infection → bronchomalacia → bronchiectasis

CLINICAL ISSUES

- Signs and symptoms
 - Recurrent pneumonia, cough, wheezing, dyspnea
- Prognosis
 - Depends on extent of bronchial wall cartilage deficiency
- Treatment
 Antibiotic prophylaxis for disease exacerbations

(Left) Graphic illustrates the airway abnormalities of Williams-Campbell syndrome, a congenital disorder characterized by bronchiectasis of 4th- to 6thgeneration bronchi due to complete or partial absence of bronchial wall cartilage. (Right) Coronal CECT of a 42year-old patient with Williams-Campbell syndrome shows bilateral bronchiectasis \supseteq of subsegmental bronchi and normal central airways. Typical presentation is in childhood, but patients may also present in adulthood.





(Left) Axial NECT of a 24-yearold patient with Williams-Campbell syndrome shows bilateral central bronchiectasis. The differential diagnosis includes cystic fibrosis, allergic bronchopulmonary aspergillosis, and primary ciliary dyskinesia. (Right) Coronal NECT of the same patient shows bilateral bronchiectasis and normal central airways 🔁 characteristic of Williams-Campbell syndrome. Multiplanar reformatted images help demonstrate the distribution of bronchiectasis.





Abbreviations

• Williams-Campbell syndrome (WCS)

Synonyms

- Bronchomalacia
- Noncystic fibrosis

Definitions

• Rare congenital syndrome characterized by partial or complete absence of cartilage in subsegmental bronchi

IMAGING

General Features

- Best diagnostic clue
- Bilateral bronchiectasis
- Location
 - Involvement of 4th- to 6th-generation bronchi (1st generation of subsegmental bronchi)
- Morphology
 - Cylindrical/cystic bronchiectasis

Radiographic Findings

• Bronchiectasis, bronchial wall thickening, and cystic lesions

CT Findings

- Diffuse bilateral cylindrical/cystic bronchiectasis
- Normal trachea, mainstem bronchi, and segmental bronchi
- Bronchial air-fluid levels may be associated with infection
- Dynamic CT
 - Inspiratory phase: "Ballooning" of bronchiectasis
 - Expiratory phase: Collapse of bronchiectatic airways (absence of cartilaginous plates)
- Virtual bronchoscopy
 - Useful for clinicians; visualization of extent of involvement
 - Highlights absence of cartilage ring impressions along bronchial walls

Imaging Recommendations

- Best imaging tool
 - CT inspiratory/expiratory phases
 - Multiplanar CT reformations to demonstrate distribution and location of bronchiectasis
 - o 3D reformations may be useful to clinicians

DIFFERENTIAL DIAGNOSIS

Cystic Fibrosis

- 80% of cases diagnosed before 5 years of age
- Diffuse cylindrical bronchiectasis with upper lobe predominance

Primary Ciliary Dyskinesia

- Variable age: Infancy to 50 years
- Varicoid bronchiectasis with middle lobe and lingular predominance
- Kartagener syndrome: Situs inversus totalis, bronchiectasis, and sinusitis

Allergic Bronchopulmonary Aspergillosis

• Most affected patients have asthma or cystic fibrosis

- Asthma + peripheral blood eosinophilia + skin reactivity or presence of serum IgE to Aspergillus fumigatus + precipitating antibodies or serum IgG to A. fumigatus + elevated serum IgE (> 1,000 kU/L)
- Bronchiectasis with central/upper lung zone distribution, mucoid impaction: Finger-in-glove opacities
 Hyperattenuating mucus secondary to calcium deposits

PATHOLOGY

General Features

- Etiology
 - Congenital syndrome
 - Acquired hypothesis: Adenovirus infection → bronchomalacia → bronchiectasis
- Associated abnormalities
 - Congenital heart disease, bronchial isomerism, situs inversus, polysplenia, malrotation of abdominal viscera

Gross Pathologic & Surgical Features

- Defective or completely absent cartilages of 4th- to 6thorder bronchi
- Cartilage deficiency is limited to airways

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Recurrent pneumonia
 - Cough, wheezing

Demographics

• Children, occasionally adults

Natural History & Prognosis

• Prognosis depends on extent/severity of cartilage deficiency

Treatment

- Pulmonary resection if bleeding or severe infection
- Respiratory physiotherapy
- Antibiotic prophylaxis for disease exacerbation

DIAGNOSTIC CHECKLIST

Consider

- Distribution of bronchiectasis for formulation of differential diagnosis
 - Central: Allergic bronchopulmonary aspergillosis
 - Upper lobe: Cystic fibrosis
 - o Middle lobe, lingula, lower lobe: Primary ciliary dyskinesia

Image Interpretation Pearls

 Trachea, mainstem bronchi, and segmental bronchi are normal in patients with WCS

- Singh A et al: Bronchiectasis revisited: imaging-based pattern approach to diagnosis. Curr Probl Diagn Radiol. 48(1):53-60, 2019
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- Milliron B et al: Bronchiectasis: mechanisms and imaging clues of associated common and uncommon diseases. Radiographics. 35(4):1011-30, 2015

Broncholithiasis

KEY FACTS

TERMINOLOGY

• Calcified or ossified endoluminal material, usually due to bronchial wall erosion by adjacent calcified lymph node

IMAGING

• Radiography

- Nonspecific peribronchial ca++; postobstructive changes
- CT
 - Endobronchial, transbronchial, peribronchial ca⁺⁺ nodule
 - Extraluminal gas nearly diagnostic of bronchial wall erosion
 - Positional change or disappearance of preexistent endobronchial or peribronchial ca⁺⁺
 - Signs of bronchial obstruction
 - Atelectasis (66%)
 - Postobstructive pneumonitis (33%)
 - Bronchiectasis (33%)
 - Air-trapping (5%)
 - Mucoid impaction

TOP DIFFERENTIAL DIAGNOSES

- Carcinoid
- Airway hamartoma
- Tracheobronchopathia osteochondroplastica
- Airway amyloidosis

PATHOLOGY

• Bronchial wall erosion by adjacent calcified lymph nodes

CLINICAL ISSUES

- Nonproductive cough
- Hemoptysis (may be massive)
- Lithoptysis: Expectoration of calcified material
- Complications: Recurrent pneumonia, bronchiectasis, bronchostenosis, fistula (aortotracheal, mainstem bronchus-to-mainstem bronchus, pulmonary artery-tobronchial artery)
- Treatment depends on clinical scenario: Observation, bronchoscopic removal, surgery

(Left) Composite image with coronal NECT (left) and coronal CECT (right) obtained years later shows a calcified subcarinal lymph node \supseteq that eroded into the left mainstem bronchus 🔁 with a transbronchial configuration. Most broncholiths represent calcified lymph nodes that erode into the airway, as in this case. (Right) Clinical photograph shows broncholith expectorated by the same patient who presented with cough and lithoptysis. Completely endobronchial broncholiths may be treated with bronchoscopic retrieval.





(Left) Axial CECT of a patient with broncholithiasis involving the bronchus intermedius shows a densely calcified nodule within the bronchus intermedius \supseteq and associated right lower lobe consolidation 🔁 secondary to postobstructive pneumonitis and a moderate right pleural effusion 🔁. (Right) Axial NECT of the same patient 3 years after bronchoscopic retrieval of the broncholith shows interval development of shortsegment bronchostenosis \implies , a known complication of broncholithiasis.





Definitions

• Calcified or ossified endoluminal material, usually due to bronchial wall erosion by adjacent calcified lymph node

IMAGING

General Features

- Best diagnostic clue
 - Endobronchial or peribronchial calcified nodule with signs of bronchial obstruction
- Location
 - Most common: Middle lobe and upper lobe anterior segmental bronchi
 - o Right > left (2:1)
 - May occur anywhere from trachea to subsegmental airways but most common in lobar and segmental airways
- Size
- o 2-15 mm
- Morphology
 - Irregular shape, angular margins
 - o Predominant ca++, minimal soft tissue component

Radiographic Findings

- Broncholiths typically not discernible; manifest as nonspecific ca⁺⁺
- Airway obstruction
 - o Atelectasis
 - Mucoid impaction
 - Finger-in-glove opacities
 - o Bronchiectasis
 - Expiratory air-trapping
- Calcified mediastinal &/or hilar lymph nodes

CT Findings

- Endobronchial, transbronchial, or peribronchial calcified nodule
 - o Distortion and narrowing of adjacent airway (50%)
 - Complete airway obstruction (50%)
 - Extraluminal gas nearly diagnostic of bronchial wall erosion
 - o Usually solitary, rarely multiple
 - No enhancement with intravenous contrast
 - Absence of soft tissue mass (critical for differentiation from fibrosing mediastinitis)
 - Positional change or disappearance of preexistent peribronchial ca⁺⁺
- Signs of bronchial obstruction
 - o Atelectasis (66%)
 - Postobstructive pneumonitis (33%)
 - o Bronchiectasis (33%)
 - o Air-trapping (5%)
 - o Mucoid impaction

Imaging Recommendations

- Best imaging tool
 - Thin-section CT is optimal imaging modality to document endobronchial location

DIFFERENTIAL DIAGNOSIS

Carcinoid

- 39% of carcinoids exhibit ca++ or ossification
- May enhance with intravenous contrast; typically dominant soft tissue component

Airway Hamartoma

• May exhibit internal ca++ &/or fat attenuation

Tracheobronchopathia Osteochondroplastica

- Submucosal osteocartilaginous nodules
 - Anterior and lateral tracheal margins
 - o Calcified nodules; usually numerous and diffuse

Airway Amyloidosis

- Localized or diffuse tracheobronchial involvement
- Airway stenosis due to submucosal amyloid deposits
- ca++ usually amorphous or stippled
- Usually diffuse and multifocal rather than solitary

PATHOLOGY

General Features

- Etiology
 - Bronchial wall erosion by adjacent calcified lymph nodes
 Common: Tuberculosis, histoplasmosis
 - Silicosis: Few reported cases
 - Uncommon: Retained foreign bodies, sarcoidosis, cryptococcosis, coccidioidomycosis, endobronchial aspergillosis, endobronchial nocardiosis, and Mycobacterium kansasii pulmonary infection

Gross Pathologic & Surgical Features

- Calcium phosphate (85%), calcium carbonate (15%)
- May be peribronchial, endobronchial or transbronchial

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonproductive cough
 - Hemoptysis (may be massive)
 - Lithoptysis: Expectoration of calcified material
 - o Airway obstruction (rare)
- Other signs/symptoms
 - Recurrent pneumonia, bronchiectasis, bronchostenosis, fistula (aortotracheal, mainstem bronchus-to-mainstem bronchus, and pulmonary artery-to-bronchial artery)

Treatment

- Observation (for asymptomatic or minimally symptomatic)
- Bronchoscopic retrieval: Loose endoluminal broncholith; transbronchial broncholith at risk of massive hemoptysis, only attempt with surgical back-up
- Lobectomy or segmentectomy: Failed bronchoscopic retrieval or bronchiectasis of adjacent lung

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 Alshabani K et al: Broncholithiasis: a review. Chest. 156(3):445-55, 2019
 Jin YX et al: Diagnosis and treatment evaluation of 48 cases of broncholithiasis. Thorac Cardiovasc Surg. 64(5):450-5, 2016

KEY FACTS

TERMINOLOGY

- Centrilobular emphysema (CLE)
- Synonyms
 Centriacinar emphysema
 - o Proximal acinar emphysema
- Destruction and enlargement of respiratory bronchioles near center of secondary pulmonary lobule

IMAGING

- Radiography
 - o Mild disease: May be normal
 - Advanced disease: Heterogeneous lung density, vascular distortion/disruption
 - Hyperinflated and hyperlucent lungs
- CT/HRCT
 - o Centrilobular low attenuation, no discernible wall
 - May visualize central lobular artery surrounded by destroyed lung (**central dot sign**)

TOP DIFFERENTIAL DIAGNOSES

- Panlobular emphysema
- Paraseptal emphysema
- Cystic lung disease
- Constrictive bronchiolitis
- Asthma

PATHOLOGY

• Precursor may be respiratory bronchiolitis

CLINICAL ISSUES

- Symptoms: Dyspnea, shortness of breath
- Strongly associated with cigarette smoking
- Treatment
 - Smoking cessation
 - Lung volume reduction/endobronchial valves
 - Lung transplantation
- Complications: Pneumothorax, hemoptysis, pneumonia, chronic obstructive pulmonary disease exacerbation

(Left) AP chest radiograph of a 63-year-old-man with advanced destructive emphysema (ADE) and apical bullous disease shows lung hyperinflation, increased biapical lucency, as well as distortion and basilar displacement of vascular markings. (Right) Lateral chest radiograph of the same patient shows the characteristic findings of emphysema with flattening of the hemidiaphragms 🖂, increased AP diameter of the chest, as well as increased retrosternal 🔁 and retrocardiac 🛃 spaces.











- Abbreviations
- Centrilobular emphysema (CLE)

Synonyms

- Centriacinar emphysema
- Proximal acinar emphysema

Definitions

• Enlargement and destruction of respiratory bronchioles near center of secondary pulmonary lobule

IMAGING

General Features

- Best diagnostic clue
 - Well-defined round lucencies in centrilobular component of secondary pulmonary lobule on HRCT
 - Anatomical borders of secondary pulmonary lobule preserved
- Location

• Upper lung zone predominant

- Lung apices, lower lobe superior segments
- Size
 - o Mild: 1- to 2-mm centrilobular "holes"
 - Advanced: May occupy entire secondary pulmonary lobule and mimic panlobular emphysema
 CLE with panlobular features
- Morphology
 - Lung destruction near lobular arteriole and bronchiole
 - Well-defined margins between normal and emphysematous lungs with resultant heterogeneous attenuation

Radiographic Findings

- Radiography
 - o Mild: Radiography insensitive, may be normal
 - Weak correlation between functional indices and radiographic findings
 - Advanced: May be visible on radiography
 - Heterogeneous lung density; apical lucency
 - Basilar displacement of vasculature from upper lung hyperinflation
 - Increased branching angle of remaining vessels

• Hyperinflation

- Flat hemidiaphragms
- Increased thoracic AP diameter
- Enlarged retrosternal and retrocardiac spaces
- Small narrow heart
- Secondary manifestations

Pulmonary arterial hypertension

- Enlarged pulmonary trunk and central pulmonary arteries
- Abrupt tapering and attenuation of pulmonary vessels (peripheral arterial pruning)

CT Findings

- HRCT
 - More sensitive than radiography
 - o Detection of clinically and functionally asymptomatic CLE

- Low-attenuation areas in center of secondary pulmonary lobule
 - No discernible wall
 - Pseudo-wall may be present due to surrounding atelectatic lung
 - Surrounded by normal lung
 - Visualization of central lobular artery surrounded by destroyed lung: Central dot sign
 - Preserved borders of secondary pulmonary lobule
- Objectively measured by assuming that lung with threshold HU < -950 is emphysema

Imaging Recommendations

- Best imaging tool
 - HRCT is imaging modality of choice for assessment and characterization of emphysema
- Protocol advice
 - Acquire scans at end inspiration
 - Expiratory scans of little value in CLE
 - Careful evaluation of lung apices and lower lobe superior segments
 - Minimum-intensity projection (MinIP) images increase sensitivity for detecting mild disease
 - CT quantification analysis more accurate at grading extent of disease compared to subjective visual grading

MR Findings

- Inhaled hyperpolarized Helium-3 and Xenon-129 contrast agents
 - Areas of emphysematous lung show abnormally increased ADC values
- May detect regional emphysematous changes prior to clinical symptoms
- Rarely used in clinical practice; ongoing research

DIFFERENTIAL DIAGNOSIS

Panlobular Emphysema

- Pattern of destruction more homogeneous than CLE
- Uniform destruction of secondary pulmonary lobule
- Lower lung predominance early, progression to diffuse involvement

Paraseptal Emphysema

- Distal acinar destruction and enlargement of airspaces
- Single tier of thin-walled subpleural cystic spaces of varying sizes
- Often seen in association with CLE

Cystic Lung Disease

- Cysts with definable walls (e.g., lymphangioleiomyomatosis)
- Nonvisualization of central lobular artery

Langerhans Cell Histiocytosis

- s Smoking-related interstitial lung disease
 - Stellate centrilobular nodules \rightarrow cavitation \rightarrow irregular shaped, thick-walled cysts
 - Upper/mid lung zone distribution
 - Concurrent CLE often also present

Constrictive Bronchiolitis

• No parenchymal destruction, mosaic attenuation

• Air-trapping on expiratory CT

Asthma

- No parenchymal destruction
- Hyperinflation may be reversible

PATHOLOGY

General Features

- Etiology
 - CLE strongly associated with cigarette smoking - Severity related to extent of exposure
 - CLE also occurs after inhalation of industrial dusts (silica)
- Genetics
 - Potential genetic predisposition to CLE
 - Could explain varying extent of lung destruction in individuals with comparable smoking habits
- Associated abnormalities
 - Respiratory bronchiolitis
 - Chronic bronchitis
 - Secondary pulmonary hypertension
- Pathologic functional correlation
 - Patients may have anatomic emphysema without alteration of pulmonary function
 - Functional deterioration after ~ 30% lung destruction
 - o Pulmonary function usually determined by structural integrity of lower lung zones
 - Pulmonary function tests are global summation of airways and lung; HRCT provides regional information

Staging, Grading, & Classification

- HRCT allows objective quantification of emphysema based on attenuation
- Fleischner Society CT-based visual classification of CLE
 - Trace: Minimal lucency, < 0.5% of lung zone
 - Mild: Scattered lucencies with large areas of normal lung, 0.5-5% of lung zone
 - Moderate: Numerous well-defined lucencies. > 5% of lung zone
 - Confluent: Coalescent lucencies spanning several lobules, without parenchymal distortion or significant lobule hyperexpansion
 - o Advanced destructive emphysema (ADE): Panlobular lucencies, hyperexpanded lobules, distortion of pulmonary architecture

Gross Pathologic & Surgical Features

- Centrilobular location
 - o Dilatation of 2nd-order respiratory bronchioles
 - Primarily involves upper lung zones
 - Respiratory bronchiolitis may be precursor

Microscopic Features

- Enlargement and destruction of alveolar walls
- Emphysematous spaces become confluent within acinus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Mild disease
 - Often asymptomatic
 - May be incidental finding on CT

- o Moderate/advanced disease
 - Dyspnea, shortness of breath
 - Increased total and residual lung volumes
 - Residual volume > 120% predicted
 - FEV1 < 80% predicted
 - ↓ diffusion capacity < 80% predicted</p>
 - CLE **most common** form of emphysema associated with symptomatic or fatal chronic obstructive pulmonary disease (COPD)
- Other signs/symptoms
 - Pulmonary hypertension

Demographics

- Age
 - o Incidence peak between 45-75 years
- Sex
 - Slight male predominance (due to smoking habits)
- Epidemiology
 - o Very common disease in industrialized world
 - Geographic variations according to regional smoking habits

Natural History & Prognosis

- With smoking cessation: Stabilization or slow progression
- Without smoking cessation: Accelerated progression to clinically symptomatic form requiring treatment

Treatment

- Smoking cessation: Continued decline of pulmonary function
- Bronchodilators; antibiotics to prevent infection
- Pulmonary rehabilitation: Improved functional exercise • capacity and quality of life
- Lung volume reduction surgery
 - Candidates with ADE
- Endobronchial valve placement in advanced emphysema o Bronchoscopically placed 1-way valve
 - Allows air to exit but not enter treated bronchus
 - o Modest improvement of pulmonary function, exercise tolerance, symptoms
 - o Complications: Pneumothorax, hemoptysis, pneumonia, COPD exacerbation
- Single or bilateral lung transplantation
 - Select patients with advanced disease but preserved functional status
 - Survival benefit: Improves physiologic and functional outcomes
 - Limited by organ availability and complications

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- CLE is very common "incidental" CT finding in smokers
 - o Focal low-attenuation areas with imperceptible walls
 - Upper lung zone predominance
 - Optimally evaluated on HRCT

SELECTED REFERENCES

El Kaddouri B et al: Fleischner Society visual emphysema CT patterns help predict progression of emphysema in current and former smokers: results from the COPDGene study. Radiology. 298(2):441-9, 2021

Centrilobular Emphysema





(Left) Axial CECT of a 69-yearold-man with confluent centrilobular emphysema shows centrilobular lucencies ➡ surrounded by normal lung *increased increased increased* attenuation, accentuated by superimposed pulmonary edema in this patient. (Right) Axial NECT of a 59-year-old smoker with dyspnea and obstructive pulmonary function tests shows upper lobe predominant lucencies with imperceptible walls \square , surrounding centrilobular pulmonary arteries (central dot), characteristic of centrilobular emphysema.





(Left) Axial CECT of a patient with ADE and superimposed multifocal infection 🔁 is shown. Emphysematous lung with consolidation should not be confused with cystic lung disease or honeycombing. (Right) Coronal minIP reformatted image of a 64year-old female smoker with moderate centrilobular emphysema shows the apical predominant centrilobular lucencies 🔁 as a result of centriacinar destruction and airspace enlargement. Paraseptal emphysema \supseteq is often seen concurrently.





(Left) Sagittal NECT of a 66year-old man shows the characteristic craniocaudal distribution of centrilobular emphysema, which most significantly affects the upper lobes \supseteq and superior segments \bowtie of the lower lobes. (Right) Axial NECT of a 59-year-old smoker with progressive dyspnea shows scattered lucencies in the upper lobes without discernible walls, surrounding centrilobular pulmonary arteries 🔁 (central dot). Minimal paraseptal emphysema 🗃 also present.

Paraseptal Emphysema

KEY FACTS

TERMINOLOGY

- Paraseptal emphysema (PSE)
- Synonym: Distal acinar emphysema
- Permanently enlarged distal acinus with destruction of alveolar ducts and sacs
- Bullae: Dilated, thin-walled peripheral airspaces > 1 cm

IMAGING

• Radiography

- May be normal; mild PSE difficult to detectPeripheral lung lucencies with thin walls
- CT/HRCT
 - Subpleural and peribronchovascular single tier of cystic spaces
 - Separated by intact interlobular septa
 - Minimum-intensity projection (minIP) images may improve detection
 - HRCT is imaging modality of choice

TOP DIFFERENTIAL DIAGNOSES

- Cystic lung disease
- Centrilobular emphysema
- Panlobular emphysema
- Honeycomb lung (pulmonary fibrosis)

PATHOLOGY

• 1 incidence: Smokers, IV drug users, HIV(+) patients

CLINICAL ISSUES

- Often incidentally detected
- Treatment
 - Smoking cessation
 - Pleurodesis for recurrent pneumothorax
 - Lung volume reduction for severe bullous disease

DIAGNOSTIC CHECKLIST

• Consider PSE as cause of spontaneous pneumothorax

(Left) Axial NECT of a 65-yearold male smoker with paraseptal emphysema shows typical apical subpleural cystic changes, mostly composed of a single tier of cysts 🔁 separated by intact interlobular septa. Mild centrilobular emphysema 🔁 often coexists. (Right) Coronal NECT of the same patient shows the upper lung zone predominant and subpleural location of cystic spaces \supseteq as well as along bronchovascular structures $\overline{\nearrow}$, typical of paraseptal emphysema.





(Left) Coned-down PA chest radiograph of a 58-year-old man with paraseptal emphysema shows upper lung subpleural lucencies and thin linear opacities 🔁. (Right) Coronal HRCT of the same patient shows upper lung predominant, peripheral 🖂, fissural \square , and subpleural cystic spaces as a result of distal acinar destruction. Unlike honeycombing with basilar, multi-tiered and thickwalled cysts, paraseptal emphysema typically manifests with a single tier of cystic spaces separated by intact interlobular septa.





Abbreviations

• Paraseptal emphysema (PSE)

Synonyms

• Distal acinar emphysema

Definitions

- Destruction located in lung periphery adjacent to pleura or along interlobular septa
- Permanently enlarged distal airspaces with destruction
- Bulla: Dilated airspace measuring > 1 cm
 - Bullae: Circumscribed, thin-walled, coalescent destroyed acini
- Vanishing lung syndrome: Severe PSE and large bullae (> 1/3 of hemithorax) compression of adjacent lung

IMAGING

General Features

- Best diagnostic clue
 - Small subpleural lucencies arranged as single tier of "cystic" spaces
- Location
 - Upper lung predominant

Radiographic Findings

- Radiography
 - May be normal; mild PSE difficult to detect
 - Peripheral lung lucencies with thin walls

CT Findings

- HRCT
 - Subpleural and peribronchovascular arcades of cystic spaces
 - Cystic spaces separated by intact interlobular septa
 - Minimum-intensity projection (minIP) images may improve detection

Imaging Recommendations

- Best imaging tool
 - HRCT is imaging modality of choice for assessment and characterization of emphysema

DIFFERENTIAL DIAGNOSIS

Cystic Lung Disease

- Thin-walled cysts
- Not confined to subpleural location

Centrilobular Emphysema

- Most common type of emphysema
- Frequently associated with PSE
- Low-attenuation foci with imperceptible walls

Panlobular Emphysema

- Diffuse regions of low attenuation with paucity of vascular structures
- Lower lung predominant hyperlucency

Honeycomb Lung (Pulmonary Fibrosis)

- Multiple tiers of subpleural cysts; thicker walls
- Lower lung predominant

PATHOLOGY

General Features

Etiology

- o Pathogenesis unclear
 - Animal models with pleural surface capillary changes and pulmonary perfusion deficiency → subpleural destruction

• Association with tall and thin body habitus

- Postulated mechanism: ↑ gravitational pull on lungs with greater negative pleural pressure at lung apices
- ↑ incidence in **smokers**, IV drug users, HIV(+) patients
- Marijuana cigarettes may be more highly associated
- Often coexists with centrilobular emphysema

Microscopic Features

- Peripheral components of acinus dominantly and selectively involved
 - o Destruction and dilation of alveolar ducts and sacs
 - Adjacent to pleural surfaces and interlobular septa

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Often asymptomatic; minimal effect on pulmonary function in early/mild disease
- Other signs/symptoms
 - Acute dyspnea and chest pain with **spontaneous pneumothorax**

Demographics

- Classically occurs in **male smokers**; 4th decade
- Prevalence: 3% in community \rightarrow 15% of smokers

Natural History & Prognosis

- Progression with advancing age
- Progression with cumulative smoking pack-years

Treatment

- Smoking cessation
- Pleurodesis for recurrent pneumothorax
- Lung volume reduction: Surgical bullectomy or endobronchial occlusion

DIAGNOSTIC CHECKLIST

Consider

• PSE as potential cause of spontaneous pneumothorax

Image Interpretation Pearls

• Characteristic subpleural location allows differentiation from lymphangioleiomyomatosis and Langerhans cell histiocytosis, which affect a similar population that may present with spontaneous pneumothorax

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Panlobular Emphysema

KEY FACTS

TERMINOLOGY

- Panlobular emphysema (PLE)
- Enlargement and destruction of entire acinus or secondary pulmonary lobule

IMAGING

- Radiography
 - o Very insensitive
 - May be normal
 - Hyperinflation, flat diaphragm, increased retrosternal space
- HRCT
 - o Diffuse areas of low attenuation with paucity of vesselso Difficult distinction between normal and affected lung

TOP DIFFERENTIAL DIAGNOSES

- Centrilobular emphysema (advanced)
- Paraseptal emphysema
- Asthma

PATHOLOGY

- α-1-antitrypsin deficiency (α1AD)
- Destruction of entire acinus

CLINICAL ISSUES

- Mild disease
 - Often asymptomatic
 - May be incidental finding on HRCT
- Advanced disease
- o Dyspnea
- > 3 million people worldwide with severe a1AD
- Treatment
 - Bronchodilators and prevention of infection
 - Lung volume reduction: Surgery or endobronchial valves
 - May require surgery or transplant; may recur

DIAGNOSTIC CHECKLIST

• Consider PLE in patients with diffuse homogeneous decreased lung attenuation on CT/HRCT

(Left) AP chest radiograph of a 53-year-old man with a 40 pack-year smoking history shows marked hyperexpansion and hyperlucency throughout both lungs with distortion and paucity of vascular structures. (Right) Coronal NECT of the same patient shows the lower lung predominant, diffuse low $attenuation \ge of the lung$ with paucity of small-caliber intrinsic vascular structures. This patient was found to be a heterozygote carrier of the a-1-antitrypsin deficiency gene. Lung destruction was compounded by the patient's cigarette smoking.











Abbreviations

- Panlobular emphysema (PLE)
- α-1-antitrypsin deficiency (α1AD or AATD)

Synonyms

• Panacinar emphysema

Definitions

• Enlargement and destruction of entire acinus or secondary pulmonary lobule

IMAGING

General Features

- Best diagnostic clue
 - Ill-defined areas of abnormal lucency and paucity of vessels
 - Difficult distinction of normal lung from PLE
- Location
 - o Diffuse lung disease with lower lobe predominance

Radiographic Findings

- Radiography
 - o Mild disease: Very insensitive, may be normal
 - Advanced disease: Vascular distortion and disruption, paucity of vascular markings
 - Hyperinflation
 - Flattened hemidiaphragms
 - Increased AP diameter of thorax
 - Increased retrosternal/retrocardiac spaces

CT Findings

- HRCT
 - **Diffuse regions of lucency** with paucity of vessels in affected areas
 - o Difficult to distinguish between normal lung and PLE
 - o Bronchiectasis

Nuclear Medicine Findings

- V/Q scan
 - o Ventilation imaging with Xe-133 or Tc-99m DTPA
 - Abnormal wash-in/equilibrium phase
 - Heterogeneous radiotracer distribution
 - Abnormal washout
 - Radiotracer retention in affected lung as result of obstructive air-trapping

Imaging Recommendations

- Best imaging tool
 - HRCT for optimal visualization and assessment of PLE

DIFFERENTIAL DIAGNOSIS

Centrilobular Emphysema

- Upper lung; centrilobular lung destruction
- Normal vs. emphysema distinction more apparent

Paraseptal Emphysema

- Single tier of subpleural cystic airspaces
- Bullae often present

Cystic Lung Disease

• Cysts with discrete, definable walls

Asthma

- Mosaic attenuation/air-trapping, bronchial wall thickening
- No parenchymal destruction

PATHOLOGY

General Features

- Etiology
 - ο Highly associated with α1AD
 - Protease enzyme responsible for inhibition of neutrophil elastase
 - □ Encoded by genes PI *(GSTP1)*, MIM *(MTSS1)* + 107400; > 100 alleles identified
 - Homozygous carriers most severely affected; heterozygotes less so
 - o Idiopathic PLE does occur; 5-10% of random autopsies
 - Less common causes
 - Intravenous methylphenidate abuse ("Ritalin lung")
 - Elastin abnormalities: Ehlers-Danlos, cutis laxa
- Associated abnormalities
 - Chronic bronchitis and recurrent infection
 - Secondary pulmonary hypertension
 - **Smokers with a1AD** often have concomitant centrilobular or paraseptal emphysema

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Mild disease: Often asymptomatic
 - o Advanced disease: Progressive dyspnea
 - Abnormal pulmonary function
 - □ Increased total and residual lung volume
 - □ ↓ FEV1 < 80% predicted
 - □ ↓ diffusion capacity < 80% predicted

Demographics

- Epidemiology: Underrecognized disease
 - > 3 million people worldwide have severe α1ADOnder-recognized disease
- Age: a1AD typically diagnosed in 3rd to 4th decade
- Sex: Slight male predominance

Natural History & Prognosis

• Rapid progression if untreated

Treatment

- Bronchodilators and prevention of infection
- Lung volume reduction: Surgery or endobronchial valves
- Lung transplantation in severely affected; may recur

DIAGNOSTIC CHECKLIST

Consider

• PLE in patients with diffuse homogeneously decreased lung attenuation on CT/HRCT

SELECTED REFERENCES

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Infectious Bronchiolitis

KEY FACTS

TERMINOLOGY

• Cellular bronchiolitis resulting from bacterial, fungal, or viral infection

IMAGING

- Centrilobular nodules: ≤ 3-mm regularly spaced nodules that spare subpleural lung; represent bronchiolar filling in central secondary pulmonary lobules
- Acute
 - Centrilobular nodules
 - Solid, discrete, associated with tree-in-bud pattern
 - Bronchial wall thickening
 - ± ground-glass or consolidation
 - ± air-trapping
- Chronic
 - Nontuberculous mycobacteria (NTMB) and Pseudomonas
 - Bronchiectasis
 - Middle lobe and lingula tend to exhibit more advanced disease

- Tuberculosis and cavitary NTMB
 - Upper lobe predominant involvement
 - Tree-in-bud nodules + cavitation + nodules, masses, or consolidations

TOP DIFFERENTIAL DIAGNOSES

- Aspiration bronchiolitis
- Diffuse panbronchiolitis

PATHOLOGY

• Acute bronchiolar injury, epithelial necrosis, bronchiolar wall inflammation and edema, intraluminal exudate

CLINICAL ISSUES

- Acute: Clinical symptoms similar to those of acute pneumonia
- Chronic
 - NTMB: Often asymptomatic, chronic coughTuberculosis: Chronic cough, weight loss, fever
- Treatment: Supportive care, antimicrobials

(Left) PA chest radiograph of a patient with acute infectious bronchiolitis secondary to respiratory syncytial virus (RSV) shows bilateral illdefined reticulonodular opacities. (Right) Coronal HRCT of the same patient shows diffuse bilateral centrilobular micronodules, tree-in-bud opacities, and scattered upper lobe groundglass opacities 🔁. RSV is the most common viral cause of acute infectious bronchiolitis. RSV infection in children has been linked with an increased incidence of asthma.





(Left) PA chest radiograph of a patient with infectious bronchiolitis shows bilateral patchy and reticulonodular basilar opacities 🔁 without lobar consolidation or pleural effusion. (Right) Axial CECT of the same patient shows centrilobular nodules 🔁 and patchy ground-glass opacities corresponding to the radiographic abnormalities. The lower lobe and posterior distribution of the bronchiolitis raises aspiration as a possible etiology, typically distinguished from infection based on clinical presentation.





Abbreviations

- Nontuberculous mycobacteria (NTMB)
- Respiratory syncytial virus (RSV)

Definitions

• Cellular bronchiolitis resulting from bacterial, fungal, or viral infection

IMAGING

General Features

- Best diagnostic clue
 - CT: Centrilobular &/or tree-in-bud nodules
- Morphology
 - o Centrilobular nodules, usually solid
 - Ground-glass nodules may occur in viral bronchiolitis

Radiographic Findings

- Acute
 - o May be normal
 - Normal to increased lung volume
 - Nodular or reticulonodular opacities
 - Bronchial wall thickening
- Chronic
 - NTMB and Pseudomonas. Reticulonodular opacities
 - Tuberculosis (postprimary pattern) and cavitary NTMB: Upper lobe cavitary nodules, masses, or consolidations

CT Findings

- **Centrilobular nodules**: ≤ 3-mm regularly-spaced nodules spare subpleural lung; represent bronchiolar filling in central secondary pulmonary lobules
 - **Tree-in-bud pattern**: Subset of centrilobular nodules with coexistent centrilobular and branching X- or Yshaped opacities
- Acute
 - Centrilobular nodules
 - Usually solid and discrete, often with associated treein-bud pattern
 - May exhibit ground-glass attenuation
 - Bronchial wall thickening
 - ± ground-glass opacities or consolidations
 - May be lobular, particularly when caused by Mycoplasma pneumoniae
 - Consolidation common in infections from Adenovirus, *M. pneumoniae*, and mycobacteria
 - ± air-trapping
 - Common in viral infections, particularly RSV
- Chronic
 - NTMB and Pseudomonas
 - Bronchiectasis
 - Mosaic attenuation, air-trapping
 - Middle lobe and lingula tend to exhibit more advanced disease
 - Tuberculosis and cavitary NTMB
 - Upper lobe predominant involvement
 - Tree-in-bud nodules + cavitation + nodules, masses or consolidations

DIFFERENTIAL DIAGNOSIS

Aspiration Bronchiolitis

- Often indistinguishable from infectious bronchiolitis
- Risk factors for aspiration (e.g., esophageal dysmotility, neurologic impairment, head and neck malignancies)

Predilection for dependent lung Diffuse Panbronchiolitis

• Common clinical context: Asian patients (e.g., from Japan or Korea)

PATHOLOGY

General Features

- Etiologies
 - o Acute
 - Viral (e.g., RSV, parainfluenza, rhinovirus, metapneumovirus)
 - Bacterial (e.g., *M. pneumoniae, Haemophilus influenzae*)
 - Immune compromise: Fungal (Aspergillus fumigatus)
 - o Chronic
 - Mycobacteria (tuberculosis and NTMB)
 - Pseudomonas species

Gross Pathologic & Surgical Features

- Histopathology: Acute bronchiolar injury, epithelial necrosis, bronchiolar wall inflammation and edema, intraluminal exudate
- ± injury to mucosa, bronchiolar wall fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute: Similar to acute pneumonia
 - o Chronic
 - NTMB: Often asymptomatic, chronic cough
 - Tuberculosis: Chronic cough, weight loss, fever

Demographics

- Most common cause of hospitalization among infants in USA
- Adult disease varies with immune status
 Immunocompetent: Bacteria (*Mycoplasma*), viruses (parainfluenza), mycobacteria (tuberculous and NTMB)
 - Immunocompromised with human immunodeficiency virus infection: Fungi (*A. fumigatus*), tuberculosis
 - Immunocompromised after stem cell transplant: Viruses (RSV, parainfluenza)

Treatment

• Supportive care, antimicrobials

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- Tanaka N et al: Infection in immunocompromised hosts: imaging. J Thorac Imaging. 33(5):306-21, 2018
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(Left) AP chest radiograph of a patient with postprimary pattern of tuberculosis shows right greater than left upper lobe heterogeneous opacities with intrinsic lucency 🖂, concerning for cavitation. (Right) Axial NECT of the same patient shows extensive bilateral centrilobular nodules and tree-in-bud opacities and a right upper lobe cavitary lesion \supseteq . The findings are classic for active pulmonary tuberculosis. Affected patients should be immediately isolated until tuberculosis is excluded to avoid dissemination of disease.





(Left) Axial CECT of a patient with cavitary (classic) nontuberculous mycobacterial infection shows multifocal bilateral upper lobe cavities $rac{1}{2}$ on a background of emphysema 🔁. (Right) Axial CECT MIP reformatted image of the same patient shows bilateral centrilobular nodules and tree-in-bud opacities. Cavitary nontuberculous mycobacterial infection is indistinguishable from the postprimary pattern of tuberculosis. Common related mycobacteria include M. avium complex and M. kansasii.





(Left) PA chest radiograph of a patient with bronchiectatic nontuberculous mycobacterial infection shows left greater than right mid and lower lung zone linear and micronodular opacities. Note obscuration of the right and left heart borders that indicates middle lobe and lingular involvement, respectively. (Right) Axial HRCT of the same patient shows extensive bronchiectasis and volume loss involving the middle lobe ᠫ and lingula \supseteq and bilateral lower lobe centrilobular micronodules and tree-in-bud opacities 🔁.





Infectious Bronchiolitis





(Left) Axial NECT of a patient with chronic bronchiectatic nontuberculous mycobacterial infection shows middle lobe 🖻 and lingular 🔁 bronchiectasis and volume loss and subtle bilateral lower lobe centrilobular nodules 🖂, some of which exhibit a branching tree-in-bud configuration. (Right) Coronal CECT of a patient with acute M. pneumoniae pneumonia ground-glass ᠫ centrilobular nodules and multifocal bilateral lower lobe nodular consolidations 🔁.





(Left) Axial CECT of a patient with acute herpes virus bronchiolitis shows multiple punctate ill-defined centrilobular nodules \supseteq and subtle ground-glass opacities ∠ Note scattered areas of hyperlucency 🖾, suggestive of air-trapping. Air-trapping is a common marker of small airways disease and is often present in viral infectious bronchiolitis. (Right) Axial CECT of a patient with adenovirus pulmonary infection shows a dense right lower lobe consolidation 🔁 surrounded by centrilobular micronodules $\overline{\rightarrow}$.





(Left) PA chest radiograph of a young woman with a postprimary pattern of tuberculosis shows a right upper lobe heterogeneous consolidation and volume loss. Note adjacent ill-defined right lower lobe nodular opacities □ (Right) Axial CECT MIP reformatted image of the same patient shows right upper lobe tree-in-bud opacities, consolidation 🖂, and a thick-walled cavity 🖂, characteristic of postprimary pattern of tuberculosis. The presence of tree-in-bud nodules is consistent with active tuberculosis infection.

KEY FACTS

TERMINOLOGY

• Constrictive bronchiolitis (CB)

IMAGING

- Best diagnostic clue: Mosaic attenuation and expiratory airtrapping on HRCT
- Radiography
 - o Normal chest radiographs
 - Hyperinflation, peripheral attenuation of vascular structures, multiple small nodules, air-trapping on expiratory radiography
- HRCT
 - Mosaic attenuation: Alternating areas of decreased and increased lung attenuation
 - Inspiratory CT may be normal
 - Air-trapping on expiratory CT
 - Bronchial dilatation, bronchiectasis, bronchial wall thickening
 - Scattered centrilobular nodules

TOP DIFFERENTIAL DIAGNOSES

- Panlobular emphysema
- Pulmonary artery hypertension
- Asthma

PATHOLOGY

- Etiologies
 - o Postinfectious
 - Lung and heart-lung transplantation
 - Hematopoietic stem cell transplantation
 - Connective tissue disease

CLINICAL ISSUES

• Chronic and slowly progressive course

DIAGNOSTIC CHECKLIST

• Consider CB in patients with HRCT findings of mosaic attenuation and air-trapping in the appropriate clinical setting

(Left) Graphic illustrates the CT findings of constrictive bronchiolitis characterized by alternating increased \square and decreased \square lung attenuation with borders that conform to the contours of underlying secondary pulmonary lobules. (Right) Axial inspiratory NECT of a patient status post lung transplantation for cystic fibrosis shows mosaic attenuation, which is an imaging manifestation of constrictive bronchiolitis. The most common symptoms at the time of clinical presentation are dyspnea and chronic cough.





(Left) Axial expiratory HRCT of a patient with rheumatoid arthritis and constrictive bronchiolitis shows left lung mosaic attenuation and expiratory air-trapping 🖂. Scattered centrilobular micronodules \blacksquare are also present. (Right) Axial CECT of a 66-year-old woman with diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) shows mosaic attenuation from constrictive bronchiolitis and small lung nodules \square that correlate with pulmonary neuroendocrine proliferations.





Definitions

- **Bronchiolitis**: Inflammatory and fibrotic processes that affect small airways
 - o Multiple classification schemes
 - Clinical features, setting, etiologies
 - Histologic and HRCT findings
- Bronchiolitis obliterans
 - Constrictive bronchiolitis (CB)
 - Irreversible peribronchiolar fibrosis with resultant bronchiolar narrowing or obstruction
 - Collagen deposition extrinsic to airway lumen
 - Cryptogenic organizing pneumonia (COP)
 - Previously known as bronchiolitis obliterans organizing pneumonia (BOOP)
 - Fibroblastic proliferation mainly involving alveolar ducts and alveolar spaces
 - Typically responds to steroids
- **Obliterative bronchiolitis**: Clinical syndrome of airflow obstruction, may be associated with CT or HRCT findings of small airways disease
- Swyer-James-MacLeod syndrome: Unilateral or focal postinfectious CB
- Bronchiolitis obliterans syndrome (BOS): Clinical syndrome of chronic rejection after lung transplantation

IMAGING

General Features

- Best diagnostic clue
 - Mosaic attenuation and expiratory air-trapping on HRCT

Radiographic Findings

- Radiography
 - Chest radiographs are usually normal
 - Nonspecific findings
 - Hyperinflation
 - Peripheral attenuation of vascular structures
 - Multiple small nodules
 - o Swyer-James-MacLeod syndrome
 - Unilateral hyperlucent lung
 - Decreased pulmonary vascularity
 - Normal or decreased volume of affected lung
 - Small ipsilateral hilum
 - Air-trapping on expiratory radiography

CT Findings

- HRCT
 - **Mosaic attenuation**: Alternating areas of decreased and increased lung attenuation
 - Decreased lung attenuation
 - Decreased vessel caliber from hypoxic vasoconstriction
 - □ No decrease in lung cross-sectional area
 - Increased (normal) lung attenuation
 - Increased vessel caliber and blood flow
 - $\circ~$ Air-trapping on expiratory CT
 - May be lobular, segmental, or lobar
 - Large confluent areas of decreased attenuation may be present

- Not diagnostic of CB in absence of functional abnormalities
- Mild expiratory air-trapping may be seen in normal patients
- Inspiratory CT in CB may be completely normal
- Ancillary findings
 - Bronchial dilatation, bronchiectasis, bronchial wall thickening
 - Scattered centrilobular nodules
 - Pulmonary nodules
 - Consider diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH)

Swyer-James-MacLeod syndrome

- Focal lung hyperlucency and decreased vascularity
- Normal or decreased volume of affected lung
- Air-trapping in affected lung on expiratory CT
- Areas of air-trapping and hyperlucency typically found in other lobes and contralateral lung

MR Findings

- Hyperpolarized 3-Helium MR imaging
 - Delineates extent of air-trapping
 - Earlier detection of disease than with spirometry or HRCT

Imaging Recommendations

- Best imaging tool
 - Expiratory HRCT for detection and characterization of air-trapping

DIFFERENTIAL DIAGNOSIS

Panlobular Emphysema

- Parenchymal destruction and vascular distortion
- Decreased lung attenuation

Decreased vessel caliber

• Diffuse or lower lung zone predominance

Pulmonary Artery Hypertension

- Mosaic lung attenuation (perfusion)
 - Decreased vessel caliber in areas of low attenuation
 Increased vessel caliber in areas of high attenuation
- Air-trapping may occur
- Enlarged pulmonary trunk and pulmonary arteries

Asthma

- Reversible reactive small airway obstruction
- Common disease: 5% of adults, 10% of children
- Mosaic attenuation less frequent than in CB
- Severe asthma may be indistinguishable from CB
- Severe cases: Bronchial wall thickening, bronchial dilatation, mucus plugging

PATHOLOGY

General Features

- Etiology
- Postinfectious
 - Childhood infection
 - Viral: Adenovirus type 7 most common; also respiratory syncytial virus (RSV), measles, parainfluenza, influenza

- 🗆 Bacterial: Mycoplasma pneumoniae
- Swyer-James-MacLeod syndrome
 - Subset of affected patients
 - Typically unilateral involvement following childhood viral bronchiolitis
- Cystic fibrosis
- Sequela of recurrent episodes of pulmonary infection
- Lung and heart-lung transplantation
 - Chronic rejection or graft-vs.-host disease
 Prevalence of 50% in survivors 5 years post transplantation
 - Severe infection; cytomegalovirus pneumonia

• Hematopoietic stem cell transplantation

- Manifestation of graft-vs.-host disease
- Classically described in allogeneic transplants
 Less common in autologous transplants
- Connective tissue diseases
- Rheumatoid arthritis
 - □ Middle-aged women with longstanding disease
 - \Box ± association with penicillamine therapy
- Systemic lupus erythematosus
- Scleroderma
- Sjögren syndrome

• Inhalational lung diseases

- Nitrous gases: NO, NO₂, N₂O₂
- Sulfur dioxide: SO2
- Ammonia, chlorine, phosgene
- Occupational exposure to diacetyl (e.g., popcorn flavoring)
- Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia
 - Proliferation of pulmonary neuroendocrine cells
 - Tumorlets manifesting as pulmonary nodules
 - Nodular proliferations > 5 mm: Carcinoid tumors
 - Women > 40 years of age with asthma-like symptoms
- Idiopathic
 - Older women; very poor prognosis
 - Variable history of cigarette smoking
- Miscellaneous conditions
 - Ingestion of uncooked Sauropus androgynous
 - Inflammatory bowel disease
 - Paraneoplastic pemphigus
 - Gold and penicillamine therapy

Microscopic Features

- Narrowing of membranous and respiratory bronchioles
 - Concentric involvement
 - Inflammation and fibrosis of submucosal and peribronchiolar tissues
 - No polyps or granulation tissue
- Lung or heart-lung transplantation
- Chronic rejection: Submucosal and intraepithelial lymphocytic and histiocytic infiltrates

CLINICAL ISSUES

Presentation

Most common signs/symptoms
 Dyspnea, chronic cough

- Other signs/symptoms
 - Symptoms of lower respiratory tract infection
 - Mid inspiratory squeaks, wheezes, crackles on auscultation
 - o Swyer-James-MacLeod syndrome
 - Affected patients may be asymptomatic
 - Cough, recurrent infection, or hemoptysis
 - o Inhalational lung disease
 - Mild symptoms
 - May progress to pulmonary edema and acute respiratory distress syndrome
 - Patients who recover may initially become asymptomatic
 - Subsequently develop progressive cough, dyspnea, and hypoxemia

Natural History & Prognosis

- Chronic and slowly progressive course is most common
- Rapidly progressive course has been described
 More common in idiopathic CB
 - Eventual respiratory failure
- Pulmonary function tests
 - Mixed restrictive and obstructive abnormalities
- Lung transplantation
 - Median time between transplantation and CB: 16-20 months
 - Leading cause of death after 1st year post transplantation
 - o Survival after CB: 30-40%
- Graft-vs.-host disease
 - o Mortality: 12% at 5 years; 18% at 10 years

Treatment

- Limited success of treatment regimens
- Treatment of concomitant infection
- Macrolide antibiotics for chronic inflammatory lung diseases
- Corticosteroids and augmentation of immunosuppression in transplant recipients
- Extracorporeal photopheresis
 - Prophylaxis and treatment of acute rejection in heart transplantation
 - Preliminary results in lung transplantation encouraging
 - Significant reduction in rate of decline of lung function and improved forced expiratory volume in 1 second (FEV₁)

DIAGNOSTIC CHECKLIST

Consider

• CB in patients with HRCT findings of mosaic attenuation and air-trapping in the appropriate clinical setting

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Constrictive Bronchiolitis





(Left) PA chest radiograph of a patient with Swyer-James-MacLeod syndrome demonstrates hyperinflation of the left lung, which is also more lucent and contains vessels of smaller caliber compared to the right lung. (Right) Coronal CECT of the same patient demonstrates , hyperinflation and hyperlucency of and decreased vascularity throughout the left lung. Swyer-James-MacLeod syndrome is a rare entity associated with postinfectious constrictive bronchiolitis occurring in childhood that affects a subset of patients.





(Left) Axial HRCT of a patient with chronic graft-vs.-host disease shows mosaic attenuation on inspiratory HRCT. Areas of increased lung attenuation contain larger caliber pulmonary vessels 🄁 and alternate with lowattenuation areas Ξ . (Right) Axial HRCT of the same patient shows accentuation of mosaic attenuation on expiratory HRCT, consistent with expiratory air-trapping. The normal lung exhibits increased attenuation $\overline{\boldsymbol{\boldsymbol{\varnothing}}}$, while the abnormal lung exhibits decreased attenuation \supseteq .





(Left) Axial expiratory HRCT of a patient who is status post smoke inhalation in a house fire shows multifocal bilateral air-trapping ➡. Air-trapping is not diagnostic of constrictive bronchiolitis, and small degrees of lobular air-trapping may be seen in normal patients. (Right) Coronal NECT of a patient with cystic fibrosis and constrictive bronchiolitis shows multifocal mosaic attenuation with alternating areas of increased and decreased lung attenuation associated with bronchial wall thickening ₽, bronchiectasis \blacksquare , and mucus plugs.

KEY FACTS

TERMINOLOGY

- Swyer-James-MacLeod syndrome (SJM)
- Constrictive bronchiolitis secondary to childhood infectious bronchiolitis
- Constrictive bronchiolitis: Irreversible obstructive small airways disease; submucosal and peribronchiolar fibrosis with small airways destruction and scarring

IMAGING

- Radiography
 - Hyperlucent lobe or lung without hyperexpansion
 - Decreased vascular markings in regions of hyperlucency
- CT
 - Hyperlucent lung with small intrinsic pulmonary vessels
 Typically bilateral; entire lung, lobe, or several pulmonary segments
 - Mosaic attenuation (perfusion)
 - Expiratory air-trapping
 - Frequent bronchiectasis

TOP DIFFERENTIAL DIAGNOSES

- Asthma
- Bronchiectasis
- Congenital interruption of pulmonary artery
- Panlobular emphysema

PATHOLOGY

• Epithelial injury caused by lower respiratory tract infection → peribronchiolar fibrosis → small airways obstruction

CLINICAL ISSUES

- Typically asymptomatic
- Wheezing, cough, dyspnea on exertion
- History of childhood respiratory infection; often unknown

DIAGNOSTIC CHECKLIST

 consider SJM in asymptomatic patient with unilateral hyperlucent lung on radiography and multifocal areas of hyperlucent lung, bronchiectasis, and air-trapping on CT

(Left) PA chest radiograph of a 35-year-old woman with a childhood history of occult foreign body aspiration that resulted in recurrent infections shows a hyperlucent left hemithorax, without significant hyperexpansion and decreased vascularity 🔁 throughout the left lung. (Right) Axial CECT of the same patient shows a hyperlucent left lung with paucity of smallcaliber vessels \supseteq in the left upper and lower lobes, consistent with Swyer-James-MacLeod syndrome due to repetitive airway insults in early childhood.





(Left) Coronal NECT of an asymptomatic 18-year-old patient with prior respiratory syncytial virus infection in infancy and presumptive Swyer-James-MacLeod syndrome shows multifocal regions of hyperlucency \supseteq with intrinsic small pulmonary vessels. (Right) Coronal NECT of a patient with severe Adenovirus infection in childhood shows a hyperlucent left lung, paucity of smallcaliber pulmonary vessels ₽, and mild bronchial wall thickening 🔁. Clinical diagnosis was Swyer-James-MacLeod syndrome.





Abbreviations

• Swyer-James-MacLeod syndrome (SJM)

Synonyms

- Swyer-James syndrome
- MacLeod syndrome
- Controversy regarding eponyms to be ascribed to syndrome
 - MacLeod presented report of 9 patients with "abnormal transradiancy of 1 lung," which was "small or normal size" at British Thoracic Society meeting in London in February of 1952
 - Swyer and James published case of "unilateral pulmonary emphysema" in 1953
 - o MacLeod published his work in 1954

Definitions

- Constrictive bronchiolitis as result of childhood infectious bronchiolitis (typically from Adenovirus infection)
- Constrictive bronchiolitis: Irreversible obstructive small airways disease characterized by submucosal and peribronchiolar fibrosis with resultant destruction and obliterative scarring of small airways
- Mosaic attenuation (perfusion): Geographic regions of increased parenchymal attenuation with intrinsic large pulmonary vessels adjacent to regions of decreased attenuation with intrinsic small pulmonary vessels

IMAGING

General Features

- Best diagnostic clue
 - Unilateral small or normal-sized lung
 - Diminished pulmonary vascularity
 - Areas of expiratory air-trapping
 - Bronchial wall thickening and bronchiectasis
- Location
 - o May be localized to single lobe or affect entire lung
 - May affect 1 or more pulmonary segments
 - Involvement typically bilateral
 - Radiographic abnormalities may appear unilateral
 - Bilateral involvement on CT
- Morphology
 - Original published description by Swyer and James in 1953
 - Unilateral hyperlucent lung
 - Small ipsilateral pulmonary artery
 - Incomplete filling of ipsilateral peripheral bronchioles with contrast material at bronchography
 - Decreased size and number of pulmonary artery branches within affected lung
 - Bronchiectasis often present

Radiographic Findings

- Hyperlucent lobe or lung without hyperexpansion (small to normal-sized affected lung)
- No ipsilateral volume loss or change in density on expiratory imaging as result of air-trapping
- Decreased vascular markings within regions of hyperlucency

• Small ipsilateral hilum

CT Findings

- Regions of hyperlucency with small associated vascular structures
 - Hyperlucent foci affecting **both lungs**
 - 1 lung typically more severely involved
 - Radiographic misconception of unilateral involvement
- Mosaic attenuation (perfusion)
- Expiratory air-trapping
- Some degree of bronchiectasis in majority of cases
 Saccular bronchiectasis described
- ± bronchial stenosis or luminal obliteration

Nuclear Medicine Findings

- Perfusion imaging with Tc-99m MAA
 - Areas of photopenia
 - Hypoxic vasoconstriction in early acute phase of bronchiolar inflammation
 - Microvascular obstruction in late chronic phase
- Ventilation imaging with Xe-133 or Tc-99m DTPA
 Abnormal wash-in/equilibrium phase: Areas of
 - photopenia Narrowing of small airways in oastwastyte phas
 - Narrowing of small airways in early acute phase of bronchiolar inflammation
 - Bronchiolar occlusion in late chronic phase
 - Abnormal washout: Radiotracer retention in affected lobes as result of obstructive air-trapping

Imaging Recommendations

- Best imaging tool
 - HRCT most sensitive for evaluation and identification of
 - Mosaic attenuation
 - Air-trapping
 - Bronchiectasis
- Protocol advice
 - Inspiratory and expiratory HRCT
 - Expiratory HRCT critical for identifying areas of airtrapping

DIFFERENTIAL DIAGNOSIS

Asthma

- Diffuse bilateral pulmonary involvement
- May exhibit mild mosaic attenuation on CT
- Cylindrical bronchiectasis described in asthma
 Saccular bronchiectasis favors SJM

Bronchiectasis

- Cystic fibrosis, primary ciliary dyskinesia, immunodeficiencies
- Bronchiolectasis may be associated with hypoxic vasoconstriction with resultant hyperlucent lung and small vessels
- Often significant tree-in-bud centrilobular nodules from mucoid impaction or infection within dilated bronchioles
- Frequently diffuse and bilateral involvement

Congenital Interruption of Pulmonary Artery

- Proximal pulmonary artery completely absent or terminates abruptly
- Small hilum and lung, ipsilateral mediastinal shift

• Mosaic attenuation without air-trapping

Panlobular Emphysema

- Lower lobe predominant hyperlucent lung with small scant pulmonary vessels
- Association with α-1-antitrypsin deficiency
- Mild cylindrical bronchiectasis may be present

Congenital Lobar Overinflation

- Usually affects single lobe
 Left upper lobe most frequently affected
- Primary bronchial abnormality resulting in luminal narrowing and air-trapping
 - Hyperlucent and hyperexpanded lung
 - Resultant mass effect on mediastinum/adjacent lung
- Almost all diagnosed prenatally or infancy: 50% of affected patients present in first 2 days of life
 - Occasional incidental finding in adulthood
 - Associated congenital heart disease (15%)

Primary Unilateral Pulmonary Hypoplasia

- Small lung and ipsilateral pulmonary artery
- No air-trapping

PATHOLOGY

General Features

- Proposed pathogenesis
 - Epithelial injury caused by lower respiratory tract infection
 - Insult precedes alveolar maturation (< 8 years)
 - Severely injured epithelial cells release interleukin 8 and other proinflammatory mediators
 - Neutrophils and other inflammatory cells recruited to small airways
 - Cytokines and mediators released from inflammatory cells with
 - Matrix degradation and collagen deposition
 - Fibroblast proliferation and resultant **peribronchial** fibrosis
 - Fibrosis of peribronchiolar alveolar septa obstructs pulmonary capillary bed
 - Decreased blood flow to affected pulmonary artery segments
 - Compounded by hypoxic vasoconstriction
- Clinical severity determined by degree of epithelial injury and inflammation
- Unclear whether degree of morphologic CT abnormalities are directly related to degree of impairment on pulmonary function tests

Staging, Grading, & Classification

- Diagnosis most often rests on clinical criteria
 - History of severe respiratory infection during childhood, especially early childhood
 - Obstructive pattern on pulmonary function tests
 - → forced expiratory flow at 25-75% of forced vital capacity
 - Consistent with small airways obstruction
 - Unresponsive to systemic steroids or bronchodilators
 - Imaging findings supportive of diagnosis
 - Exclusion of other chronic lung diseases

Microscopic Features

- Bronchial submucosal accumulation of mucopolysaccharide proteins
- Patchy submucosal and peribronchiolar fibrosis
 - Fibrosis surrounds airway with resultant extrinsic luminal narrowing
 - Patchy involvement can yield false negative tissue sampling

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Most patients asymptomatic
 - Chronic wheezing, productive cough, dyspnea on exertion
 - Symptomatology depends on percentage of lung parenchyma involved
 - Obstructive pattern on pulmonary function tests
- Other signs/symptoms
 - Hemoptysis (rare)
 - Recurrent infections (rare)

Demographics

- Respiratory infection most often occurs in early childhood
 - Associated pathogens: Adenovirus, measles virus, influenza virus, respiratory syncytial virus, and Mycoplasma pneumoniae
- Most patients diagnosed as adults
 - Often incidental imaging finding

Natural History & Prognosis

- CT findings of constrictive bronchiolitis may develop as early as 9 months after infection
- Excellent prognosis as most affected patients are asymptomatic
- Chronic intermittent wheezing and cough with large areas of pulmonary involvement
- Bronchiectasis predisposes to repeated infections

Treatment

- Systemic or inhaled corticosteroids for wheezing and chronic cough
- Lung volume reduction surgery (LVRS) rarely required
 - Reserved for select patients with recurrent infections due to bronchiectasis

DIAGNOSTIC CHECKLIST

Consider

• SJM in asymptomatic patients with unilateral hyperlucent lung on radiography and multifocal areas of hyperlucent lung, bronchiectasis, and air-trapping on CT

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- 2. Gomes de Farias LP et al: Swyer-James-MacLeod syndrome: the hyperlucent lung. Radiol Cardiothorac Imaging. 2(3):e190246, 2020
- Kawasuji H et al: Multimodal imaging findings in an adult case of Swyer-James-MacLeod syndrome. Respirol Case Rep. 5(4):e00236, 2017
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(Left) PA chest radiograph of an asymptomatic patient with Swyer-James-MacLeod syndrome shows right upper lung hyperlucency \supseteq with intrinsic decreased pulmonary vascularity. The left lung appears normal. (Right) Axial HRCT of the same patient shows that the radiographic abnormality corresponds to right upper lobe hyperlucency amid scattered areas of relatively normal pulmonary attenuation 🔁. The right upper lobe pulmonary vessels \supseteq are diminutive when compared to those in the left upper lobe 🖂





(Left) Axial HRCT of the same patient shows right upper and right lower lobe hyperlucency with intrinsic bronchiectasis ➡ and a small size of intrinsic pulmonary vessels. While the left lung is relatively normal, there is a small hyperlucent area \supseteq in the left lower lobe superior segment. (Right) Axial expiratory HRCT of the same patient shows no significant increase in the attenuation of the hyperlucent lung (including the left lower lobe superior segment 🖂), consistent with air-trapping. CT typically reveals bilateral pulmonary involvement.





(Left) PA chest radiograph of a patient with Swyer-James-MacLeod syndrome secondary to prior severe neonatal pneumonia who presented with chronic cough shows right lung hyperlucency and paucity of pulmonary vascular markings. (Right) Coronal CECT of the same patient shows multifocal regions of of left lung hyperlucency with intrinsic small pulmonary vessels and bronchial wall thickening 🔁. The diagnosis was made based on history, imaging findings, and clinical features of obstructive smallairways disease.

Asthma

KEY FACTS

TERMINOLOGY

• Reversible airway obstruction, chronic airway inflammation, and nonspecific airway hyperreactivity

IMAGING

• Radiography

- Bronchial wall thickening
- Hyperinflation: Transient or fixed
- o Atelectasis, pneumothorax, pneumonia

• CT

- Bronchiectasis: Cylindrical, mucoid impaction
- Assessment of extent and severity of airway wall thickness/luminal narrowing
- Bronchiolitis: Mosaic attenuation on inspiration, expiratory air-trapping, small centrilobular nodules
- Identification of associated conditions
- Primary role of imaging is to identify complications (not to make diagnosis)

TOP DIFFERENTIAL DIAGNOSES

- Vocal cord paralysis
- Tracheobronchial obstruction
- Constrictive bronchiolitis

PATHOLOGY

- Chronic inflammation of mid and small-sized bronchi
- Bronchiolar findings: Constrictive bronchiolitis

CLINICAL ISSUES

- "Not all that wheezes is asthma"
- Symptoms/signs
- Cough, shortness of breath, wheezing, and chest discomfort
- Affects 7% of USA population
- Children, adolescents, and adults
- Treatment: Combination of anti-inflammatory drugs and bronchodilators

(Left) PA chest radiograph of a patient with longstanding asthma shows bilateral lung hyperinflation and nonspecific bilateral reticular opacities. (Right) Lateral chest radiograph of the same patient shows flattening of the diaphragm and enlargement of the retrosternal clear space, consistent with marked hyperinflation. Note diffuse peribronchial cuffing. While nonspecific, hyperinflation and peribronchial cuffing are common findings in patients with asthma.





(Left) Axial NECT of the same patient shows extensive bronchiectasis, bronchial wall thickening \blacksquare , and branching opacities that represent mucoid impactions 🔁. (Right) Coronal NECT MIP image of the same patient shows bronchiectasis, mucoid impactions 🛃, and tree-in-bud $opacities \Longrightarrow from bronchiolar$ mucoid impactions. Cylindrical bronchiectasis is more common in asthma, and cystic or varicoid bronchiectasis is more common in allergic bronchopulmonary aspergillosis. (Courtesy S. Rossi, MD.)





Definitions

• Reversible airway obstruction, chronic airway inflammation, and nonspecific airway hyperreactivity

IMAGING

General Features

- Best diagnostic clue
 - Imaging is for identification of complications (not for diagnosis)

Radiographic Findings

- Bronchial wall thickening or peribronchial cuffing (most common)
- Hyperinflation: Transient or fixed
- Complications
 - **Atelectasis**: Often from mucoid impaction, middle lobe commonly affected
 - o Pneumonia
 - Pneumothorax and pneumomediastinum

CT Findings

- Assessment of extent and severity of airway wall thickness/luminal narrowing
 - \circ \uparrow thickness correlates with disease severity
- Bronchiectasis
 - Typically 1 or few dilated bronchi
 - Signet ring sign, absence of bronchial tapering
 - o Mucoid impactions
 - Cylindrical bronchiectasis more likely in asthma without allergic bronchopulmonary aspergillosis (ABPA)
 - Central cystic or varicoid bronchiectasis, mucoid impaction, and centrilobular nodules suggest ABPA

• Bronchiolitis

- Mosaic attenuation during inspiration
- Expiratory air-trapping
- Small centrilobular nodules
- Identification of associated conditions (e.g., ABPA) and mimics (e.g., hypersensitivity pneumonitis)

Imaging Recommendations

- Best imaging tool
- Consider imaging only if complications suspected
- Protocol advice
 - Indications for chest radiography
 - Chronic obstructive pulmonary disease
 - Fever or temperature > 37.8° C
 - History of intravenous drug use
 - Seizures
 - Immunosuppression
 - Clinical suspicion of pneumothorax

DIFFERENTIAL DIAGNOSIS

Vocal Cord Paralysis

- Severe symptoms, inspiratory/expiratory stridor, episodic hoarseness
- No bronchial wall thickening
- Laryngoscopic diagnosis

Tracheal or Carinal Obstruction

- Tumor, post-intubation tracheal stenosis, vascular ring, foreign body, sarcoidosis, granulomatosis with polyangiitis, amyloidosis, relapsing polychondritis
- Imaging studies for identification and assessment of obstructing lesion

Constrictive Bronchiolitis

- Idiopathic, post-infectious, autoimmune disease, asthma
- Often refractory to bronchodilators
- May be radiologically indistinguishable from asthma

PATHOLOGY

General Features

- Etiology
 - Common asthma triggers: Animals (pet hair or dander), dust, weather changes, air or food chemicals, exercise, mold, pollen, respiratory infections (e.g., common cold), emotional stress, tobacco smoke, medications (e.g., aspirin)
- Associated abnormalities
 - o ABPA
 - Bronchocentric granulomatosis
 - Chronic eosinophilic pneumonia
 - Churg-Strauss syndrome

Microscopic Features

- Chronic inflammation of mid and small-sized bronchi
- Bronchiolar findings
 Constrictive bronchiolitis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough, shortness of breath, wheezing, and chest discomfort

Demographics

- Age
 - o Children, adolescents, and adults
- Epidemiology
 - Affects 7% of USA population

Treatment

• Complex; combination of anti-inflammatory drugs (e.g., corticosteroids, cromolyn), bronchodilators

DIAGNOSTIC CHECKLIST

Consider

• "Not all that wheezes is asthma" when interpreting imaging studies of affected patients

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- Ash SY et al: The role of imaging in the assessment of severe asthma. Curr Opin Pulm Med. 23(1):97-102, 2017
- Richards JC et al: Imaging of asthma. Immunol Allergy Clin North Am. 36(3):529-45, 2016

(Left) Axial inspiratory HRCT of a patient with asthma shows a very subtle pattern of bilateral mosaic attenuation. (Right) Axial expiratory HRCT of the same patient shows scattered bilateral subsegmental air-trapping, consistent with small airways disease. This finding often correlates with severity of asthma and is associated with a history of asthma-related hospitalization, intensive care unit admissions, &/or mechanical ventilation.





(Left) PA chest radiograph of a young patient with asthma shows mild elevation of the right hemidiaphragm and obscuration of the right cardiac border secondary to atelectasis of the middle lobe. (Right) Lateral chest radiograph of the same patient shows a band-like $opacity \blacksquare caudal to the$ inferiorly displaced horizontal fissure that confirms middle lobe atelectasis. Atelectasis is one of the most common abnormalities found on chest radiographs of patients with asthma.





(Left) PA chest radiograph of a patient with asthma shows a right upper lobe opacity with elevation of the minor fissure *▶* and a juxtaphrenic peak \blacksquare , consistent with right upper lobe atelectasis. (Right) Coronal CECT of the same patient shows sublobar right upper lobe atelectasis 🔁. Atelectasis in patients with asthma is typically associated with mucous plugs and does not necessarily imply acute illness, infection, or worsening asthma.





Asthma





(Left) PA chest radiograph of a patient with asthma who presented with dyspnea, fever, and leukocytosis shows obscuration of the left heart border 🚬, consistent with lingular pneumonia given the history. (Right) PA chest radiograph of the same patient shows post-treatment resolution of the lingular consolidation. Pneumonia is a common complication of asthma and an indication for imaging asthmatic patients. Since asthma is so prevalent, an effort should be made to image affected patients as little as possible.

(Left) PA chest radiograph of a patient with asthma who presented with acute dyspnea and chest pain shows extensive

pneumomediastinum 🔁 and subcutaneous air 🔁 in the neck. (Right) Coronal CECT of the same patient shows pneumomediastinum and subcutaneous air in the neck. Pneumomediastinum as a complication of asthma is more common in children and more frequent than pneumothorax. Rarely, pneumomediastinum may be associated with air within the spinal canal.







patient with asthma shows a , pneumothorax manifesting with a visible visceral pleural line \blacksquare at the right lung apex. (Right) Coronal MR with hyperpolarized ¹²⁹Xe of an asthmatic patient shows heterogeneous distribution of ¹²⁹Xe due to extensive ventilation defects. ³He and ¹²⁹Xe have been used successfully in research studies designed to assess ventilatory abnormalities and are promising techniques for future clinical practice. (Courtesy H. P. McAdams, MD.)

(Left) PA chest radiograph of a



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Introduction

Imaging of pulmonary infection is challenging due to the numerous infectious organisms that may produce diseases with protean imaging manifestations. The radiologist is often the first healthcare provider to raise the possibility of pulmonary infection, as imaging studies are often performed before microbiologic and immunologic testing results become available. In some cases, the radiologist may be able to suggest an unsuspected pulmonary infection &/or a specific pulmonary pathogen. For example, identification of upper lobe cavitary disease should suggest active tuberculosis, and the radiologist must promptly alert the referring physician &/or other members of the clinical team so that airborne pathogen isolation precautions can be instituted. Thus, radiologists may play a critical role in the identification, assessment, and management of patients with pulmonary infection. Although imaging features may not allow the diagnosis of a specific pathogen, communication with members of the healthcare team may lead to the formulation of a focused differential diagnosis or the identification of a likely causative microorganism, which may positively impact early treatment and recovery.

Chest radiography remains a reasonable first step in the identification of suspected pulmonary infection, particularly in the immunocompetent patient. CT and more invasive procedures are usually reserved for complicated cases. Nevertheless, immunocompromised patients may benefit from early thin-section CT evaluation if they have signs and symptoms of infection and normal chest radiographs.

Immune Status

Diagnostic algorithms used in patients with pulmonary infection must take into account various aspects of the patient's history and demographic characteristics. In all cases, host immunity is an important consideration and is used to stratify a population of potentially infected patients into two groups: Patients with normal immunity and immunocompromised patients. Knowledge of the patient's immune status allows healthcare providers to significantly narrow the differential diagnosis. For example, a patient with acquired immunodeficiency syndrome (AIDS) who presents with symptoms may be suffering from one or more infectious, inflammatory, or neoplastic processes. However, when such a patient exhibits diffuse bilateral hazy pulmonary opacities on chest radiography and bilateral ground-glass opacities on chest CT, the most likely diagnosis is infection with Pneumocystis jirovecii, also known as Pneumocystis pneumonia (PCP).

The radiologist must be familiar with the various types of immunosuppression, which may affect surface barriers (skin, mucosa), humoral immunity, and cell-mediated immunity. Pulmonary pathogens vary with the type of immune suppression affecting a given patient. For example, patients with AIDS are unlikely to develop PCP when CD4 levels are > 500 cells/mm³. However, in patients with CD4 levels < 500 cells/mm³, the rate of PCP infection increases significantly. On the other hand, patients with other forms of immunosuppression, such as steroid therapy, neutropenia, and diabetes, are at risk of developing specific pulmonary infections related to the nature of their immune compromise.

Community-Acquired vs. Hospital-Acquired Infection

There are well-recognized differences between infections acquired in the community and nosocomial infections that affect hospitalized patients. Overall, community-acquired pneumonia often manifests on chest radiography as lobar (lobar pneumonia) or multifocal consolidation (e.g., bronchopneumonia) due to microorganisms that include *Pneumococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila,* and viral agents, such as influenza and respiratory syncytial virus.

Nosocomial (hospital-acquired) pneumonia should be considered if the patient acquires the pulmonary infection at least 48 hours after admission to the hospital. The most common pathogens include gram-negative bacilli (e.g., *Pseudomonas aeruginosa* and *Enterobacter* spp.) and *S. aureus*. These infections often exhibit extensive and aggressive imaging abnormalities on chest radiography.

Clinical Manifestations and Laboratory Findings

The clinical presentation of an infected patient may vary with the offending organism. Patients with bacterial pneumonia typically present with acute onset of chest pain, fever, productive cough, and neutrophilia. Patients with viral and mycoplasmal pneumonias may exhibit mild fever, productive cough, and mildly elevated white blood cell counts. Febrile neutropenia following bone marrow transplant should suggest angioinvasive fungal infection.

Recently, there has been emphasis on **biomarkers** that allow early treatment decisions of affected patients before microbiologic studies are available. For example, procalcitonin is typically elevated in bacterial infection but not or marginally elevated in viral and fungal infections. Thus, in a patient with multifocal opacities on imaging secondary to influenza or SARS-CoV-2, low procalcitonin levels allow the clinician to refrain from antibiotic therapy. Procalcitonin also helps guide antibiotic therapy; for example, patients with rapidly decreasing levels may be treated for shorter periods of time, whereas those with increasing or plateauing procalcitonin levels have a poor prognosis and may require more aggressive treatment. Another important FDA-approved biomarker is **Fungitell**. It was initially developed to allow early diagnosis of angioinvasive aspergillosis, which has significant morbi-mortality in affected transplant recipients. Elevated titers in the appropriate clinical context are virtually diagnostic. Other fungal infections may also exhibit elevated Fungitell, allowing differentiation from bacterial and viral infections.

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Pneumonia in Immunocompromised Host: **HIV Infection**



Pneumonia in Immunocompromised Host: **HIV Infection**



Community-Acquired Pneumonia

(Left) PA chest radiograph of a patient with human *immunodeficiency virus (HIV)* infection, elevated procalcitonin and Pneumococcus pneumoniae pneumonia shows a sublobar right upper lobe consolidation E. (Right) Axial NECT of the same patient shows a right upper lobe consolidation with an intrinsic air bronchograms ∠. The CD4 count was > 500 cells/mm³. Correlation with CD4 levels is always suggested in patients with HIV infection to formulate an appropriate and focused differential diagnosis.

Community-Acquired Pneumonia



Pneumonia in Immunocompromised Host: Neutropenia





Pneumonia in Immunocompromised Host: Neutropenia



(Left) PA chest radiograph of a neutropenic patient with angioinvasive aspergillosis secondary to Aspergillus flavum and elevated Fungitell after bone marrow transplant shows a right lower lobe cavitary mass 🔁. (Right) Axial NECT of the same patient confirms a right lower lobe cavitary mass \blacksquare with nodular cavity walls. A. flavum is the 2nd most common pathogen to cause angioinvasive aspergillosis after Aspergillus fumigatus and is considered 100x more virulent in terms of the inoculum required for infection.

Infections

(Left) PA chest radiograph of a patient with upper respiratory symptoms due to Mycoplasma pneumoniae pneumonia shows multifocal heterogeneous airspace disease. (Right) Axial CECT of the same patient better characterizes the extent of pulmonary involvement by consolidation and shows associated groundglass opacities 🔁. Mycoplasma pneumonia is a common cause of communityacquired pneumonia in children and frequently exhibits discordance between imaging findings and clinical disease severity.

Bronchopneumonia

KEY FACTS

TERMINOLOGY

- Lobular pneumonia
- Multifocal bronchiolocentric inflammatory exudate

IMAGING

• Radiography

- Multifocal lobular or confluent consolidations
- Aspiration pneumonia (dependent lungs)
- Air bronchograms usually absent
- Cavitation (abscess)
- Pneumatoceles (S. aureus or P. jirovecii)
- CT
 - Centrilobular nodules and tree-in-bud opacities
 - Patchy airspace nodules (4-10 mm)
 - Lobular, subsegmental, segmental ground-glass opacities and consolidations
 - Identification of necrosis/cavitation

TOP DIFFERENTIAL DIAGNOSES

- Aspiration
- Alveolar hemorrhage
- Organizing pneumonia

PATHOLOGY

- S. aureus, E. coli, P. aeruginosa, K. pneumoniae, S. pneumoniae, H. influenzae, anaerobes, viral and fungal pathogens
- Aspiration of secretions from colonized trachea

CLINICAL ISSUES

- Symptoms/signs
 - Acute onset of fever, chills, cough, sputumElevated white blood cell count with left-shift
- Any age, but young children and older adults at increased risk
- Treatment: Antibiotics and empyema drainage if present
- Nonsmokers and outpatients: Resolution in 2-3 weeks

(Left) *PA chest radiograph of a 55-year-old*

immunocompromised woman shows patchy bilateral nodular opacities and right lung confluent consolidations suggestive of bronchopneumonia. (Right) Axial NECT of the same patient shows multifocal centrilobular nodules 🖂 lobular consolidations 🖂, and confluent consolidations 🔁 with surrounding ground-glass opacities. These findings in a febrile immunocompromised patient are highly suggestive of bronchopneumonia.





(Left) Coronal NECT of a 70year-old man with S. aureus bronchopneumonia shows multifocal bilateral lobular consolidations , ill-defined ground-glass opacities \square , and clustered centrilobular nodules \square , indicating endobronchial spread of infection. (Right) Axial CECT of a 37-year-old woman with aspiration bronchopneumonia who sleeps left-side down shows gravitational distribution of asymmetric lingular and left lower lobe centrilobular nodules, and lobular consolidations \supseteq with areas of confluence 🔁.





Synonyms

• Lobular pneumonia

Definitions

• Multifocal bronchiolocentric inflammatory exudate

IMAGING

General Features

- Best diagnostic clue
 - Acute multifocal lobular or confluent consolidation in febrile patient
- Location
 - Typically multifocal and bilateral; may affect certain lobes more than others
 - Aspiration pneumonia: Dependent portions of lungs
 - Usually multilobar and bilateral
 - Upper lobe posterior segments (supine)
 - Lower lobe basilar segments (upright)

Radiographic Findings

- Radiography
 - Multifocal patchy or confluent peribronchovascular illdefined nodular opacities or consolidations: Air bronchograms usually absent
 - ± pneumatoceles (S. aureus or P. jirovecii)
 - t cavitation (abscess): More common in upper lobes
 S. aureus, Haemophilus influenzae anaerobes, gramnegative bacteria

CT Findings

- NECT
 - Centrilobular nodules and tree-in-bud opacities
 - Peribronchovascular airspace (4- to 10-mm) nodules
 - Lobular, subsegmental, segmental ground glassopacities and consolidations
 ± cavitation
- o ± cavit
- CECT
 - Necrosis: Low-attenuation areas ± cavitation and rim enhancement (isolated or in consolidations)

Imaging Recommendations

- Best imaging tool
 - Chest radiography: Useful for detection of disease and documentation of response to therapy
 - CT: Sensitive and specific for detection of underlying structural abnormalities and complications
- Protocol advice
 - CECT or CTA useful to assess necrotic areas and possible coexistent pulmonary thromboembolism

DIFFERENTIAL DIAGNOSIS

Alveolar Hemorrhage

- Bilateral diffuse airspace disease, may be centrilobular
- Anemia, hemoptysis

Organizing Pneumonia

- Peribronchovascular &/or perilobular opacities
- Unresponsive to antibiotics, but highly responsive to steroids

PATHOLOGY

General Features

- Etiology
 - S. aureus, E. coli, P. aeruginosa, K. pneumoniae, S.
 - *pneumoniae, H. influenzae*, anaerobes, viruses and fungi • Aspiration of secretions from colonized trachea

Gross Pathologic & Surgical Features

- Exudate centered on terminal bronchioles (centrilobular)
- Patchy distribution: Adjacent lobules may be normal

Microscopic Features

- Bronchial inflammation with epithelial ulcerations and fibrinopurulent exudate
- Spread to contiguous pulmonary lobules

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute onset fever, chills, productive cough
 - Leukocytosis with left-shift; elevated procalcitonin
 - Identification of etiology in < 50%
- Clinical profile
 - o Associated with hospital-acquired pneumonia
 - *S. aureus, P. aeruginosa, E. coli,* anaerobes, gramnegative organisms
 - *Pseudomonas aeruginosa*: Most common and lethal form of hospital-acquired pneumonia
 - Associated conditions
 - COPD: P. aeruginosa, H. influenzae, M. catarrhalis
 - Cystic fibrosis: P. aeruginosa
 - Biomarkers
 - Procalcitonin: Elevated in bacterial infection; normal or marginally elevated in viral or fungal infection; the higher the level, the higher the risk of sepsis; rapidly decreasing levels may allow a shorter antibiotic course
 - **Fungitell**: Elevated in many fungal infections; helpful to differentiate from bacterial and viral infection

Demographics

• Age

• Any age; children < 5 years, older adults > 65 years

Natural History & Prognosis

- Children < 5 years, older patients > 65 years, and immunocompromised patients most susceptible
 - This is the leading cause of death from infection in patients < 5 years
- Prognosis depends on organism virulence, antibiotic susceptibility, host response
- Resolution: Nonsmokers and outpatients within 2-3 weeks

Treatment

• Appropriate antibiotics and empyema drainage if present

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KEY FACTS

TERMINOLOGY

- Community-acquired pneumonia (CAP)
 Acute pulmonary infection acquired outside hospital
- IMAGING
- Radiography
 - Detection of abnormality, assessment of disease extent, detection of complications, evaluation of treatment response
 - Limited value in predicting causative organism
 - Immunocompromised, especially if neutropenic, may have normal radiographs
- CT
 - Problem-solving tool for nondiagnostic chest radiographs, unresolved pneumonia, or suspected complications
- Complications
 - o Cavitation, abscess formation
 - o Empyema

TOP DIFFERENTIAL DIAGNOSES

- Cardiogenic pulmonary edema
- Alveolar hemorrhage
- Acute lung injury in SARS-CoV-2 (COVID-19)
- Aspiration
- Organizing pneumonia

PATHOLOGY

- Common: *Streptococcus pneumoniae* (50%), viral pneumonia (20%), *Haemophilus influenzae* (20%), *Chlamydia pneumoniae* (15%), *Mycoplasma pneumoniae* (5%), *Moraxella catarrhalis*
- Acute lung damage due to SARS-CoV-2: Cause of pulmonary opacities; may simulate CAP

CLINICAL ISSUES

• Symptoms/signs: Fever, chills, cough, sputum

DIAGNOSTIC CHECKLIST

• Careful imaging assessment of patients with CAP for early detection of complications, such as abscess and empyema

(Left) PA chest radiograph of a patient with pneumococcal pneumonia shows a focal consolidation \blacksquare in the periphery of the right lung. S. pneumoniae is the most common cause of communityacquired pneumonia and typically manifests as a lobar consolidation. (Right) PA chest radiograph of a patient with pneumococcal pneumonia shows a heterogeneous left upper lobe consolidation with air bronchograms 🛃 and central bronchial wall thickening 🔁.





(Left) PA chest radiograph of a patient with bacterial community-acquired pneumonia shows a diffuse lingular consolidation 🔁. Extension of pulmonary infection into adjacent lung lobes depends on whether the interlobar fissure is complete and may follow collateral pathways, such as the pores of Kohn and canals of Lambert. (Right) Axial HRCT of a patient with community-acquired Adenovirus pneumonia shows tiny miliary nodules and mild mosaic attenuation of the lung parenchyma.





Abbreviations

• Community-acquired pneumonia (CAP)

Definitions

• Acute pulmonary infection acquired outside hospital

IMAGING

General Features

- Best diagnostic clue
 Consolidation(s) in patient with fever
- Location
- Single or multiple lobes
- Size
- Range: Small opacity to lobar/multilobar consolidationsMorphology
 - Range: Ground-glass opacity to frank consolidation

Radiographic Findings

- High sensitivity
 - Immunocompromised, especially if neutropenic, may have normal radiographs
- Typical distribution: Unilateral or bilateral segmental consolidation
- Significant interobserver variability in pattern recognition
- Various patterns; range of ground-glass opacity to consolidation
- Pattern not diagnostic of specific organism
- Single organism may cause multiple patterns
- Lobar pneumonia vs. bronchopneumonia
 - Pathologic designation difficult to reliably identify radiographically
- Unusual patterns
 - Hyperinflation common with viral pneumonia (distal airway obstruction)
 - Lobar enlargement with bulging fissures: *Klebsiella* pneumonia
 - Round pneumonia is common pattern of CAP in children
 - Pneumatoceles: Develop later in disease (classically *S. aureus*), may persist for months, resolve spontaneously
 - Hilar lymphadenopathy
 - Rare; differential diagnosis includes tuberculosis, mycoplasma, fungi, mononucleosis, measles, plague, tularemia, anthrax, pertussis
- Complications
 - o Cavitation
 - Suggests bacterial disease (*S. aureus*, gram-negative bacteria, anaerobes)
 - o Empyema
 - Pleural effusion in 20-60%, reactive parapneumonic effusion
 - Up to 5% progress to empyema
 - Suspect if effusion enlarges or becomes loculated
- Resolution
 - Delayed with advanced age and multilobar involvement
 - Faster resolution in nonsmokers and outpatientsExpected timetable
 - 50% resolve in 2 weeks; 66% in 4 weeks; 75% in 6 weeks

- Follow-up imaging of resolving CAP (symptoms resolve in 5-7 days) is controversial
- Mortality associated with 2 radiographic abnormalities
 Bilateral pleural effusions
 - o Multilobar disease

CT Findings

- Ground-glass opacity
- Consolidation
- Nodules
 - Diffuse or patchy tree-in-bud opacities highly suggestive of infectious bronchiolitis (especially *Mycoplasma* and viruses)
- More sensitive and specific for detection of complications • Abscess vs. empyema
 - Abscess: Thick, irregular wall; round shape; small area of contact with chest wall
 - Empyema: Thin, uniform wall; lenticular shape; broad area of contact with chest wall; pleural thickening and enhancement; edema of adjacent extrapleural fat
- Recurrent pneumonia
 - Lung cancer, bronchiectasis, chronic obstructive pulmonary disease
 - Intralobar sequestration if recurrent posterior basilar left lower lobe involvement
 - CECT: Systemic blood supply typically from descending thoracic aorta
- Acute lung injury in context COVID-19 (highly suggestive, not pathognomonic)
 - Ground-glass opacities ± consolidation
 - o Peripheral, bilateral, multifocal
 - Perilobular pattern

Imaging Recommendations

- Best imaging tool
 - Chest radiography for identification of abnormality, assessment of disease extent, detection of complications, and evaluation of treatment response
 - Limited value in predicting causative organism
- Protocol advice
 - CT: Problem-solving tool for nondiagnostic chest radiographs; unresolved pneumonia or suspected complications

DIFFERENTIAL DIAGNOSIS

Cardiogenic Pulmonary Edema

- Cardiomegaly and pulmonary venous hypertension
- Edema shifts with patient position
- Focal right upper lobe edema with mitral regurgitation

Alveolar Hemorrhage

- Patients may be anemic and have hemoptysis
- Multifocal bilateral ground-glass opacities

Acute Lung Injury in SARS-CoV-2 (COVID-19)

- Opacities may simulate multifocal pneumonia, but represent acute lung injury
 - Perilobular opacities with features of organizing pneumonia
- Procalcitonin is low or normal unless there is concomitant bacterial infection

Aspiration

- ± predisposing condition, such as esophageal motility disorder
- Gravity-dependent location of airspace disease

Organizing Pneumonia

- Often treated for pneumonia for variable length of time
- Patchy, chronic, or migratory bibasilar consolidation

Chronic Eosinophilic Pneumonia

- Typically chronic peripheral upper lobe consolidation: "Photographic negative of pulmonary edema"
- Asthma, eosinophilia

Hypersensitivity Pneumonitis

- History of antigen exposure
- Chest radiography often normal
- CT: Diffuse ground-glass opacities, poorly-defined centrilobular nodules, geographic lobular hyperinflation

Pulmonary Infarction

• Melting snowball sign with resolution; pneumonia resolves rapidly

Atelectasis

• Fissural displacement or indirect signs of volume loss

PATHOLOGY

General Features

- Etiology
 - Common pathogens: Streptococcus pneumoniae (50%), viral pneumonia (20%), Haemophilus influenzae (20%), Chlamydia pneumoniae (15%), Mycoplasma pneumoniae (5%)
 - Offending organism cultured in < 50%
- Portal of entry: Inhalation or aspiration of oral secretions
- Important trends
 - Decline in *S. pneumoniae* incidence
 - COVID-19 pandemic
 - Acute lung injury: Important cause of pulmonary opacities during pandemic
 - Increased recognition of respiratory viruses
 - Detected in 1/3 of CAP when using molecular methods
 - Discovery of lung microbiome
 - May play role in development of pneumonia
- **Procalcitonin**: Differentiation of bacterial from viral/fungal infection
 - Increased in bacterial infection
 - The higher the value, the higher the risk of sepsis
 - Rapidly decreasing levels may allow shortened antibiotic treatment

Staging, Grading, & Classification

- CAP only seen on CT (not on radiography): Similar pathogens and outcomes compared to those detected on radiography
 - Same management principles apply to patients with CTonly pneumonia and those with radiographic pneumonia
- Health care-associated pneumonia (pneumonia acquired in health care facilities or after recent hospitalization); term is no longer used

Gross Pathologic & Surgical Features

- Lobar vs. bronchopneumonia
 - o Lobar
 - Alveolar flooding with inflammatory exudate, especially neutrophils
 - Rapidly spreads throughout lobe, only stopped by intact fissures
 - Usually peripheral
 - Bronchopneumonia
 - Exudate centered on terminal bronchioles (centrilobular)
 - Respects septal boundaries
 - Patchy: Adjacent secondary pulmonary lobules may be normal, patchwork quilt pattern

Microscopic Features

- Nonspecific acute &/or chronic inflammatory cells
- Organisms identified with special stains (such as Gram or acid fast)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - No individual or combinations of signs and symptoms on history or physical examination can reliably confirm or exclude the presence of pneumonia
 - Classic findings: Fever, chills, cough, sputum
 - Empyema: Patient may be surprisingly free of toxic symptoms
 - Pulmonary cavity in patient with poor dentition suggests lung abscess

Demographics

- Age
 - o Anyage
- Epidemiology
 - o 8-15/1,000 persons/year

Natural History & Prognosis

- Depends on virulence of organism, antibiotic susceptibility, host immune factors
- Pneumonia is 6th most common cause of death

Treatment

- Appropriate antibiotics
- Drain empyemas, not abscesses

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Absence of parenchymal abnormality excludes pneumonia (except in immunocompromised subjects)

Reporting Tips

- Diagnosis of CAP is based on culture
- Careful imaging assessment of patients with CAP for early detection of complications, such as lung abscess and empyema

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(Left) AP chest radiograph of a patient with communityacquired pneumococcal pneumonia shows bilateral multilobar consolidations 乏. Note sharp demarcation of the minor fissure 🔁 by adjacent middle lobe consolidation. (Right) Axial HRCT of the same patient shows multifocal consolidations with adjacent ground-glass opacities and air bronchograms \square , and small nodular ground-glass opacities 🛃 in the left lung. Note the sharp demarcation of the right major fissure 🔁 by adjacent right lower lobe consolidation.





(Left) Axial HRCT of a patient with community-acquired pulmonary infection shows clusters of small centrilobular nodules 🛃 and mild bronchial wall thickening 🛃. Mycoplasma, chlamydia, and viruses are common causes of this pattern. (Right) Axial CECT of a patient with a lung abscess shows a cavitary right lower lobe mass \supseteq with irregular nodular cavity walls, bilateral lower lobe patchy ground-glass opacities \blacksquare , and a small poorly-defined left lower lobe cavitary nodule 🔁





(Left) Axial CECT of a patient with empyema secondary to community-acquired pneumonia shows a multiloculated left pleural effusion with intrinsic gas \blacksquare from associated bronchopleural fistula and extrapleural fat edema 🔁. (Right) Axial NECT of a patient with community-acquired pneumonia-related empyema shows a multiloculated right pleural effusion and adjacent atelectasis 🛃. Note that the extrapleural fat \bowtie is hazy as compared to the deep chest wall fat. This finding is highly suggestive of empyema.

KEY FACTS

TERMINOLOGY

- Hospital-acquired pneumonia (HAP): Infection after ≥ 48 hours of hospitalization
- Ventilator-associated pneumonia (VAP): HAP in patients mechanically ventilated for > 48 hours

IMAGING

• Radiography

- Lobar consolidation: Focal or multifocal, nonsegmental
- Bronchopneumonia pattern
 - Multifocal, lobular, subsegmental, segmental consolidation, bronchial wall thickening
- o Cavity
- Pneumatocele
- o Pleural effusion
- CT
 - Ground-glass opacities/consolidations
 - Centrilobular nodules
 - o Tree-in-bud opacities

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary edema
- Diffuse alveolar hemorrhage
- Pulmonary embolism
- Aspiration

CLINICAL ISSUES

- Symptoms/signs
 - Fever or hypothermia, cough, purulent sputum
 - Oxygenation impairment
 - Leucocytosis or leukopenia
- HAP incidence: 5 to > 20 cases/1,000 hospital admissions
- VAP incidence: 1-2.5 cases (North America) and 18.3 cases (Europe)/1,000 ventilator-days

DIAGNOSTIC CHECKLIST

• Consider HAP in hospitalized patient with new pulmonary opacity on imaging and compatible clinical features and laboratory data

(Left) AP chest radiograph of a patient with hospital-acquired pneumonia shows bilateral peripheral multilobar nonsegmental consolidations. Methicillin-resistant Staphylococcus aureus was isolated from blood cultures. (Right) Coronal NECT of the same patient obtained 2 days later shows rapid progression of multifocal multilobar consolidations \square . The patient developed acute respiratory distress syndrome and died. Patients with hospitalacquired pneumonia exhibit an 8.4x increased risk of death.





(Left) AP chest radiograph of a 32-year-old patient with head trauma who required mechanical ventilation shows no pulmonary abnormalities. (Right) AP chest radiograph of the same patient obtained 5 days later to evaluate fever and purulent respiratory secretions shows patchy bilateral pulmonary opacities with coalescence in the right upper lobe 🖘 Blood cultures demonstrated Acinetobacter baumannii pneumonia.





Abbreviations

- Hospital-acquired pneumonia (HAP)
- HAP requiring mechanical ventilation (V-HAP)
- Ventilator-associated pneumonia (VAP)

Synonyms

• Nosocomial pneumonia (includes HAP and VAP)

Definitions

- HAP
 - Infection acquired after at least 48 hours of hospitalization
- VAP
 - Subcategory of HAP that occurs in patients who have been mechanically ventilated for > 48 hours

IMAGING

General Features

- Best diagnostic clue
 - Focal/multifocal consolidation in hospitalized patient with fever and purulent sputum

Radiographic Findings

- Lobar consolidation
 - Focal or multifocal, nonsegmental
- Bronchopneumonia pattern
- Multifocal, lobular, subsegmental, and segmental consolidations
- Bronchial wall thickening
- Cavity
- Pneumatocele
- Pleural effusion

CT Findings

- Ground-glass opacity, consolidation
- Centrilobular nodules
- Tree-in-bud opacities
- Cavity
- Pleural effusion

Imaging Recommendations

- Best imaging tool
 - Chest radiography is imaging study of choice in patients with suspected HAP but has low sensitivity and specificity
 - Low-dose chest CT has gained acceptance in the diagnosis of HAP due to greater sensitivity than radiography with a comparable radiation dose

DIFFERENTIAL DIAGNOSIS

Pulmonary Edema

- Abnormal extravascular lung fluid
- Variable distribution according to etiology

Hemorrhage

• Hemoptysis and anemia may suggest diagnosis, but not always present

Pulmonary Infarction

• Basilar predominance, broad pleural base

Aspiration

• Consolidation in dependent lung parenchyma

PATHOLOGY

General Features

- Etiology
 - Pharyngeal bacterial aspiration associated with severe impairment of respiratory physiology
 - Microbiological evidence more frequently documented in VAP than in HAP
 - Pathogens responsible for VAP and HAP are similar
 - Klebsiella pneumoniae and Staphylococcus aureus predominate in HAP
 - Acinetobacter baumannii and Pseudomonas aeruginosa predominate in VAP
 - New molecular diagnosis test may allow rapid identification of causative microorganism

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Fever or hypothermia
 - o Cough
 - Purulent sputum
 - Oxygenation impairment
 - o Leukocytosis or leukopenia
 - Complications
 - Lung abscess
 - Empyema

Demographics

• Age

- Most common in older adult patients
- Epidemiology
 - HAP incidence: 5 to > 20 cases/1,000 hospital admissions
- VAP incidence
 - North America: 1-2.5 cases/1,000 ventilator-days
 - Europe: 18.3 cases/1,000 ventilator-days

Natural History & Prognosis

- Patients with HAP exhibit an 8.4x increased risk of death
- V-HAP has high mortality rate at day 28 (27.8%)

Treatment

- Antibiotic treatment based on
 - o Mortality risk (low or high)
 - Presence or absence of septic shock
 - Risk of multidrug resistant organisms

DIAGNOSTIC CHECKLIST

Consider

• HAP in hospitalized patient with new pulmonary opacity on imaging and compatible clinical features and laboratory data

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KEY FACTS

TERMINOLOGY

• Lung necrosis secondary to microbial infection

IMAGING

- Radiography
 - Spherical thick-walled cavity surrounded by consolidation
 - o Equal air-fluid level length on frontal and lateral
 - radiographyO Usually related to aspiration
 - Gravitationally dependent lung
 - Oravitationally dependent if
 Pleural effusion common
- CT
 - Abscess: Thick irregular wall, spherical, narrow contact with chest wall, bronchovascular markings extend to abscess
 - Empyema: Thin uniform wall, lenticular shape, broad contact with chest wall, split pleura sign

TOP DIFFERENTIAL DIAGNOSES

- Tuberculosis
- Infected bulla
- Lung cancer
- Granulomatosis with polyangiitis
- Hydatidosis

PATHOLOGY

• Aspiration: Mixed aerobic and anaerobic polymicrobial bacterial infection originating in gingiva

CLINICAL ISSUES

- Cough, foul-smelling sputum, periodontal disease
- Responds to antibiotics in contrast to abscesses elsewhere that usually require drainage

DIAGNOSTIC CHECKLIST

 Consider CT to assess complications, such as empyema and bronchopleural fistula

(Left) PA chest radiograph of a 51-year-old man with poor dentition shows a mass-like opacity 🔁 with central lucency, consistent with cavitation overlying the right hilum. The lesion exhibits the hilum overlay sign, which indicates that it is not in the hilum. (Right) Lateral chest radiograph of the same patient shows the mass-like opacity \blacksquare in the superior segment of the right lower lobe. Although tuberculosis should be considered based on location, lung abscess must also be included in the differential diagnosis.





(Left) Coronal CECT of the same patient shows a spherical lesion with lobulated borders, intrinsic cavitation, and a thick, nodular cavity wall surrounded by a groundglass opacity halo 🛃. (Right) Axial CECT of the same patient shows the cavitary lesion \blacksquare in the superior segment of the right lower lobe abutting the right paravertebral region with associated mildly enlarged reactive right hilar lymph nodes 🔁. The location in the dependent aspect of the right lower lobe suggests aspiration in the supine position.





Synonyms

• Necrotizing pneumonia, pulmonary gangrene

Definitions

- Liquefactive lung necrosis secondary to microbial infection
- Cavity: Air-containing lesion with relatively thick wall (> 4 mm) ± surrounding consolidation or mass

IMAGING

General Features

- Best diagnostic clue
 - Irregular thick-walled lung cavity, often contains air, fluid, air-fluid level
- Location
 - Gravitationally dependent segments in cases of aspiration
- Morphology
 - Spherical thick-walled cavity with relatively smooth inner margin

Radiographic Findings

- 7- to 14-day evolution from pneumonia to abscess cavity
- Pulmonary cavity
 - o Often solitary
 - Wall thickness: < 4 mm (5%); 5-15 mm (80%); > 15 mm (15%)
 - o Air-fluid level in 75%
 - Often surrounded by consolidation (50%)
- Location usually related to aspiration in gravitationally dependent locations
 - Supine position: Upper lobe posterior segments, lower lobe superior segments
 - Decubitus position: Upper lobe posterior segments, lower lobe lateral basilar segments
 - Upright position: Lower lobe basilar segments, middle lobe
- Lower lobe abscesses usually larger than upper lobe abscesses
- Pleural effusions common (50%); may evolve to empyema
- Multiple abscesses
 - Bronchogenic spread from initial abscess
 - Daughter abscesses usually smaller than parent
 - Located in areas gravitationally that are dependent from parent abscess
 - Lemierre syndrome
 - Sore throat and internal jugular vein thrombosis
 - Usually secondary to Fusobacterium
- Distinction of lung abscess from empyema
 - Cavity: Spherical shape, equal length of air-fluid levels on orthogonal radiography, acute angles with chest wall
 - Empyema: Lenticular shape, unequal length of air-fluid levels on orthogonal radiography, obtuse angles with chest wall
 - o 33% of lung abscesses accompanied by empyema
- Slow resolution with treatment; often months
 The larger the abscess, the longer the time to resolution

CT Findings

• Optimal visualization and assessment of lung abscess

- Abscess may be fluid-filled
- Air-fluid level or internal air indicates bronchial communication
- Cavity wall thickness: Variable, 4 mm to < 15 mm; thick wall more common
 - o Internal wall usually smooth (90%), shaggy (10%)
- Surrounding airspace or ground-glass opacity may exhibit air bronchograms or tiny air bubbles
- Abscess vs. empyema
 - Abscess: Thick irregular wall, spherical, narrow contact with chest wall, bronchovascular markings extend toward abscess
 - Empyema: Thin uniform wall, lenticular shape, broad contact with chest wall, split pleura sign, adjacent compressed lung
- Frequent reactive hilar and mediastinal lymphadenopathy, usually < 2.5-cm short axis diameter
- Bronchopleural fistula: Development of hydropneumothorax
- Air crescent: Suggests invasive aspergillosis or mycetoma in preexisting cavity

Imaging Recommendations

- Best imaging tool
 - CT for differentiation of lung abscess from empyema and exclusion of lung cancer
- Protocol advice
 - Antibiotics should be continued until chest radiography shows resolution or stability

DIFFERENTIAL DIAGNOSIS

Pneumatocele

• Difficult distinction from abscess, especially in staphylococcal pneumonia

Tuberculosis

• Upper lobe consolidation with cavitation

May be bilateral

Infected Bulla

- Emphysema and history of smoking
- Thin-walled bulla with air-fluid level
- Considered pneumonia variant, responds to antibiotics

Lung Cancer

- Lung cavity in edentulous patient more likely due to cancer than abscess
- Thickest portion of cavity wall > 15 mm suggests malignancy
- Nodular cavity wall
- Less likely to exhibit surrounding consolidation

Septic Emboli

- Endocarditis, extrathoracic site of infection, indwelling catheter, IV drug use
- Often multiple nodules/consolidations, rapidly evolve into cavities (24 hours)

Granulomatosis With Polyangiitis

- Associated sinus and renal disease
- Nodules or masses ± cavitation, air-fluid levels rare
- ± subglottic stenosis

Necrobiotic Nodules

- History of rheumatoid arthritis &/or dust inhalation
- Few, small, subpleural cavitary nodules

Intralobar Sequestration

- Recurrent pneumonia in same location, typically lower lobe basilar segments
- May exhibit intrinsic air, air-fluid levels, fluid
- Supplied by systemic artery(ies)

Hydatidosis

• Crescent sign if air enters potential space between pericyst and endocyst and separates parasitic membranes

PATHOLOGY

General Features

- Etiology
 - Aspiration: Mixed aerobic and anaerobic polymicrobial bacterial infection originating from gingiva
 - o Abscess-forming organisms
 - Anaerobes: Peptostreptococcus, Bacteroides, Fusobacterium, microaerophilic streptococci
 - Aerobes: Staphylococcus aureus, Streptococcus pyogenes, Klebsiella pneumoniae, Haemophilus influenzae, Actinomyces, Nocardia, Mycobacterium species
 - Parasites: Paragonimus, Entamoeba
 - Fungi: Aspergillus, Cryptococcus, Histoplasma, Blastomyces, Coccidioides
- Associated abnormalities
 - o May progress to empyema and bronchopleural fistula

Gross Pathologic & Surgical Features

- Parenchymal destruction: Heals with scarring, bronchiectasis, cyst formation
- Uncommon complication: Pulmonary gangrene with necrotic lung fragments in abscess cavity (pulmonary sequestrum)

Microscopic Features

- Most are secondary to polymicrobial infection
- 1/2 of cases due to or include anaerobic organisms; must be cultured with anaerobic technique
- Sputum gram stain classically polymicrobial with many neutrophils
- Tuberculosis and *Nocardia* detected with acid-fast stain; fungi detected with silver stain

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Often subacute illness of weeks to monthsFever
 - Leukocytosis in 90% of patients
 - o Cough, foul-smelling sputum
 - Periodontal disease
 - Hemoptysis may occur, may be fatal

Demographics

- Age
 - Any age, but more common in older adults

- Sex
 - o M:F = 4:1
- Epidemiology
 - High risk: Poor dentition, seizure disorder, alcoholism
 - Predisposing conditions: Immune deficiency, bronchiectasis, malignancy, emphysema, steroid treatment
 - May develop in patients with inappropriate/inadequate antibiotic treatment of pneumonia
 - 70-80% are smokers; 12% have associated lung cancer; infected lung cancer rare

Diagnosis

- Image-guided aspiration
 - No bronchoscopy in acute phase for abscesses > 4 cm because of potential spillover of contents to normal lung

Natural History & Prognosis

- Good prognosis with early diagnosis and treatment (< 10% mortality)
 - o 33% mortality if untreated
- Aspiration → pneumonia → progression to lung abscess in 7-14 days
 - Slower resolution compared to noncavitary pneumonia
 - Heals with scarring, bronchiectasis, cystic change
 - Higher mortality in older debilitated
 - immunocompromised patients with large abscesses

Treatment

- Broad-spectrum antibiotics due to polymicrobial etiology (clindamycin) or combination of antibiotics (ampicillin-sulbactam, amoxicillin-clavulanate)
- Bronchoscopy to exclude endobronchial lesion or foreign body if failed medical treatment
- < 10% require surgery (abscess > 6 cm)
- Percutaneous drainage (controversial), endoscopic drainage
 - Reserved for nonresolving abscess or empyema that abuts chest wall (10-20%)

DIAGNOSTIC CHECKLIST

Consider

- Lung cancer in edentulous patient (most abscesses arise from periodontal bacteria)
- CT to evaluate complications, such as empyema and bronchopleural fistula

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Lung Abscess





(Left) Axial CECT of a 61-yearold alcoholic man with productive cough and dyspnea shows a heterogeneous left upper lobe consolidation with central lucencies 🖾, consistent with cavitation and suggestive of necrotizing pneumonia. Blood cultures revealed Streptococcus pneumoniae. (Right) Axial NECT of the same patient obtained 2 months later shows improved but persistent left upper lobe cavitary disease with a thick, nodular abscess wall \rightarrow .





(Left) Coronal NECT of a patient with hemoptysis shows a complex left upper lobe abscess \blacksquare secondary to methicillin-sensitive Staphylococcus aureus infection. The loculated left , pleural effusion 🛃 represented an empyema, which required decortication. (Right) Axial NECT of a 62year-old man with fever and cough shows a right lung cavitary lesion $\overline{\supseteq}$ with a thick, nodular wall and intraluminal debris. Culture of bronchoalveolar lavage specimens showed coccidioidomycosis.





(Left) Axial CECT of an 84year-old man shows a large right upper lobe mass-like $consolidation \blacksquare$ with a central low-attenuation spherical component with intrinsic air bubbles. The lesion was thought to represent a lung abscess rather than a pulmonary neoplasm. (Right) Axial NECT of the same patient obtained 2 months later after antibiotic treatment shows marked interval improvement with resolution of the mass-like lesion and a residual linear scar 🔁 at the site of the previously noted lung abscess.

Septic Emboli

KEY FACTS

TERMINOLOGY

• Infected embolic material seeding lung from extrapulmonary source; often foreign body or infective endocarditis

IMAGING

- Radiography
 - Peripheral, poorly-marginated, 1- to 3-cm, nodular or wedge-shaped opacities
 - Rapid cavitation, often within 24 hours
 - Pleural effusions, may be loculated
- CT
 - Multifocal peripheral and basilar lung nodules
 - Cavities in various stages of evolution (thick- to thinwalled)
 - Subpleural wedge-shaped consolidations due to hemorrhage or infarction
 - o Empyema

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary emboli
- Pneumonia
- Pulmonary metastases

PATHOLOGY

- *Staphylococcus aureus* is most common organism related to foreign bodies and IV drug use
- Etiology: Infective endocarditis, Lemierre syndrome, infected venous catheters or pacemaker wires
- Risk factors: IV drug use, indwelling catheters

CLINICAL ISSUES

• Symptoms/signs: Fever, dyspnea, chest pain

DIAGNOSTIC CHECKLIST

• Consider septic emboli in IV drug user or patient with indwelling catheter with multiple lung nodules

(Left) AP chest radiograph of a patient with a history of IV drug use, cough, and fevers shows bilateral patchy, wedge-shaped opacities \square , many with cavitation \boxtimes . This radiographic pattern is characteristic of pulmonary septic emboli. This clinical context should prompt a dedicated search for cavitary disease that can be subtle. (Right) Coronal NECT of the same patient shows multifocal bilateral wedge-shaped and nodular consolidations \square , many with central lucency and cavitation 🔁. CT optimally shows disease extent.





(Left) AP chest radiograph of a patient with endocarditis shows multiple bilateral peripheral wedge-shaped $opacities \longrightarrow with subtle$ associated lucencies 🔁. Note left internal jugular central venous catheter
. (Right) Axial CECT of the same patient shows bilateral peripheral nodular and wedgeshaped opacities 🔁 with cavitation \boxtimes , consistent with septic emboli. Right heart endocarditis is an important cause of septic emboli, and valve vegetations should be excluded when septic emboli are suspected on imaging.





Definitions

• Lung seeding by infected embolic material from extrapulmonary source; often foreign body or infective endocarditis

IMAGING

General Features

- Best diagnostic clue
 - Multiple nodules or patchy consolidations with rapid cavitation
- Location
 - Peripheral and basilar predominance
- Size
 - Usually small (< 3 cm in diameter)

Radiographic Findings

- Radiography
 - Peripheral, poorly-marginated 1- to 3-cm nodular or wedge-shaped opacities
 - May change in number or appearance (size or degree of cavitation) from day to day
 - Target sign: Thin-walled cyst with central density
 - Usually basilar (gravity and blood flow)
 - Rapid evolution, frequent cavitation within 24 hours (50%)
 - Cavity wall often thick
 - Absence of air-fluid level
 - Cavities in various stages of evolution
 - Complications
 - Loculated pleural effusion
 - Pneumothorax (rare)

CT Findings

• Multiple discrete nodules

- Average number: 15
- Size: 0.5-3.5 cm; larger nodules rare
- Peripheral and bilateral
- \circ Cavitation
 - Cavities in various stages of evolution (thick- to thinwalled)
- Air bronchograms
 - More common in gram-positive septic emboli
- Ground-glass halo
 - More common in gram-negative septic emboli
- Subpleural wedge-shaped consolidations
 - $\circ~$ Occlusion of pulmonary arteries by septic emboli $\rightarrow~$ hemorrhage or infarction
 - Cavitation slightly more common in nodules than in wedge-shaped consolidations
- Feeding vessel sign: Vessel leading directly to nodule or wedge-shaped opacity
 - 60-70% of patients with nodules, less common with wedge-shaped opacities
 - Multiplanar reformatted images often show that vessel actually courses around nodule
 - o "Feeding vessel" sometimes represents draining vein
- Mediastinal lymphadenopathy in 20%
- No intravascular clots

Pleural effusion, may be loculated in 80%
 Often evolves to empyema

Echocardiographic Findings

Detection of valve vegetations/endocarditis as source of septic emboli

Nuclear Medicine Findings

• PET/CT may be useful in patients with cardiac device infection

Imaging Recommendations

- Best imaging tool
 - CT for characterization of nodules initially detected on radiography and assessment of complications
 - Chest radiographs usually sufficient for monitoring response to therapy

DIFFERENTIAL DIAGNOSIS

Pulmonary Emboli

- Infarct: Airspace opacities from hemorrhage
 Hampton sign: Subpleural wedge-shaped opacities
 - Pulmonary infarct may cavitate (rare)
 - Cavity usually single and large (> 4 cm)
 - Evolution from ill-defined consolidation to well-defined opacity
- CTA: Filling defect(s) in pulmonary arterial system

Pneumonia

- Bacterial, fungal, mycobacterial
 - Solitary or multiple nodules &/or consolidations
 - Not necessarily peripheral in location
 - *M. tuberculosis* and classic atypical mycobacterial infection with upper lobe predominance
 - Cavitation or pneumatoceles common with *Staphylococcus*, gram-negative organisms (such as *Klebsiella*), fungal, and mycobacterial infection
 - Invasive aspergillosis
 - Ground-glass opacity halo
 - Air crescent sign

Pulmonary Metastases

- Multiple variably sized pulmonary nodules
 - Tend to be peripheral; 80% within 2 cm of pleural surface
 - o Usually sharply marginated in contrast to septic emboli
 - o May exhibit feeding vessel sign
 - Indistinct margins or ground-glass opacity halo in hemorrhagic metastases: Renal cell carcinoma, choriocarcinoma, melanoma
 - Cavitation common in metastases from squamous cell carcinoma or sarcoma
 - Less common: Primary gastrointestinal tract adenocarcinomas
- Do not rapidly evolve

Pneumatoceles

- Transient, usually follow known insult
 - o Trauma
 - o Infection
 - Hydrocarbon ingestion
- May evolve rapidly

Septic Emboli

• Typically thin-walled without air-fluid level

ANCA-Positive Granulomatosis With Polyangiitis

- Nodules with varying degrees of cavitation
 Do not rapidly evolve
- ± subglottic airway stenosis

Laryngeal Papillomatosis

- Multiple solid and cystic nodules • Grow extremely slowly
- Perihilar and central in location
- Laryngeal infection with human papillomavirus

PATHOLOGY

General Features

- Etiology
 - Organisms
 - *Staphylococcus aureus* is the most common organism related to foreign bodies and IV drug use
 - Burn patients: Pseudomonas aeruginosa most common
 - Other organisms
 - □ Streptococci
 - Fungi: ICU patients on broad-spectrum antibiotics and IV drug users
 - □ Gram-negative rods (*Serratia*)

• Infective endocarditis

- Tricuspid valve most commonly affected, aortic valve may also be involved
- Nonbacterial thrombotic endocarditis with injury to endothelial surface of heart
- Transient bacteremia leads to seeding of lesions with adherent bacteria
- Subsequent development of infective endocarditis

• Lemierre syndrome

- Uncommon but potentially life-threatening complication of acute pharyngotonsillitis
- Jugular vein septic thrombophlebitis from adjacent peritonsillar abscess leads to septic emboli
- Anaerobic infection from gram-negative bacilli (*Fusobacterium* most common)
- Immunocompetent host
- Infected venous catheters or pacemaker wires
- Pelvic thrombophlebitis
- Osteomyelitis

Gross Pathologic & Surgical Features

Necrotic infected lung
 Usually sharply demarcated from adjacent normal lung

Microscopic Features

- Acute inflammatory cells and necrosis are not specific and can be seen in infections, neoplasms, etc.
- May see colonies of organisms

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Fever
 - o Dyspnea
 - Chest pain

- Hemoptysis
- Other signs/symptoms
 - Endocarditis
 - **Osler nodes**: Tender subcutaneous nodules usually found on distal pads of digits
 - Janeway lesions: Nontender maculae on palms and soles
 - Roth spots: Retinal hemorrhages with small, clear centers
 - Petechiae, splinter hemorrhages (dark red linear lesions in nailbeds)

• Lemierre syndrome

- Sore throat
- Neck pain, swelling
- Cervical lymphadenopathy
- Cord sign (palpable thrombosed jugular vein)

Demographics

- Epidemiology
 - Risk factors
 - Indwelling venous catheters
 - Intravenous drug use
 - Immunologic deficiencies, particularly lymphoma, organ transplants
 - Periodontal disease
 - Burns

Natural History & Prognosis

- Radiographic abnormalities may precede positive blood cultures
- Mean duration of symptoms before diagnosis: 18 days

Treatment

- Therapy with broad spectrum antibiotics
 - o In cases of infective endocarditis: 6-8 weeks
- Drainage of associated empyema
- Surgery
 - Remove source of infection; drain abscess
 - Replace heart valves

DIAGNOSTIC CHECKLIST

Consider

- Septic emboli in intravenous drug user or patient with longterm indwelling catheter with multiple pulmonary nodules
- Echocardiography to exclude right heart valve vegetation when septic emboli are suspected on imaging

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Septic Emboli





(Left) Coronal CECT of a patient who presented with sore throat, neck pain, and dyspnea shows thrombosis of the right external jugular vein \blacksquare and enhancement of the vessel walls, consistent with thrombophlebitis. (Right) Axial CECT of the same patient shows multiple subpleural nodules (2 of which are shown here), consistent with septic emboli. Blood culture grew Fusobacterium necrophorum. These findings are consistent with Lemierre syndrome, an uncommon cause of septic emboli.





(Left) Coronal CECT of a patient who presented with fever shows a retained catheter fragment ⊇ in the right brachiocephalic vein. (Right) Axial CECT of the same patient shows multiple bilateral small predominantly peripheral pulmonary nodules ⊇, consistent with pulmonary emboli. Blood culture was positive for Staphylococcus aureus. An infected central line is a common cause of pulmonary septic emboli.





(Left) Axial NECT of an IV drug user with tricuspid endocarditis and Staphylococcus aureus bacteremia shows multiple cavitary lesions of varying sizes and variable wall thicknesses, consistent with septic emboli. (Right) Axial CECT of the same patient obtained 2 weeks later shows focal dilatation of a pulmonary artery branch 🛃, consistent with pulmonary artery pseudoaneurysm (a rare complication of septic embolism).

KEY FACTS

TERMINOLOGY

• Lung infection caused by *Streptococcus pneumoniae*

IMAGING

- Radiography
 - o Lobar consolidation (81%)
 - Homogenous consolidation that crosses segmental boundaries and involves only one lobe
 - o Bronchopneumonia (19%)
 - Nonconfluent heterogeneous consolidation
 - o Pleural effusion (10-15%)
 - More common in severe pneumonia
- CT
 - Ground-glass attenuation (86%)
 - Consolidation (75.6%)
 - o Bronchial wall thickening (25.6%)
 - Centrilobular nodules (19.8%)
 - Pleural effusion (18.6%)

TOP DIFFERENTIAL DIAGNOSES

- Other bacterial pneumonias
- Viral pneumonia
- Pulmonary infarction
- Hemorrhage
- Pulmonary edema
- Aspiration

PATHOLOGY

• Streptococcus pneumoniae (pneumococcus) is catalasenegative gram-positive coccus

CLINICAL ISSUES

- Acute onset, fever, chills, productive cough, pleuritic chest pain
- *S. pneumoniae* is most frequent pathogen that produces pneumonia, regardless of patient location (outpatient, hospitalized, ICU), age group, or comorbidities

(Left) PA chest radiograph of a 28-year-old patient with pneumococcal pneumonia who presented with cough and fever shows a left perihilar consolidation 🔁. Lobar pneumonia is the most common imaging manifestation of Streptococcus pneumoniae pneumonia. (Right) Axial CECT of the same patient shows a dense confluent left lower lobe consolidation \supseteq with intrinsic air bronchograms 🖂. Procalcitonin is a helpful biomarker, which is typically elevated in bacterial infections.





(Left) AP chest radiograph of a 64-year-old patient with pneumococcal pneumonia shows multifocal right lung consolidations \square and obliteration of the right costophrenic angle 🔁 Multifocal pneumonia can also occur in the context of Streptococcus pneumoniae. (Right) Axial CECT of the same patient shows middle lobe and right lower lobe $consolidations \supseteq$ with intrinsic air bronchograms and bilateral pleural effusions 🖂





Infections

Abbreviations

• Community-acquired pneumonia (CAP)

Synonyms

• Streptococcal or pneumococcal pneumonia

Definitions

• Lung infection caused by Streptococcus pneumoniae

IMAGING

General Features

- Best diagnostic clue
 - Focal or multifocal lobar consolidation ± air bronchograms

Radiographic Findings

- Radiography
 - o Lobar consolidation (81%)
 - Homogenous consolidation, crosses segmental boundaries, involves only one lobe
 - ± air bronchograms
 - May be multifocal
 - Bronchopneumonia (19%)
 - Nonconfluent heterogeneous consolidation
 - Bronchial wall thickening
 - Pleural effusion (10-15%)
 - Free or loculated
 - More common in severe pneumonia
 - Round pneumonia
 - Spherical consolidation; may simulate mass
 - More frequent in children
 - o Rare complications: Lung abscess, empyema

CT Findings

- Ground-glass attenuation (86%)
- Consolidation (75.6%)
- Bronchial wall thickening (25.6%)
- Centrilobular nodules (19.8%)
- Interlobular septal thickening (9.3%)
- Reticular opacity (9.3%)
- Nodules (8.1%)
- Bronchiectasis (2.3%)
- Pleural effusion (18.6%)
- Lymphadenopathy (15.1%)

Ultrasonographic Findings

• Ultrasonography useful for detection and characterization of pleural effusion

Imaging Recommendations

- Best imaging tool
 - Chest radiography: First-line imaging in patient with suspected pneumonia
 - CT: Detection of complications in patient with unexpected clinical course
- Protocol advice
 - Contrast administration helpful for evaluation of patients with pleuropulmonary disease

DIFFERENTIAL DIAGNOSIS

Other Bacterial Pneumonia

- Radiologic manifestations may be similar to those of pneumonia caused by other bacteria
- *Klebsiella pneumoniae* and *Haemophilus influenzae* pneumonia may exhibit indistinguishable radiologic manifestations, but are less frequent

Viral Pneumonia

- Similar imaging findings
- Frequent ground-glass opacities, centrilobular nodules ± surrounding ground-glass opacity, bronchial wall thickening

Pulmonary Infarction

- Pulmonary hemorrhage and ischemia secondary to pulmonary embolism
- 15% of patients with pulmonary embolism
- Basilar predominance, wedge-shaped, abuts pleura

Pulmonary Edema

- Abnormal extravascular lung water
- Variable distribution according to etiology
 Bat wing distribution of edema of sudden onset
 - Central and basilar predominance in cardiogenic pulmonary edema
 - Bilateral upper lobe predominant consolidation in neurogenic pulmonary edema

Lung Cancer

- Invasive mucinous adenocarcinoma
 Lepidic growth pattern
- Focal or multifocal consolidation
- Nodules, interlobular septal thickening, bronchovascular bundle thickening from disseminated malignancy
- Constitutional symptoms and hemoptysis in some patients

Pulmonary Lymphoma

- Primary or secondary
- Focal or multifocal consolidations &/or masses with air bronchograms
- Mediastinal lymphadenopathy present in most affected patients
- Subacute or chronic clinical manifestations with type B symptoms

Organizing Pneumonia

- Chronic clinical manifestations
- Basilar predominant peribronchovascular or subpleural consolidation
- May exhibit migratory behavior
- Reversed halo sign

Aspiration

- Critically ill patient
 - Consolidation in dependent lung parenchyma
 - Rapid progression
 - May be complicated by bacterial pneumonia or acute respiratory distress syndrome (ARDS)

PATHOLOGY

General Features

- Etiology
 - Streptococcus pneumoniae (Pneumococcus): Catalasenegative gram-positive coccus
 - Produces toxin called pneumolysin (PLY) (alphahemolysin)
 - Metabolizes hemoglobin to greenish pigment
 - Allows classification as alpha-hemolytic streptococci
 - Polysaccharide capsule
 - Most important virulence factor of *Streptococcus pneumoniae*
 - Determines serotype of microorganism
 - Target for current pneumococcal vaccines
 - Virulence factors
 - Capsular polysaccharide (CPS): Major surface antigen
 - Prevents entrapment by mucus during colonizationInhibits opsonophagocytosis
 - ChoP on teichoic acid (PAFR ligand)
 - Binds PAFR on epithelial and endothelial cell surfaces
 - Ply (pore-forming toxin)
 - Cytotoxic and pro-apoptotic for wide variety of host cells
 - PLY contributes to immunopathogenesis of invasive pneumococcal disease
 - Associated with prothrombotic activity and immunosuppression

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute onset
 - o Fever
 - o Chills
 - Productive cough
 - Pleuritic chest pain
 - Dullness to percussion
 - Egophony and pectoriloquy in areas of consolidation
- Other signs/symptoms
 - Middle ear infection (acute otitis media)
 Children (6-36 months)
 - o Sinusitis
 - o Meningitis
 - o Endocarditis
 - Peritonitis
 - Septic arthritis
 - Austrian syndrome
 - Disseminated Streptococcus pneumoniae infection
 - Classic triad: Pneumonia, endocarditis, meningitis
 - Alcoholism is principal risk factor

Demographics

- Age
 - Bimodal distribution
 - Children and older adults
- Epidemiology
 - o 40-50% of adults are asymptomatic carriers

- S. pneumoniae remains most frequent pathogen that produces pneumonia, regardless of patient location (outpatient, hospitalized, ICU), age group, or comorbidities
- Dominant manifestation of pneumococcal CAP is nonbacteremic/non-invasive disease
- o Invasive infection (1/4 of cases)
- Other pathogens may be co-detected in individuals with pneumococcal disease (viruses, bacteria, &/or helminths)
- Risk factors for pneumococcal pneumonia
 - Extreme ages (young and older patients)
 - Alcoholism
 - Immunosuppression
 - Chronic heart or lung disease
 - Prior splenectomy
 - Cirrhosis
 - Malignancy (especially hematopoietic)
 - Dementia
 - Smoking and exposure to second-hand smoke

Natural History & Prognosis

- Variable clinical course
- Most patients respond to conventional antibiotics, but in some cases, there is disease progression
- Complications
 - Necrotizing pneumonia
 - o Empyema
 - o ARDS
- **Elevated procalcitonin** often indicates bacterial etiologies; the higher the level, the higher the risk of sepsis

Treatment

- Polyvalent polysaccharide vaccination recommended for high-risk patients
- Vaccines that contain purified capsular polysaccharides (PPVs) effective against invasive disease in adults
- The 10-valent (PCV10) and 13-valent (PCV13) formulations of PCV have replaced 7-valent version
- Vaccine efficacy against non-invasive pneumonia remains controversial
- Macrolide or doxycycline commonly used in outpatient setting
- Multi-drug-resistant strains becoming more common

DIAGNOSTIC CHECKLIST

Consider

- *Streptococcus pneumoniae (Pneumococcus)* is most common bacterial etiology of CAP
- Pneumococcal pneumonia must be considered in differential diagnosis of patient with lobar consolidation, acute respiratory symptoms, and fever

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- Okada F et al: Thin-section CT findings of patients with acute Streptococcus pneumoniae pneumonia with and without concurrent infection. Br J Radiol. 85(1016):e357-64, 2012

Pneumococcal Pneumonia





(Left) PA chest radiograph of a 32-year-old patient with fever and cough shows no abnormality. While chest radiography is the study of choice to assess suspected pneumonia, it may fail to reveal subtle pulmonary abnormalities. (Right) Axial NECT of the same patient shows a spherical left upper lobe consolidation \supseteq with intrinsic air bronchograms. Sputum culture revealed pneumococcal pneumonia. CT has greater sensitivity for detection of subtle pneumonias, but is rarely used.





(Left) AP chest radiograph of a 55-year-old patient who presented with fever and chest pain shows a right upper lobe consolidation \supseteq and a loculated right pleural effusion 🖾 (Right) Axial CECT of the same patient shows a cavitary right lower lobe $consolidation \supseteq$ and bilateral pleural effusions 🖾. Right parietal pleural thickening and enhancement 🖂 are consistent with empyema. Pleural thickening and enhancement in the setting of pneumonia should raise suspicion for empyema and prompt pleural fluid analysis.





(Left) AP chest radiograph of a 87-year-old patient with chronic obstructive pulmonary disease and pneumococcal pneumonia shows multifocal multilobar consolidations 🖂, radiolucent areas 🖂, and small pleural effusions 🔁. (Right) Axial CECT of the same patient shows multifocal , consolidations 🔁 on a background of severe emphysema 🖾 and left larger than right pleural effusions Pleural effusions are often parapneumonic and not infected. Signs of empyema include pleural thickening, enhancement, and loculation.

KEY FACTS

TERMINOLOGY

- Lung infection caused by *Staphylococcus aureus*
- Methicillin-resistant *Staphylococcus aureus* (MRSA); methicillin-sensitive *S. aureus* (MSSA)

IMAGING

- Radiography
 - Consolidation: Segmental, patchy, or homogeneous depending on disease severity
 - Cavitation: Varies according to published series
 - Pleural effusion: Free or loculated
 - Complications: Lung abscess, pneumatocele, empyema
- CT
 - o Ground-glass opacities: MRSA (79.4%); MSSA (80.7%)
 - Consolidation: MRSA (58.8%); MSSA (51.8%)
 - Bronchial wall thickening: MRSA (60.3%); MSSA (75.9%)
 - Centrilobular nodules: MRSA (47.1%); MSSA (63.9%)
 - o Cavitation: MRSA (2.9%); MSSA (3.6%)
 - o Pleural effusion: MRSA (70.6%); MSSA (40.8%)

TOP DIFFERENTIAL DIAGNOSES

- Other bacterial pneumonias
- Viral pneumonia
- Aspiration
- Hemorrhage
- Pulmonary edema

PATHOLOGY

• *S. aureus:* Gram-positive, facultative anaerobic bacterium of Staphylococcaceae family

CLINICAL ISSUES

- Children and older adults more susceptible
- Women may a have higher rate of colonization by S. aureus
- 1.6-3% prevalence among patients with communityacquired pneumonia who require hospitalization
- 16% of nosocomial pneumonias
- Mortality of staphylococcal pneumonia is usually associated with inadequate initial antibiotic therapy

(Left) AP chest radiograph of a 41-year-old patient who presented with fever and cough shows multilobar basilar predominant consolidations (Right) Coronal NECT of the same patient shows rapid progression of bilateral lower lobe consolidations (Blood cultures confirmed the diagnosis of methicillinsensitive Staphylococcus aureus (MSSA) pneumonia.





(Left) AP chest radiograph of a 42-year-old patient with methicillin-resistent Staphylococcus aureus (MRSA) pneumonia shows patchy nonsegmental multilobar basilar predominant consolidations ⇒. (Right) Axial CECT of the same patient obtained 3 days later shows a right upper lobe cavitary mass-like consolidation ⇒, left upper lobe peribronchovascular illdefined nodules ⇒, and bilateral pleural effusions ⇒.





Abbreviations

- Methicillin-resistant Staphylococcus aureus (MRSA)
- Methicillin-sensitive S. aureus (MSSA)
- Community-acquired pneumonia (CAP)

Synonyms

• S. aureus pneumonia

Definitions

• Lung infection caused by S. aureus

IMAGING

General Features

- Best diagnostic clue
 - Bronchopneumonia (lobular pneumonia)
 - Bilateral, patchy, or segmental areas of consolidation

Radiographic Findings

- Radiography
 - Consolidation
 - Bilateral
 - Segmental, patchy, or homogeneous according to disease severity
 - o Cavitation
 - Low-attenuation area within pulmonary consolidation
 - Varies according to series
 - Pleural effusion
 - Free or loculated
 - Unilateral or bilateral
 - Complications
 - Recent data shows lower incidence of lung abscess and pneumatocele
 - Lung abscess
 - Circumscribed area of pus or necrotic debris in lung parenchyma
 - Cavitary lung mass
 - Pneumatocele
 - Round, thin-walled airspace in lung
 - Empyema
 - Pus in pleural cavity; abscess in pleural cavity
 - Thickening and enhancement of pleura and striation of extrapleural fat suggest pleural infection
 - Pneumothorax: Associated with pneumatoceles

CT Findings

- Ground-glass opacities: MRSA (79.4%); MSSA (80.7%)
- Consolidation: MRSA (58.8%); MSSA (51.8%)
- Bronchial wall thickening: MRSA (60.3%); MSSA (75.9%)
- Centrilobular nodules: MRSA (47.1%); MSSA (63.9%)
- Tree-in-bud: MRSA (23.5%); MSSA (44.6%)
- Reticular opacities: MRSA (33.8%); MSSA (25.3%)
- Bronchiectasis: MRSA (13.2%); MSSA (12.0%)
- Interlobular septal thickening: MRSA (8.8%); MSSA (8.4%)
- Cavitation: MRSA (2.9%); MSSA (3.6%)
- Pleural effusion: MRSA (70.6%); MSSA (40.8%)
- Distribution of parenchymal abnormalities
 O Unilateral: MRSA (35.3%); MSSA (36.1%)

- o Bilateral: MRSA (64.7%); MSSA (63.1%)
- o Basilar predominance: MRSA (69.1%); MSSA (60.2%)
- Peripheral predominance: MRSA (70.6%); MSSA (53.0%)
- Centrilobular nodules, tree-in-bud opacities, and bronchial wall thickening are more frequent in patients with MSSA pneumonia than in those with MRSA

Ultrasonographic Findings

• Ultrasonography useful for detection and characterization of pleural effusion

Imaging Recommendations

- Best imaging tool
 - Chest radiography: Initial imaging in patient with suspected pneumonia
 - CT: Identification and assessment of complications in patients with unexpected clinical course
- Protocol advice
 - Contrast administration useful in evaluation of patients with pleuropulmonary disease

DIFFERENTIAL DIAGNOSIS

Other Bacterial Pneumonias

- Radiological manifestations similar to those of pneumonia caused by other bacteria
- *S. pneumoniae*, gram-negative bacilli, and *Enterobacter* spp. should be considered in initial differential diagnosis

Viral Pneumonia

- Radiological manifestations of staphylococcal pneumonia may be similar to those seen in pneumonia caused by viruses
- Centrilobular nodules, tree-in-bud opacities, and groundglass opacities are frequent imaging abnormalities of viral pneumonia

Aspiration

- Critically-ill patient
- Parenchymal opacities in dependent portions of lung

Hemorrhage

- Hemoptysis and anemia may suggest diagnosis, but are not always present
- Diffuse or patchy multifocal consolidation

Lung Cancer

- Invasive mucinous adenocarcinoma
- Focal or multifocal consolidation
- Nodules, interlobular septal thickening, and bronchovascular bundle thickening may be present in patients with tumor dissemination

Pulmonary Edema

- Abnormal extravascular lung water
- Bat wing distribution in edema of sudden onset
- Central and basilar predominance of abnormalities in cardiogenic pulmonary edema

Small Vessel Vasculitis

- Multifocal ground-glass opacities and consolidation
- Cavitary nodules
- ANCA(+)

PATHOLOGY

General Features

- Etiology
 - *S. aureus:* Gram-positive, facultative anaerobic bacterium of Staphylococcaceae family
 - Non-motile bacterium, no sporulation, and generally no capsule (although some strains develop slime capsule)
 - Ability of staphylococci to produce catalase, allows their differentiation from *Streptococcus* and *Enterococcus* genera
 - o *S. aureus* colonizes nasopharynx of healthy individuals
 - Bacterial toxins contribute to lung infection morbidity
 - Pore-forming hemolysin (Hla)
 - Leukocidins (Panton-Valentine leukocidin)
 - Phenol-soluble modulins (PSMs)
 - o MRSA
 - Ability to make penicillin-binding protein 2A (PBP-2A) through mecA gene

Microscopic Features

• Gram-positive cocci in clusters

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Cough
 - o Sputum
 - o Fever
 - o Dyspnea
 - General weakness
- Other signs/symptoms
 - o *S. aureus* bacteremia
 - 28% of bacterial bloodstream infections
 - Related to skin-soft tissue infections or pneumonia
 - May produce metastatic infections
 - Infective endocarditis
 - Vertebral osteomyelitis
 - Iliopsoas abscess
 - Septic arthritis
 - Identification of metastatic infections denotes change in duration of antibiotic therapy

Demographics

- Age
 - o Children and older adults more susceptible
- Sex
 - Women may have higher rate of colonization by S. aureus
- Epidemiology
 - 1.6-3% prevalence among CAP patients requiring hospitalization
 - 0.7% with MRSA
 - 1% with MSSA
 - o 16% of nosocomial pneumonias
 - Increased incidence
 - Cigarette smoking
 - Alcoholism
 - Cardiovascular disease
 - Diabetes mellitus

- Pulmonary emphysema
- Malignancy
- Risk factors for community-acquired MRSA
 - Low socioeconomic status
 - Intravenous drug use
 - Previous MRSA infection or colonization
 - Recurrent skin infections
 - Severe pneumonia
- Community-acquired staphylococcal pneumonia is usually seen in patients recovering from influenza
- Community-acquired MRSA more likely to affect healthy populations with no predisposing risk factors
- 13.5% of bacterial pneumonias that arise as complication of COVID-19 infection

Natural History & Prognosis

- Community-acquired MRSA commonly associated with rapid progression and clinical deterioration
- Mortality of staphylococcal pneumonia is usually associated with inadequate initial antibiotic therapy

Treatment

- Effective antibiotics for treatment of community-acquired MRSA are not part of initial empiric therapy for management of CAP
- Guidelines for diagnosis and treatment of adults with CAP: Empiric coverage for MRSA only in patients with validated risk factors
- Empiric treatment option: Vancomycin (15 mg/kg every 12 h, adjusted based on levels) or linezolid (600 mg every 12 h)
- Identification of MRSA in respiratory tract within prior year predicts very high risk of MRSA identification in patients who present with CAP
- Major additional risk factors for MRSA: Hospitalization and parenteral antibiotic exposure in last 90 days
- Development of diagnostic tests capable of rapidly and accurately identifying *S. aureus* could greatly improve current approach to CAP management and reduce overuse of anti-MRSA antibiotics

DIAGNOSTIC CHECKLIST

Consider

- Prevalence of staphylococcal pneumonia in patients with CAP is low
- Staphylococcal pneumonia should be considered in patients with bronchopneumonia pattern on imaging (bilateral, patchy, or segmental areas of consolidation and bronchial wall thickening)

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Staphylococcal Pneumonia





(Left) AP chest radiograph of a 77-year-old patient with chronic obstructive pulmonary disease and methicillinsensitive Staphylococcus aureus (MSSA) pneumonia shows bilateral patchy right lung predominant consolidations 🖂 (Right) Coronal NECT of the same patient shows right lung . multilobar peribronchovascular . consolidations 🔁, bilateral centrilobular nodules and treein-bud opacities, and bronchiectasis 🔁





(Left) AP chest radiograph of a 69-year-old patient who presented with fever and chest pain shows a large loculated right pleural effusion ∋. (Right) Axial CECT of the same patient shows a loculated right pleural effusion ∋ and thickening and enhancement ▷ of the parietal pleural surface. Pleural fluid analysis confirmed empyema secondary to Staphylococcus aureus.





(Left) Coronal NECT of a 54year-old patient with methicillin-sensitive Staphylococcus aureus bacteremia shows a large right upper lobe cavitary consolidation ⇒ and left upper lobe centrilobular nodules ⇒. (Right) Sagittal NECT of the same patient shows spondylodiscitis involving the L2 vertebral body ⇒ as a complication of hematogenous dissemination of infection.

Klebsiella Pneumonia

KEY FACTS

TERMINOLOGY

• Pulmonary infection caused by Klebsiella pneumoniae

IMAGING

- Acute pneumonia
 - Consolidation
 - Right upper lobe predominance
 - o Cavitation
 - Lower incidence in recent literature
- Acute pneumonia complications
 - o Lung abscess
 - Cavitary lung mass
 - Pulmonary gangrene
 - Massive necrosis and sloughed lung
 - Chronic pneumonia
 - Consolidation in right upper lobe apical and posterior segments and right lower lobe superior segment

TOP DIFFERENTIAL DIAGNOSES

- Other bacterial pneumonias
- Tuberculosis

CLINICAL ISSUES

- Symptoms/signs
- High fever, chills, and flu-like symptoms
 Cough with sputum (currant-jelly sputum)
- Risk factors
 - Alcohol abuse, cigarette smoking
 - o Diabetes
- High mortality rate in alcoholics (50-60%)
- Higher mortality in *Klebsiella* pneumonia combined with other bacterial infections

DIAGNOSTIC CHECKLIST

• Consider *Klebsiella* pneumonia in alcoholic patient with severe community-acquired pneumonia

(Left) PA chest radiograph of a 77-year-old alcoholic patient with Klebsiella pneumoniae pneumonia shows a dense right upper lobe consolidation. (Right) Sagittal CECT of the same patient shows a dense consolidation of the right upper lobe posterior segment, a bulging morphology $\overline{\longrightarrow}$ of the adjacent right posterior major fissure, and a small right pleural effusion 🔁. While bulging of interlobar fissures has been historically associated with Klebsiella pneumonia, it may occur with pulmonary infection by various other microorganisms.





(Left) PA chest radiograph of an 84-year-old diabetic patient with Klebsiella pneumoniae pneumonia shows a right lower lobe cavitary mass 🔁 secondary to lung abscess formation. (Right) Axial CECT of the same patient shows a right lower lobe pulmonary mass with central low attenuation and gas bubbles ⇒, consistent with tissue necrosis. Klebsiella pneumonia is often associated with necrotizing pulmonary infection with resultant necrotizing pneumonia and abscess formation.





Synonyms

Friedländer pneumonia

Definitions

• Pulmonary infection caused by Klebsiella pneumoniae

IMAGING

Radiographic Findings

- Acute pneumonia
 - Consolidation
 - Lobar distribution
 - Right upper lobe predominance
 - Bulging of interlobar fissures
 - □ Related to bulky inflammatory exudate
 - Described in old published literature
 - May be seen in pneumonia due to other microorganisms
 - o Cavitation
 - Low-attenuation area within pulmonary consolidation
 - Lower incidence in recent series
 - Pleural effusion
 - Unilateral (39.9%)
 - Bilateral (13.1%)
- Acute pneumonia complications
 - Lung abscess
 - Circumscribed area of pus or necrotic debris in lung parenchyma
 - Cavitary lung mass
 - Pulmonary gangrene
 - Secondary to central vascular obstruction and bronchial obstruction
 - Massive necrosis and sloughed lung
 - Chronic pneumonia
 - Consolidation in right upper lobe apical and posterior segments and right lower lobe superior segment

CT Findings

- Acute pneumonia
 - o Ground-glass attenuation (100%)
 - o Consolidation (91.4%)
 - o Intralobular reticular opacities (85.9%)
 - Bronchial wall thickening (26.3%)
 - o Interlobular septal thickening (9.6%)
 - o Centrilobular nodules (4.0%)
 - o Bronchiectasis (4%)
 - o Cavitary lesions (0.5%)
- Chronic pneumonia
 - o Low-attenuation area within pulmonary consolidation

Imaging Recommendations

- Best imaging tool
 - Chest radiography for initial evaluation of patient with suspected pneumonia
 - CT: Identification of complications and evaluation of patients with unexpected or complicated clinical course

DIFFERENTIAL DIAGNOSIS

Other Bacterial Pneumonias

- Similar radiologic manifestations in pneumonia caused by variety of organisms
- Anaerobic bacterial pneumonia should be considered in alcoholic patients with cavitary lung disease

Tuberculosis

• Distribution of parenchymal abnormalities described in chronic *Klebsiella* pneumonia may mimic tuberculosis

PATHOLOGY

General Features

- Etiology
 - *K. pneumoniae* is a nonmotile, gram-negative bacillus of the Enterobacteriaceae family
 - Usually develops capsule (determining factor in virulence of bacteria)
 - May produce carbapenemase (β-lactamase) with secondary bacterial resistance
 - Additional pathogens frequently coexist
 - 37% have methicillin-resistant *Staphylococcus aureus* (MRSA)
 - 23% have Pseudomonas aeruginosa

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute pneumonia
 - High fever, chills, and flu-like symptoms
 - Cough with sputum (currant-jelly sputum)
 - Chronic pneumonia
 - Chronic productive cough and hemoptysis

Demographics

- Sex
 - 0 M>F
- Epidemiology
 Discommon cause of com
 - Uncommon cause of community-acquired pneumonia (0.5-5%)
 - Important pathogen in etiology of nosocomial pneumonia (10%)
 - Risk factors
 - Alcohol abuse, cigarette smoking
 - Diabetes
 - Chronic pulmonary disease

Natural History & Prognosis

- High mortality rate in alcoholics (50-60%)
- Higher mortality in *Klebsiella* pneumonia combined with other bacterial infections

DIAGNOSTIC CHECKLIST

Consider

• *Klebsiella* pneumonia in alcoholic patient with severe community-acquired pneumonia

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KEY FACTS

TERMINOLOGY

- Pulmonary infection due to Pseudomonas aeruginosa
- Common cause of hospital-acquired pneumonia (HAP)

IMAGING

• Radiography

- Multifocal patchy or confluent heterogeneous opacities with nodularity
- Lobular consolidations with areas of confluence
- o ± pleural effusions
- CT
 - Peribronchovascular ground-glass opacities and clustered branching centrilobular nodules
 - Lobular, subsegmental, and segmental consolidations
 - ± cavitation
 - ± pleural effusions
 - ± bronchiectasis with bronchial wall thickening and airfluid levels

TOP DIFFERENTIAL DIAGNOSES

- Non-Pseudomonas bronchopneumonia
- Aspiration
- Alveolar hemorrhage
- Non-tuberculous mycobacterial infection

PATHOLOGY

• Centrilobular exudate, focal necrosis, hemorrhage

CLINICAL ISSUES

- Uncommon cause of community-acquired pneumonia; structural lung disease (chronic obstructive, cystic fibrosis)
- Common cause of hospital acquired and ventilatorassociated pneumonia; most lethal pulmonary nosocomial infection
- Disseminated bacteremia uncommon, but often lethal in immunocompromised patients
- Chronic infection/colonization in cystic fibrosis and other structural lung abnormalities

(Left) AP chest radiograph of a patient with emphysema who presented with right upper lobe community-acquired pneumonia shows right upper lobe consolidation with areas of intrinsic lucency \supseteq raising concern for necrosis. Blood culture grew Pseudomonas aeruginosa. (Right) Axial NECT of the same patient shows necrotizing pneumonia with large areas of cavitation 🖂. Note contralateral bronchopneumonia 🖾 and including cavitary nodules 🔁. Pre-existing lung disease, e.g., chronic obstructive pulmonary disease, is often present.





(Left) Axial CECT of a 69-yearold immunocompromised man status post heart transplant shows community-acquired Pseudomonas pneumonia that manifests with a right upper lobe confluent lobular $consolidation \supseteq and$ surrounding ground-glass opacities. (Right) Coronal NECT of the same patient obtained 1 week later shows marked progression of right greater than left consolidations, right upper lobe cavitation 🔁 bronchopleural fistula, and pneumothorax treated with a right chest tube 🔁.





Abbreviations

• Pseudomonas aeruginosa (P. aeruginosa)

Definitions

• Pulmonary infection due to gram-negative *P. aeruginosa;* common cause of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP)

IMAGING

General Features

- Best diagnostic clue
 - Bronchopneumonia in ventilated patients, particularly those with structural lung disease, heart failure, or immunosuppression
- Location
 - Multifocal, bilateral, upper lobe predominant
- Size
 - Range: Subcentimeter centrilobular nodules to lobular and confluent consolidations
- Morphology
 - Peribronchiolar ground-glass opacities and centrilobular nodules; lobular consolidations with confluence

Radiographic Findings

- Multifocal heterogeneous nodular opacities
- Lobular consolidations with confluence ± cavitation
- ± pleural effusion

CT Findings

- Peribronchovascular ground-glass opacities, clustered centrilobular nodules, tree-in-bud opacities
- Lobular and confluent consolidations ± cavitation
- ± pleural effusion
- ± bronchiectasis, bronchial wall thickening, air-fluid levels

Imaging Recommendations

- Best imaging tool
 - Chest radiography for disease detection and documentation of response to therapy
 - NECT typically sufficient for identification of underlying structural lung disease and complications

DIFFERENTIAL DIAGNOSIS

Non-Pseudomonas Bronchopneumonia

- Various other organisms may produce similar nonspecific imaging features
- *S. aureus, K. pneumoniae, S. pneumoniae, E. coli*, anaerobes, other gram-negative organisms

Aspiration

- Consolidations with gravitational distribution
- Esophageal motility disorder, alcoholism

Alveolar Hemorrhage

- Bilateral centrilobular, geographic, or diffuse airspace disease
- Anemia, hemoptysis

Non-Tuberculous Mycobacterial Infection

• Chronic *Pseudomonas* infection may exhibit bronchiectasis, bronchiolitis, lobular/confluent consolidations

PATHOLOGY

General Features

• Etiology: Aspiration of secretions from colonized trachea in susceptible hospitalized patients

Gross Pathologic & Surgical Features

• Exudate centered on terminal bronchioles, focal necrosis and hemorrhage

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Fever, chills, productive cough, systemic toxicity, leukocytosis
- Clinical profile
 - Community-acquired pneumonia (CAP)
 - Pre-existing lung disease: Chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis
 - 5-10% of severe cases

o HAP

- Frequent pathogen in intensive care unit (ICU) setting; implicated in HAP
- Most lethal form of nosocomial pulmonary infection
- Bacteremic pneumonia
 - Blood-stream invasion/spread after onset of respiratory infection in immunocompromised patients
- High mortality within 3-4 daysChronic *Pseudomonas* infection
 - Older children and adults with structural lung disease: Cystic fibrosis, COPD, bronchiectasis
 - Mucus plugging, bronchiectasis, atelectasis, fibrosis; mimics non-tuberculous mycobacterial infection

Demographics

- Any age: Older (> 65 years) and immunocompromised patients at risk for severe disease
- Predisposing factors: Immunosuppression, prior antibiotic therapy, disrupted normal mucosal barrier

Natural History & Prognosis

- Leading cause of death in patients with VAP
- Prognosis depends on virulence of organism, antibiotic susceptibility, and host response

Treatment

• Antipseudomonal antibiotic therapy

DIAGNOSTIC CHECKLIST

Consider

• *P. aeruginosa* pneumonia in ICU ventilated patients, immunosuppression, and structural lung abnormalities

SELECTED REFERENCES

 Zaragoza R et al: Update of the treatment of nosocomial pneumonia in the ICU. Crit Care. 24(1):383, 2020

Legionella Pneumonia

KEY FACTS

TERMINOLOGY

- Legionnaires disease
- Pneumonia caused by infection with any *Legionella* species, most commonly *Legionella pneumophila*

IMAGING

- Radiography
 - Rapidly progressive, asymmetric consolidation
 - Expands to occupy majority of lobe
 - Progresses to involve additional lobes or contralateral lung (3-4 days)
 - Pleural effusion in up to 2/3 of patients
- CT
 - Lobar or multilobar consolidation
 - Ground-glass opacity adjacent to consolidation
 - Perihilar > peripheral distribution
 - Pleural effusion (~ 1/3 of patients)
 - o Mild mediastinal and hilar lymphadenopathy

TOP DIFFERENTIAL DIAGNOSES

- Pneumococcal pneumonia
- Mycoplasma pneumonia
- Viral pneumonia
- Klebsiella pneumonia
- Staphylococcus pneumonia

PATHOLOGY

• Inhaled aerosolized contaminated water droplets

CLINICAL ISSUES

- Most patients have pre-existing disease
- Most common in adults > 50 years
- M:F = 2-3:1
- Prognosis varies with underlying conditions
 - Patients with impaired T-cell-mediated immunity have greatest mortality risk
- Treatment: Macrolides, fluoroquinolones

(Left) AP chest radiograph of a critically-ill patient with Legionella pneumonia who required mechanical ventilation shows a dense left lung peripheral consolidation *⊡*. (Right) Axial NECT of a patient with Legionella pneumonia shows a dense left lower lobe mass-like consolidation with surrounding ground-glass opacity. There was subsequent disease progression with eventual involvement of the right lung (not shown). Legionella pneumonia commonly exhibits progression on serial imaging.





(Left) Axial CECT of a patient with multilobar legionella pneumonia shows right upper lobe ground-glass opacities 🔁 and a dense left upper lobe consolidation 🔁 with adjacent ground-glass opacity Axial NECT of patient with multilobar Legionella pneumonia shows multifocal bilateral consolidations, some mass-like in appearance, with no cavitation or pleural effusion. Note mediastinal \supseteq and hilar 🔁 lymphadenopathy, a nonspecific finding often seen in Legionella pneumonia.





Synonyms

• Legionnaires disease

Definitions

• Pneumonia caused by infection with any *Legionella* species, most commonly *Legionella pneumophila*

IMAGING

General Features

- Best diagnostic clue
- Rapidly progressive, asymmetric consolidation
 Size
 - Initially lobar, then multilobar

Radiographic Findings

- Rapidly progressive, asymmetric lung consolidation
 - o Initially lobar, expands to occupy majority of lobe
 - Progression to involve additional lobes or contralateral lung (3-4 days)
- Less common manifestations
 - Spherical consolidation
 - Solitary or multiple mass(es), nodular- or mass-like consolidations
 - Cavitation and lymphadenopathy unusual except in immunocompromised patients
- Pleural effusion in up to 2/3 of affected patients

CT Findings

- NECT
 - Lobar or multilobar consolidation
 - Perihilar distribution more common than peripheral distribution
 - Ground-glass opacity, often adjacent to consolidation
 - Pleural effusion (~ 1/3 of patients), may be small
 - Mild mediastinal and hilar lymphadenopathy

Imaging Recommendations

- Best imaging tool
 - Chest radiography for initial diagnosis of pneumonia

DIFFERENTIAL DIAGNOSIS

Pneumococcal Pneumonia

- Consolidation usually limited to 1 lobe
 Almost always abuts visceral pleural surface
 - Air bronchograms usually present
 - Usually does not progress with appropriate therapy
 - Typically lacks extrapulmonary features, such as headache, diarrhea, and relative bradycardia

Mycoplasma Pneumonia

- Bronchopneumonia or bronchiolitis pattern more common
- Patients usually younger
- Insidious onset of symptoms

Viral Pneumonia

- Bronchopneumonia or bronchiolitis pattern more common
 Adenovirus infection may manifest as lobar pneumonia
- Cough, typically nonproductive

Klebsiella Pneumonia

- Usually nosocomial infection
- May mimic *Legionella* pneumonia
- Typically lacks extrapulmonary features, such as headache, diarrhea, and relative bradycardia

Staphylococcus Pneumonia

- Often nosocomial infection, especially in ICU
- Bronchopneumonia pattern most common
 Air bronchograms uncommon
- Abscesses in 15-30%

PATHOLOGY

General Features

- Etiology
 - Inhaled or aspirated aerosolized droplets of contaminated water

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Fever, chills, cough (initially dry), dyspnea
 - Pleuritic chest pain in ~ 30%
- Other signs/symptoms
- Headache, confusion, lethargy
- Relative bradycardia
- Loose stools or watery diarrhea
- o Microscopic hematuria, acute renal regurgitation
- Clinical profile
 - Most affected patients have pre-existing disease
 - Community-acquired: Chronic obstructive pulmonary disease and malignancy
 - Nosocomial: Malignancy, renal failure, transplantation
- Elevated procalcitonin; the higher the level, the worse the outcome

Demographics

- Age
 - May affect any age group
 - Most common in adults > 50 years
- Sex
- o M:F = 2-3:1
- Epidemiology
 - o Seasonal peak in late summer and early autumn
 - Sporadic cases associated with exposure to colonized water (construction, travel)
 - Nosocomial outbreaks related to exposure to contaminated water sources (air conditioners, showers)

Natural History & Prognosis

- Prognosis varies with underlying conditions
 - Patients with impaired T-cell-mediated immunity have greatest mortality risk

Treatment

• Doxycycline or fluoroquinolones usually effective

SELECTED REFERENCES

 Mittal S et al: Thoracic imaging features of Legionnaire's disease. Infect Dis Clin North Am. 31(1):43-54, 2017

Nocardiosis

KEY FACTS

TERMINOLOGY

• Infection by organisms in *N. asteroides* complex

IMAGING

• Radiography

- Consolidation, nodules/masses ± cavitation
- Upper lobe fibrocavitary disease
- Reticulonodular interstitial opacities
- Pleural effusion, unilateral or bilateral
- CT
 - Homogeneous consolidation (65%)
 - o Cavitation (40%)
 - Nodules (60%) &/or masses (20%)
 - Pleural effusion (30%)
 - Lymphadenopathy (15%)
- May involve extrapulmonary structures
- Best clue: Necrotizing pneumonia in immunocompromised patient

TOP DIFFERENTIAL DIAGNOSES

- Other infections that traverse tissue planes: Tuberculosis, actinomycosis, invasive aspergillosis, mucormycosis
- Lung cancer

PATHOLOGY

• Gram-positive bacilli, weakly acid-fast

CLINICAL ISSUES

- Symptoms/signs: Fever, chills, fatigue, dyspnea, productive cough, hemoptysis, sweats, weight loss
- 50% of infections in immunocompromised patient
- Underlying lung disease
- Dissemination in 50% of pulmonary infections
- Treatment: Sulfa-containing antibiotic (3-6 months)

DIAGNOSTIC CHECKLIST

• Consider brain imaging in patients with nocardiosis to exclude metastatic infection

(Left) Axial NECT of a 32-yearold patient with Fanconi anemia and Nocardia pneumonia shows a right lower lobe consolidation \square . The diagnosis was established via bronchoalveolar lavage. (Right) Axial CECT of a 66year-old man status post bilateral lung transplantation for emphysema shows middle ➡ and lower lobe pneumonia, a small right pleural effusion, and chest wall abscesses 🔁. Thoracentesis revealed nocardiosis. This infection may traverse anatomic boundaries and result in chest wall and mediastinal involvement.





(Left) Axial NECT of a 72-yearold woman with a history of immunosuppression shows a large right lower lobe cavitary mass \blacksquare , patchy left lower lobe airspace opacities \square , and trace bilateral pleural fluid. Blood cultures recovered Nocardia. (Right) Axial CECT of a young man with acquired immunodeficiency syndrome and Nocardia pulmonary infection shows multifocal nodular and mass-like consolidations \supseteq , some of which exhibit cavitation 🖂





Synonyms

• Nocardia asteroides complex: Nocardia nova, Nocardia farcinica, Nocardia transvalensis

Definitions

• Infection by organisms in *N. asteroides* complex

IMAGING

General Features

- Best diagnostic clue
 Necrotizing or cavitary pneumonia in immunocompromised patient
- Location
- Typically unilateral disease
- Morphology
 - o May traverse tissue planes

Radiographic Findings

- Radiography
 - o Consolidation, nodules/masses ± cavitation
 - Upper lobe fibrocavitary disease
 - Reticulonodular interstitial opacities
 - o Pleural effusion ~ 1/3 of cases; unilateral or bilateral

CT Findings

- NECT
 - Homogeneous consolidation (65%)
 - Lobar or diffuse, indistinct margins, frequently abuts pleura
 - Bronchopneumonia (10%)
 - Cavitation (40%)
 - Abscess, single/multiple thick-walled cavities
 - Nodules (60%) &/or masses (20%)
 - Solitary or multiple
 - Well-defined or irregular borders
 - Indolent, slowly enlarging pulmonary nodule
 - Associated reticular or fine nodular opacities
 - o Bronchiectasis (10%)
 - o Pleural effusion (30%)
 - o Lymphadenopathy (15%)
- CECT
 - Chronic infection may involve adjacent pleura, chest wall, pericardium, mediastinum, superior vena cava
 - Pleural effusion/empyema (80%)
 - Acquired immunodeficiency syndrome (AIDS): Irregular spiculated nodules and cavitary masses

Imaging Recommendations

- Best imaging tool
 - CECT optimally demonstrates involvement of chest wall and mediastinum

DIFFERENTIAL DIAGNOSIS

Other Infections That Traverse Tissue Planes

- Tuberculosis
- Actinomycosis
- Invasive aspergillosis, mucormycosis

Lung Cancer

 Pulmonary mass; may invade adjacent pleura, chest wall, mediastinum

PATHOLOGY

Microscopic Features

- Gram-positive branching beaded bacilli, weakly acid-fast, ubiquitous, soil-borne
- Slow growth: 3-5 weeks to grow in culture
- Polymerase chain reaction; rapid and reliable diagnosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Fever, chills, fatigue, dyspnea, productive cough, hemoptysis, sweats, weight loss, anorexia
- Other signs/symptoms
 - AIDS, CD4 count < 50 cells/mL, not on *Pneumocystis* prophylaxis

Demographics

- Sex
 - More common in males
- Epidemiology
 - USA: ~ 1,000 cases/year
 - o 50% of infections in immunocompromised patients
 - Transplant recipients: Kidney, lung, heart
 - Malignancy on antineoplastic therapy
 - AIDS, intravenous drug use
 - Prolonged corticosteroid or other
 - immunosuppressive treatment, such as Infliximab
 - Sternal wound infection, indwelling catheter/line infection
 - Underlying lung disease: Silicosis, pulmonary fibrosis, emphysema, alveolar proteinosis

Natural History & Prognosis

- Bacteremia with systemic dissemination in 50% of pulmonary infections
 - Brain abscess, most common site (up to 33%)
 - Retina, joints, soft tissues (psoas), liver, adrenal, skin
- Mortality with CNS involvement (up to 90%)

Treatment

- Trimethoprim-sulfamethoxazole for 3-6 months
- Surgery &/or drainage for extensive lung destruction and empyema

DIAGNOSTIC CHECKLIST

Consider

- Brain imaging in all patients with nocardiosis to exclude metastatic infection
- In severely immunocompromised patients, brain abscess may be asymptomatic for up to 3 years

SELECTED REFERENCES

- 1. Rawat D et al: Nocardiosis. StatPearls. 2020
- Ott SR et al: Pulmonary nocardiosis in Western Europe-clinical evaluation of 43 patients and population-based estimates of hospitalization rates. Int J Infect Dis. 81:140-8, 2019

Actinomycosis

KEY FACTS

TERMINOLOGY

• Granulomatous infection caused by *Actinomyces* species, most commonly *A. israelii*, gram-positive filamentous anaerobic saprophytic organism

IMAGING

- Radiography
 - Unilateral, peripheral, patchy consolidation
 - Cavitary mass/consolidation
 - Pleural effusion, chest wall involvement
- CT
 - o Focal/patchy consolidation, central low attenuation
 - Peripheral rim enhancement
 - Bronchiectatic: Bronchiectasis, bronchial wall thickening, peribronchial consolidation ± abscess formation
 - o Pleural effusion, chest wall involvement
- PET/CT: May exhibit significant FDG avidity, indistinguishable from lung cancer

TOP DIFFERENTIAL DIAGNOSES

- Bronchopneumonia
- Fungal infection
- Aspiration pneumonia
- Tuberculosis (empyema necessitatis)
- Lung cancer

PATHOLOGY

- Microabscess or necrotic material
- Actinomyces colonies or sulfur granules

CLINICAL ISSUES

- Symptoms/signs: Cough, fever, chest pain
- Treatment: Antibiotics, surgical resection

DIAGNOSTIC CHECKLIST

• Consider actinomycosis in chronic consolidations ± chest wall involvement particularly in alcoholic patients and patients with poor oral hygiene

(Left) Axial CECT of a patient with actinomycosis shows a left lower lobe consolidation with multifocal lowattenuation areas and a small loculated left pleural effusion associated with a thick enhancing parietal pleura ₽. Note low-attenuation area with peripheral ring-like enhancement , concerningfor abscess formation. (Right) Axial NECT of a patient with actinomycosis shows a middle lobe consolidation that involves the adjacent pleura \blacksquare and chest wall \blacksquare . A locally invasive neoplasm must also be considered.





(Left) Axial NECT of a patient with actinomycosis shows abnormal soft tissue obstructing the middle lobe bronchus $\overline{\Longrightarrow}$, subsegmental consolidation with intrinsic cavitation \boxtimes , and irregular bronchial dilatation $\overline{ \mathbf{ A}}$. Endobronchial actinomycosis *may mimic lung cancer.* (Right) Axial CECT of a patient with actinomycosis shows bilateral pulmonary masses with central low attenuation from necrosis. Note peripheral rim upper lobe lesion. Malignancy and vasculitis should also be considered.





Definitions

- Granulomatous infection caused by *Actinomyces* species, most commonly *A. israelii;* gram-positive filamentous anaerobic saprophytic organism
 - **Parenchymal actinomycosis**: Aspiration of endogenous oropharyngeal organisms into lungs
 - **Bronchiectatic actinomycosis**: Colonization of devitalized tissue and bronchiectasis
 - Endobronchial actinomycosis associated with broncholithiasis or foreign body: Colonization of preexisting endobronchial broncholith/foreign body

IMAGING

Radiographic Findings

- Parenchymal actinomycosis
 - o Unilateral, peripheral, patchy consolidations
 - Cavitary mass/consolidation
 - o Pleural effusion, chest wall involvement

CT Findings

- Parenchymal actinomycosis
 - CECT: Focal/patchy consolidation with central low attenuation and rim enhancement
 - o Pleural effusion
 - Chest wall involvement: Soft tissue/skeletal abnormalities
- Bronchiectatic actinomycosis
 - Localized bronchiectasis, irregular bronchial wall thickening, irregular peribronchial consolidation ± abscess formation
- Endobronchial actinomycosis associated with broncholithiasis or foreign body
 - Radiopaque endobronchial nodule/calcification with distal obstructive pneumonia
- Hilar or mediastinal lymphadenopathy

Nuclear Medicine Findings

- PET/CT
 - Lung and lymph node involvement may exhibit significant FDG avidity, indistinguishable from lung cancer

Imaging Recommendations

- Best imaging tool
 - CECT: More sensitive for characterization of extent of involvement and necrotizing changes

DIFFERENTIAL DIAGNOSIS

Bronchopneumonia

• Focal or multifocal consolidations

Fungal Infection

- Actinomycotic intracavitary lung colonization by fungus forming fungus ball
 - Imaging: Air crescent sign similar to fungus ball typically caused by *Aspergillus* species

Aspiration Pneumonia

• Gravity-dependent focal or multifocal consolidation

Tuberculosis (Empyema Necessitatis)

• Empyema that communicates with chest wall (necessitatis)

Lung Cancer

• May mimic lung cancer, as it does not respect anatomic borders

PATHOLOGY

General Features

- Etiology
 - Gram-positive anaerobic saprophytic organism in oral cavity (poor oral hygiene)

Gross Pathologic & Surgical Features

Chronic inflammation with varying degrees of fibrosis
 Microabscess or necrotic material

Microscopic Features

- Challenging isolation as may be part of normal flora
- Actinomyces colonies or sulfur granules

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Nonproductive cough, low-grade fever
- Other signs/symptoms
 Pleuritic chest pain (chest wall involvement)

Demographics

- Majority of patients are alcoholic men
- Additional risk factors: Aspiration, cigarette smoking (chronic obstructive pulmonary disease), diabetes mellitus, poor oral hygiene, periodontal disease

Natural History & Prognosis

• Good prognosis with appropriate antibiotic therapy

Treatment

- Antibiotics: High-dose intravenous penicillin or oral amoxicillin-clavulanate
- Surgical excision: Patients unresponsive to antibiotics

DIAGNOSTIC CHECKLIST

Consider

 Actinomycosis in chronic consolidations ± chest wall involvement particularly in alcoholic patients and patients with poor oral hygiene

Image Interpretation Pearls

• Chronic segmental consolidation, frequent cavitation, and chest wall involvement

Reporting Tips

• Malignancy should be excluded

SELECTED REFERENCES

- Tanaka S et al: Pulmonary actinomycosis mimicking pulmonary cancer on fluorine-18 fluorodeoxyglucose PET-CT. Cureus. 12(12):e12306, 2020
- Higashi Y et al: Pulmonary actinomycosis mimicking pulmonary aspergilloma and a brief review of the literature. Intern Med. 56(4):449-53, 2017

Melioidosis

KEY FACTS

TERMINOLOGY

• Infection caused by gram-negative bacillus *Burkholderia* pseudomallei

IMAGING

- Acute melioidosis (85%)
 - Nodules
 - Small nodules with irregular margins rapidly increase in size, coalesce, and may cavitate
 - Consolidation
 - Segmental, lobar, or multilobar ± cavitation
- Pulmonary abscess
- Chronic melioidosis (11%)
 - Mixed parenchymal opacities
 - Nodules, linear densities, and cavitation
- Other manifestations
 - o Lymphadenopathy
 - o Pleural effusions
 - o Pneumothorax

TOP DIFFERENTIAL DIAGNOSES

- Staphylococcus aureus pneumonia (acute melioidosis)
- Septic embolism (acute melioidosis)
- Tuberculosis (chronic melioidosis)

CLINICAL ISSUES

- Zoonosis that occurs in tropical countries
 - High incidence in Thailand, Singapore, and Northern Australia
 - Also described in Central America and Caribbean countries
- Mechanisms of infection: Direct bacterial inoculation via skin abrasions, inhalation of contaminated dust or water droplets, ingestion of contaminated water
- Melioidosis sepsis associated with high mortality

DIAGNOSTIC CHECKLIST

• Consider melioidosis in patients from endemic areas with febrile symptoms and pulmonary nodules

(Left) AP chest radiograph of a patient with acute melioidosis demonstrates a large cavitary mass \supseteq in the left upper lobe. (Right) Axial HRCT of the same patient shows a large left upper lobe cavitary mass-like consolidation 🖾. Most cases of melioidosis are reported in Thailand, Malaysia, Singapore, and Northern Australia. The main mechanisms of infection are direct bacterial inoculation through skin abrasions, inhalation of contaminated dust or water droplets, and ingestion of contaminated water.





(Left) PA chest radiograph of a patient with chronic melioidosis demonstrates a left mid lung zone perihilar cavitary mass 🔁. (Right) Axial NECT of the same patient shows a large left lower lobe cavitary mass $\stackrel{\frown}{\boxtimes}$ with thick and irregular cavity walls. Melioidosis can be categorized as acute or localized infection, acute pulmonary infection, acute bloodstream infection, or disseminated infection. It generally responds to antibiotic treatment, which is administered orally or intravenously depending of the disease severity.





Melioidosis

TERMINOLOGY

Definitions

• Infection caused by gram-negative bacillus *Burkholderia pseudomallei*

IMAGING

General Features

Best diagnostic clue
 Pulmonary nodules

Radiographic Findings

- Acute melioidosis (85%)
 - o Nodules
 - Associated with pneumonia or sepsis from hematogenous spread
 - Small nodules with irregular margins rapidly increase in size, coalesce, and may cavitate
 - o Consolidation
 - Segmental, lobar, or multilobar ± cavitation
 - Upper lobe predominance
 - o Abscess
 - Disease progression
- Chronic melioidosis (11%)
 - o Mixed parenchymal opacities
 - Nodules, linear densities, and cavitation

CT Findings

- Acute melioidosis
 - o Nodules
 - Variable size according to disease progression
 - o Consolidation
 - Segmental, lobar, or multilobar ± cavitation
 - o Abscess
 - < 2.5 cm (thin wall without air-fluid levels)
 - > 4 cm (thick wall and air-fluid levels)
- Chronic melioidosis
 - Mixed parenchymal opacities
 - Nodules, consolidation, and parenchymal bands
 - Cavitation
- Other manifestations
 - o Mediastinal lymphadenopathy (3%)
 - Associated with consolidation
 - Central necrosis similar to tuberculosis (TB)
 - o Pleural effusion (5-15%)
 - Pneumothorax
 - Secondary to nodule cavitation or abscess formation

DIFFERENTIAL DIAGNOSIS

Staphylococcus aureus Pneumonia

- Mimics acute melioidosis
- Similar imaging manifestations
- Pneumatocele formation

Septic Embolism

- Mimics acute melioidosis
- Similar imaging manifestations
- Evidence of distant infection

Tuberculosis

- Mimics chronic melioidosis
- Apical fibrosis
- Granuloma formation during healing

Nontuberculous Mycobacterial Infection (NTMBI)

- Imaging manifestations similar to those of TB
- Bronchiectasis

PATHOLOGY

General Features

- Etiology
 - B. pseudomallei
 - Gram-negative bacillus, non-encapsulated, motile, oxidase positive
 - Mechanisms of infection: Direct bacterial inoculation through skin abrasions, inhalation of contaminated dust or water droplets, ingestion of contaminated water

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute (10-14 days after exposure)
 - Fever with systemic inflammatory response syndrome
 - Sepsis with abscesses in other organs
 - Chronic: Symptomatic infection > 2 months
 - Fever, cough, and weight loss (90%)
- Diagnosis based on culture of *B. pseudomallei*
- Risk factors
 - Diabetes mellitus, chronic kidney failure, alcoholismImmunosuppression (primary or secondary)

Demographics

- Age
- o 40-60 years
- Sex
- o M:F = 1.4:1
- Epidemiology
 - Zoonosis that occurs in tropical countries
 - High incidence in Thailand, Singapore, and Northern Australia
 - Melioidosis also described in Central America and Caribbean countries

Natural History & Prognosis

• Melioidosis sepsis associated with high mortality

Treatment

- Intravenous: Ceftazidime, Meropenem
- Oral: Ceftazidime, Amoxicillin/clavulanic acid, or Trimethoprim-sulfamethoxazole

DIAGNOSTIC CHECKLIST

Consider

• Melioidosis in patients from endemic areas with febrile symptoms and pulmonary nodules

SELECTED REFERENCES

1. Wiersinga WJ et al: Melioidosis. Nat Rev Dis Primers. 4:17107, 2018

Tuberculosis

KEY FACTS

TERMINOLOGY

- Tuberculosis (TB); Mycobacterium tuberculosis (MTB)
 Aerobic, nonmotile, non-spore-forming acid-fast bacillus
- MTB: Airborne infection; person-to-person transmission via organism-containing droplets (1-5 μm)

IMAGING

- Radiography
 - Primary pattern: Consolidation, lymphadenopathy, pleural effusion
 - Postprimary pattern: Upper lobe/lower lobe superior segment consolidation, nodules, masses ± cavitation
- CT
 - Primary pattern: Consolidation, right hilar/paratracheal lymphadenopathy (low attenuation), effusions
 - Postprimary pattern: Upper lobe apical and lower lobe superior segment consolidations, nodules, masses
 - Identification of cavitation + centrilobular nodules virtually diagnostic of TB

TOP DIFFERENTIAL DIAGNOSES

- Nontuberculous mycobacterial infection
- Bronchopneumonia
- Necrotic lymphadenopathy
- Lung cancer
- Miliary metastases, fungal infection

CLINICAL ISSUES

- Worldwide: 1/4 of population infected; 1 of top 10 causes of death; leading cause of death from single infection
- Signs and symptoms: Cough, hemoptysis, weight loss, fatigue, malaise, fever, night sweats
- Diagnosis: Smear/culture; nucleic acid amplification tests
- Preferred treatment: Isoniazid, rifampin, ethambutol, and pyrazinamide

DIAGNOSTIC CHECKLIST

• Consider aggressive work-up of cavitary upper lobe pneumonias for exclusion of TB

(Left) PA chest radiograph of a 74-year-old man from India with diabetes mellitus and recent cough and fatigue shows a large right upper lobe irregular cavity \supseteq and diffuse bilateral nodules and consolidations. Respiratory isolation was initiated. (Right) Coronal CECT of the same patient shows a right upper lobe cavity with nodular walls and bilateral centrilobular micronodules, tree-in-bud opacities 🖂, and cavitary nodules 🔁. Tuberculosis was confirmed and treatment *initiated, but the patient* succumbed to the disease.





(Left) AP chest radiograph of a malnourished 68-year-old man who presented with cough and malaise due to tuberculosis shows a heterogeneous right upper lobe consolidation with suggestion of cavitation \square . (Right) Composite image with coronal NECT of the same patient confirms cavitation *⊠*, multifocal consolidations *⊡*, and centrilobular nodules *In the right upper lobe in the right upper lobe* apical segment and right lower lobe superior segment. Cellular bronchiolitis associated with cavitation is virtually diagnostic of active tuberculosis.





Abbreviations

- Tuberculosis (TB)
- Mycobacterium tuberculosis (MTB)
- Mycobacterium tuberculosis complex: M. tuberculosis, M. bovis, M. africanum, M. microti, M. canettii

Definitions

- MTB: Airborne infection; person-to-person transmission via organism-containing droplets (1-5 $\mu m)$
- Aerobic, nonmotile, non-spore-forming acid-fast bacillus
 Primary TB: Droplets infect alveolar macrophages → active TB within first 1-2 years (5%); contagious
- Post-primary (reactivation) TB: Infection initially controlled by immune system (5%); viable dormant organisms reactivate at later date
- Re-infection TB: Different DNA finger-printing between initial and subsequent infections
- Latent TB: Noncontagious infected individuals that do not develop symptomatic disease (~ 90%)
- Multidrug-resistant TB (MDR TB): Resistance to at least isoniazid and rifampin
- Extensively drug-resistant TB (XDR TB): Resistance to isoniazid, rifampin, any fluoroquinolone, and at least 1 of 3 injectable second-line drugs (kanamycin, capreomycin, amikacin)

IMAGING

Radiographic Findings

- Postprimary pattern of TB
 - Apical upper lobe consolidation ± cavitation
 - Slow resolution, fibronodular opacities, volume loss
 - Unilateral loculated pleural effusion
 - Tuberculous empyema; may develop bronchopleural fistula
 - May evolve to pleural Ca++ and fibrothorax
- Tuberculoma: Soft tissue or calcified nodule
- Primary pattern of TB (immunocompromised)
 Consolidation; cavitation (20-45%)
 - o Unilateral lymphadenopathy: Right hilar/paratracheal
 - Free pleural effusion
 - o Normal radiographs in immunocompromised subjects
- Miliary TB: Millet seed-sized (< 3-mm) micronodules

CT Findings

- Postprimary pattern
 - Preferential involvement of upper lobe apical segments and lower lobe superior segments
 - Centrilobular nodules and branching (tree-in-bud) opacities (95% of active TB); may involve any lobe
 - Consolidation: Ill-defined, may be multifocal, ± cavitation
 - Tuberculoma: Soft tissue nodule (5-40 mm); frequent satellite nodules and micronodules
- Primary pattern
 - o Lymphadenopathy: Right hilar/paratracheal
 - Low-attenuation center (necrosis), rim enhancement
 - Consolidation: Rare cavitation; progressive 1ary TB
 - Pleural effusion: Unilateral, free

- Chronic findings
 - Thin-walled cavities, bronchiectasis
 - Architectural distortion, fibronodular opacities
- Immunocompromised patient
 - Primary pattern; consolidation, lymphadenopathy, extrathoracic involvement
 - HIV + highly active antiretroviral therapy (HAART): Immune reconstitution inflammatory syndrome (IRIS): Paradoxical progression of consolidation, nodules, lymphadenopathy; 10-25% in acquired immune deficiency syndrome (AIDS), within 60 days of HAART
- Miliary TB: 1- to 3-mm micronodules; random distribution
- May occur with primary or postprimary TB; may progress to acute respiratory distress syndrome (ARDS)
- Airway involvement
 - Bronchial stenosis
 - Bronchial wall thickening
 - Bronchiectasis
- Pleural involvement
 - Pleural effusion; free or loculated
 - Frequent associated ipsilateral parenchymal TB
 May be complicated by bronchopleural fistula or empyema necessitatis
 - Pleural thickening, enhancement, calcification

Nuclear Medicine Findings

- PET/CT
- TB-involved tissues are typically FDG-avid

Imaging Recommendations

- Best imaging tool
 - Chest radiography is initial imaging study of choice
 - CT: May be useful for detecting subtle cavitation and cellular bronchiolitis

DIFFERENTIAL DIAGNOSIS

Nontuberculous Mycobacterial Infection

- Classic or cavitary pattern: Indistinguishable from cavitary TB on imaging
 - Presumed TB until proven otherwise

Bronchopneumonia

- Centrilobular micronodules &/or tree-in-bud opacities
- Upper lobe apical segment &/or lower lobe superior segment involvement + cavitation favor TB

Necrotic Lymphadenopathy

- Central necrosis and peripheral rim enhancement
- Other infections (fungal), metastases

Miliary Micronodules

- Other miliary infection (fungal)
- Miliary metastases

Lung Cancer

- May cavitate (e.g., squamous cell carcinoma)
- Tree-in-bud opacities not typically present

Sarcoidosis

- More extensive and symmetric mediastinal and bilateral hilar lymphadenopathy
- Cavitation rare
PATHOLOGY

General Features

- Centrilobular micronodules and tree-in-bud opacities: Caseous necrosis and granulomatous inflammation of terminal/respiratory bronchioles, alveolar ducts
- Consolidation: Granulomatous nodules (microabscesses, surrounding epithelioid histiocytes, fibrinous exudates) in alveolar spaces
- Cavitation: Caseous necrosis, epithelioid/multinucleated giant cells, granulation tissue, fibrous capsule
- Miliary nodules: Yellowish-white, intrinsic caseous necrosis; alveolar walls, interlobular septa, subpleural
- Tuberculoma: Well-defined nodule; caseous necrosis center; peripheral rim of epithelioid histiocytes, multinucleated giant cells, collagen
- Granuloma: Epithelioid histocytes and Langhans giant cells surrounded by lymphocytes
- Ghon focus: Primary site of pulmonary TB
- Ranke complex: Ghon focus + affected lymph nodes

Gross Pathologic & Surgical Features

- Cavitation: Lung disease with airway communication; subsequent expectoration of necrotic material
- Lymphadenitis: Granulomatous inflammation, lymphadenopathy

Microbiology

- MTB: Obligatory pathogen, family Mycobacteriaceae, causative agent of TB
- Highly aerobic, requires high levels of oxygen
- Ziehl-Neelsen or acid-fast stain

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough, hemoptysis, weight loss, fatigue, malaise, fever, night sweats
 - Extrapulmonary TB: Larynx, lymph nodes, pleura, GI/GU tract, CNS, bone
 - Typically not contagious except for laryngeal
- Clinical profile
 - Primary vs. postprimary patterns of TB
 - Healthy individuals develop **postprimary pattern** of TB (i.e., cavitary disease), even if never infected before
 - Immunocompromised patients develop primary pattern of TB (i.e., consolidation &/or lymphadenopathy), even if infected before
- Diagnosis
 - Smear and culture; determination of drug sensitivity
 - Sputum, induced sputum, gastric washings, bronchial washings
 - Acid-fast bacilli in sputum or tissue
 - Nucleic acid amplification tests
 - Xpert MTB/RIF: Detects MTB and rifampicin resistance; < 2 hours
 - Xpert XDR: Detection of resistance to isoniazid, injectable agents, and fluoroquinolones
 - Latent TB: Tuberculin skin test or interferon-γ release assay; single drug therapy with isoniazid or rifampicin

Demographics

• Epidemiology

- Worldwide (2019 data)
 - 1/4 of population infected: 1 of top 10 causes of death; leading cause of death from single infection
 - 10 million new cases; ~ 200,000 with HIV
 - 1.4 million deaths; ~ 200,000 with HIV
 - 2/3 of total cases: India (26%), Indonesia, China, Philippines, Pakistan, Nigeria, Bangladesh, South Africa
 - ~ 200,00 cases with MDTR TB
- o USA (2019 data)
 - 8,916 new cases
 - Highest case rates by state/city: Alaska, California, Hawaii, New York City
 - Very high case rates in some USA territories

Natural History & Prognosis

- Respiratory isolation for suspected TB
- Mortality of smear-positive untreated TB ~ 70%
- Mortality of culture-positive, smear-negative, untreated TB ~ 20%
- Untreated TB in HIV-positive individuals is rapidly fatal (mean survival: < 6 months)

Treatment

- Multiple drugs based on sensitivity; preferred treatment: Isoniazid, rifampicin, ethambutol, and pyrazinamide
- Drug resistant TB: MDR TB and XDR TB
 - Introduction of bedaquiline, delamanid, and use of repurposed agents (linezolid, clofazimine)

Prognosis

- Treatment success rate: ~ 80%
- Predictors of mortality: HIV infection, smear-positive TB, MDR TB, XDR TB, previous history of TB

Risk Factors

- Increased exposure: Immigrants from endemic regions, IV drug users, congregate settings, health care workers
- Increased risk of progression to active disease: Age < 4 years, IV drug use, immunodeficiency (HIV infection), biological agent (tumor necrosis factor α inhibitor) treatment, diabetes, silicosis, chronic renal failure, low body weight, gastrectomy/bypass surgery, alcohol/tobacco abuse, malignancy

DIAGNOSTIC CHECKLIST

Consider

- Aggressive work-up of cavitary upper lobe pneumonias for exclusion of TB
 - If questionable upper lobe cavitary disease on radiography, CT useful for confirmation
 - Isolation of patients with upper lobe cavitary disease until TB is excluded

- 1. Global Tuberculosis Report 2020. World Health Organization. 2020
- 2. Carlesi E et al: How radiology can help pulmonary tuberculosis diagnosis: analysis of 49 patients. Radiol Med. 124(9):838-45, 2019
- 3. Furin J et al: Tuberculosis. Lancet. 393(10181):1642-56, 2019

Tuberculosis





(Left) Composite image with axial HRCT (left) and axial FDG PET/CT (right) shows an FDGavid left upper lobe tuberculoma **→** surrounded by satellite micronodules *⊡*. Such lesions may mimic lung cancer on imaging, but satellite nodules are common in tuberculomas and fungal infections. (Right) Coronal NECT of a 101-year-old malnourished man previously treated for tuberculosis shows right upper lobe fibronodular $opacities \implies$ from old infection and profuse bilateral nodules, concerning for miliary tuberculosis.





(Left) Composite image with axial CECT of a 22-year-old woman with tuberculosis shows mediastinal lymphadenopathy with peripheral enhancement 🔁 and central low attenuation due to caseous necrosis. (Right) Axial CECT of a 35year-old man with severe rheumatoid arthritis treated with tumor necrosis factor inhibitors shows tuberculosis manifesting with consolidation \supseteq , centrilobular nodules 🖂, pleural effusions, and lymphadenopathy \blacksquare , typical findings seen in immunocompromised subjects.





(Left) PA chest radiograph of an asymptomatic 77-year-old woman with a history of previously treated active tuberculosis shows severe left lung volume loss, bronchiectasis, and architectural distortion. (Right) Coronal NECT of the same patient shows severe left upper lobe bronchiectasis and volume loss. The imaging abnormalities were stable, and sputum analysis was negative. Old tuberculosis may exhibit extensive radiologic abnormalities that may include fibronodular opacities and bronchiectasis.

KEY FACTS

TERMINOLOGY

- Nontuberculous mycobacteria (NTMB)
- Nontuberculous mycobacterial infection (NTMBI)
- Pulmonary infection with NTMB: Indolent and slowly progressive disease

IMAGING

- Bronchiectatic form: Middle lobe/lingular bronchiectasis and cellular bronchiolitis
- Fibrocavitary form: Upper lobe cavitary disease and pleural thickening
- Hot tub lung: Diffuse centrilobular ground-glass micronodules
- Immunocompromised patient
 - Consolidation, nodule, mass
 - Mediastinal/hilar lymphadenopathy
- Solitary nodule or mass
 Mimics lung cancer; may exhibit spiculation
- Foci of NTMBI typically FDG-avid on PET/CT

TOP DIFFERENTIAL DIAGNOSES

- Tuberculosis
- Diffuse aspiration bronchiolitis
- Hypersensitivity pneumonitis
- Lung cancer

PATHOLOGY

• Granulomatous inflammation, necrosis, fibrosis

CLINICAL ISSUES

• Symptoms: Cough, productive sputum, fatigue

DIAGNOSTIC CHECKLIST

- Consider NTMBI in older women with middle lobe/lingular bronchiectasis and cellular bronchiolitis on imaging
- Fibrocavitary NTMB may mimic tuberculosis
- Consider disseminated NTMB in patients with very low CD4 counts and lymphadenopathy
- Diagnosis: Fulfillment of clinical and microbiologic criteria

(Left) PA chest radiograph of a 72-year-old woman with bronchiectatic nontuberculous mycobacterial infection shows middle lobe and lingular heterogenous opacities 🔁 that obscure the heart borders. (Right) Axial NECT of the same patient shows bronchiectasis and volume loss *⊡* in the middle lobe and lingula and less severe bilateral lower lobe multifocal cellular bronchiolitis and bronchiectasis 🔁. These are classic imaging findings of the bronchiectatic pattern of nontuberculous mycobacterial infection.

(Left) Low-power

photomicrograph (H&E stain) of a specimen from a patient with bronchiectatic nontuberculous mycobacterial infection shows ectatic bronchi 🔁 with intraluminal exudates and mural granulomas 🖂. (Right) Fused axial FDG PET/CT of a patient with mass-like nontuberculous mycobacterial infection shows an FDG-avid left lower lobe mass 🔁. The disease may manifest as a solitary pulmonary nodule or mass, which may mimic lung cancer on radiography, CT, and PET/CT.









Abbreviations

- Nontuberculous mycobacteria (NTMB)
- Nontuberculous mycobacterial infection (NTMBI)
- Mycobacterium avium complex (MAC)

Synonyms

- Mycobacteria other than tuberculosis (MOTT)
- Lady Windermere syndrome
 Initial description of nodular bronchiectatic NTMBI

Definitions

- Pulmonary infection with NTM
 - Synonyms: Environmental mycobacteria, atypical mycobacteria, MOTT
 - No person-to-person transmission (isolation of affected patients not required)
 - Acquired from environmental sources (pipeline water supply and contaminated soil)
 - o Indolent and slowly-progressive disease

IMAGING

General Features

- Best diagnostic clue
 - Bronchiectatic form: Middle lobe/lingular bronchiectasis and cellular bronchiolitis
 - Fibrocavitary form: Upper lobe cavitary disease and pleural thickening
 - Hot tub lung: Diffuse centrilobular ground-glass micronodules

Radiographic Findings

- Fibrocavitary form
 - o Upper lobe thin-walled cavitary lesion(s)
 - Apical pleural thickening
- Bronchiectatic form
 - Middle lobe and lingular reticular or heterogenous opacities
 - o Middle lobe and lingular volume loss and bronchiectasis
- Solitary nodule/mass (may mimic lung cancer)
- Immunocompromised host
 - Consolidation, nodule, mass
 - Mediastinal/hilar lymphadenopathy

CT Findings

- Fibrocavitary form
 - Upper lobe cavitation with volume loss and apical pleural thickening
 - Typically thin cavity walls; mild wall thickening and nodular cavity walls also described
 - Ancillary findings
 - Emphysema (common)
 - Interstitial lung disease
- Bronchiectatic form
 - Classic middle lobe and lingula involvement; may affect any lobe
 - Bronchiectasis, bronchial wall thickening, mucus plugging
 - o Centrilobular micronodules (often tree-in-bud nodules)
- Mixed fibrocavitary and bronchiectatic forms common

- Hot tub lung
 - Nonfibrotic hypersensitivity pneumonitis (HP)
 - Centrilobular ground-glass micronodules
 - Mosaic attenuation and air-trapping
- Solitary nodule or mass
 - Mimics lung cancer, may exhibit spiculated borders
- Immunocompromised patient
 - o Consolidation, nodule, mass
 - Lymphadenopathy; intrinsic low-attenuation

Nuclear Medicine Findings

- PET/CT
 - Foci of NTMBI typically FDG-avid
 - Solitary nodule/mass may simulate lung cancer morphologically and based on FDG avidity

DIFFERENTIAL DIAGNOSIS

Tuberculosis

- NTMBI indistinguishable from postprimary pattern of tuberculosis (TB): Upper lobe cavities and tree-in-bud opacities
- Serial imaging: NTMB progresses over months to years, TB progresses over weeks to months

Diffuse Aspiration Bronchiolitis

- May be indistinguishable from bronchiectatic NTMBI
- Risk factors for aspiration: Achalasia, esophageal obstruction, esophageal motility disorders, gastric banding procedures, gastroesophageal reflux, neurologic conditions (e.g., dementia), etc.

Hypersensitivity Pneumonitis

• Hot tub lung: Specific type of HP indistinguishable from nonfibrotic HP

Lung Cancer

 May be morphologically indistinguishable from NTMBI manifesting as solitary nodule or mass on CT &/or PET/CT

PATHOLOGY

Microscopic Features

- General features
 - Similar to TB: Variable degrees of granulomatous inflammation, necrosis, fibrosis
 - Fibrocavitary: Large upper lobe necrotic cavities and apical pleural thickening
 - Bronchiectatic: Centrilobular nodules, branching nodular lesions, bronchiolectasis, bronchiolar wall thickening; mucus plugging of medium-sized airways

CT/histopathologic correlation

- Cavity wall: Caseous necrosis; epithelioid cells, multinucleated giant cells, granulation tissue, fibrous capsule
- Bronchiectatic: Small centrilobular nodules ± tree-in-bud opacities (granulomas and caseous necrosis in terminal or respiratory bronchioles)
- Nodules > 10 mm in diameter and lobular consolidations: Centrally located caseating granulomas, marginal nonspecific inflammation, and coalescent lymphocytic infiltrates replacing normal alveoli

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough, productive sputum, fatigue
 - Preexisting lung disease (e.g., chronic obstructive pulmonary disease, cystic fibrosis, bronchiectasis, pneumoconiosis, pulmonary fibrosis, prior TB)
 - Hot tub lung: Dyspnea, cough, fever
 - Immunocompromised patients
 - Human immunodeficiency virus (HIV) infection: Fever, weight loss, abdominal pain, diarrhea, lymphadenopathy, hepatosplenomegaly
 - Non-HIV infected: Fever, weight loss, malaise
- Clinical profile
 - o Bronchiectatic: White women in 7th and 8th decades
 - Lady Windermere syndrome
 - Based on fastidious character Lady Windermere in play titled Lady Windermere's Fan by Oscar Wilde
 - Affected patients may voluntarily suppress cough leading to poor drainage of secretions and NTMB engraftment
 - Fibrocavitary form: Preexistent lung disease (e.g., emphysema and pulmonary fibrosis)
 - Hot tub lung: MAC may grow in hot water systems (e.g., indoor pools, indoor hot tubs)
 - Thought to be hypersensitivity to MAC; but MAC may be identified in bronchoalveolar lavage fluid cultures
 - Immunocompromised host
 - HIV infected
 - □ CD4 < 200 cells/mm³
 - Disseminated NTMBI with very low CD4 (< 50 cells/µL 200 cells/mm³)
 - Non-HIV infected
 - Chemotherapy, solid-organ transplantation, chronic corticosteroids, leukemia/lymphoma

Demographics

- Epidemiology
 - o Slowly increasing prevalence worldwide
 - > than that of TB in USA and Canada
 - In USA, from 1994-1996 to 2004-2006, increased prevalence
 - □ Women, 4.5-7.5/100,000 persons; men, 3.5-4.9/100,000 persons
 - In Canada, from 1995 through 2003; overall prevalence, 3.2-4.6/100,000 persons

Diagnosis

- Clinical and microbiologic criteria for diagnosis of NTMBI
 Imaging features included in clinical criteria
- American Thoracic Society and Infectious Diseases Society of America diagnostic criteria
 - Clinical criteria (both required)
 - Pulmonary symptoms, nodular or cavitary opacities on radiography, or multifocal bronchiectasis and small nodules on CT/HRCT
 - Exclusion of other diagnoses
 - Microbiologic criteria
 - + sputum cultures from 2 separate samples or
 - + culture from at least 1 bronchial wash or lavage or

- Transbronchial or lung biopsy with granulomatous inflammation or acid-fast bacilli (AFB) and positive culture for NTM or biopsy with granulomatous inflammation or AFB and 1 or more positive culture for NTM on sputum or bronchial washings
- Transbronchial lung biopsy for diagnosis of hot tub lung
- Percutaneous or surgical lung biopsy for diagnosis of NTMB in acquired immune deficiency syndrome (AIDS)
- Ancillary tests
 - Immunohistochemistry
 - Polyclonal antibody against Mycobacterium tuberculosis and other mycobacterial species (Mycobacterium avium-intracellulare, Mycobacterium phlei, and Mycobacterium parafortuitum)
 - Detection of immunoreactive bacilli, particularly in patients with negative acid-fast staining specimen
 - o Polymerase chain reaction (PCR)
 - Amplification refractory mutational system PCR and real-time PCR methods for rapid detection of singlenucleotide polymorphisms
 - Discrimination between *M. intracellulare* and *M. avium,* differentiation of NTMB organisms resistant to clarithromycin

Natural History and Prognosis

- Radiologic progression ± treatment in ~ 50% of patients with MAC pulmonary infection
- Patients with cavitation or consolidation at initial CT more likely to progress and require treatment
- Antibiotic treatment considered when progressive involvement identified on follow-up CT imaging
- Prognosis
 - Variable response to antibiotic treatment
 - MAC infection: More severe disease with *M. intracellulare* infection; lower body mass index, more frequent respiratory symptoms and fibrocavitary disease, higher rate of smear-positive sputum, more extensive disease on CT, and worse prognosis than in *M. avium* infection

Treatment

- MAC
 - Fibrocavitary: Clarithromycin or azithromycin, ethambutol, rifampin, &/or streptomycin or amikacin
 - Bronchiectatic: Combination of clarithromycin or azithromycin, ethambutol, and rifampin
- Mycobacterium abscessus. Difficult to treat

DIAGNOSTIC CHECKLIST

Consider

 NTMBI in older women with middle lobe and lingular bronchiectasis and cellular bronchiolitis on imaging

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- Chin KL et al: Pulmonary non-tuberculous mycobacterial infections: current state and future management. Eur J Clin Microbiol Infect Dis. 39(5):799-826, 2020
- Daley CL et al: Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. Clin Infect Dis. 71(4):e1-36, 2020





(Left) PA chest radiograph of a 53-year-old man with emphysema and cavitary nontuberculous mycobacterial infection shows multifocal right lung heterogenous opacities and a right apical cavitary lesion right (Right) Axial CECT of the same patient shows upper lobe centrilobular emphysema and a thick-walled right upper lobe cavity \supseteq . The cavitary form of the disease typically affects patients with preexistent lung conditions (emphysema, interstitial lung disease), and is indistinguishable from tuberculosis on imaging.





(Left) Axial HRCT of a patient with hot tub lung shows diffuse bilateral ground-glass opacities, micronodules, and mosaic attenuation. This is a common imaging pattern of nonfibrotic hypersensitivity pneumonitis. (Right) Coronal NECT of a 37-year-old man with human immunodeficiency virus and nontuberculous mycobacterial infection shows clustered right upper lobe micronodules 🔁 and extensive left lung cavitation *⊡* The development of cavitation indicates a certain degree of preservation of host immunity.





(Left) Axial CECT of a 32-yearold man with human immunodeficiency virus and nontuberculous mycobacterial infection shows middle lobe , consolidation and right lower lobe micronodules \square , consistent with infectious bronchiolitis. (Right) Axial CECT of a patient with a history of orthotopic heart transplantation and nontuberculous mycobacterial infection shows bilateral consolidations 🔁 and surrounding micronodules 🔁. Immunosuppressed patients often develop diffuse and severe pulmonary infections.

Mycoplasma Pneumonia

KEY FACTS

TERMINOLOGY

• Pulmonary infection caused by Mycoplasma pneumoniae

IMAGING

- Radiography
 - Air-space opacification (86%)
 - Lower lung zones predominance (67%)
 - o Nodules (50%)
 - 3-10 mm (71%)
 - o Bronchovascular thickening (18%)
 - Lymphadenopathy (10%)
 - Pleural effusion (7%)
- CT
 - o Ground-glass (86%)
 - o Nodules (89%)
 - Bronchovascular bundle thickening (82%)
 - o Consolidation (79%)
 - o Interlobular septal thickening (21%)

TOP DIFFERENTIAL DIAGNOSES

- Viral pneumonia
- Other bacterial pneumonia

PATHOLOGY

- *Mycoplasma pneumoniae* is bacterium of family Mycoplasmataceae of class Mollicutes
- Intracellular pathogen characterized by lacking cell wall

CLINICAL ISSUES

- Signs and symptoms
 - Cough (initially nonproductive)
 - o Sore throat
 - Bullous myringitis
 - Encephalitis, optic neuritis, cerebellar syndrome, and aseptic meningitis
 - Erythematous maculopapular, vesicular rashes, and Stevens-Johnson syndrome
- Spreads person to person through respiratory droplets

(Left) PA chest radiograph of a 31-year-old patient with Mycoplasma pneumoniae pneumonia shows bronchial wall thickening and left basilar predominant ill-defined nodular opacities \supseteq . (Right) Axial HRCT of the same patient shows a right lower lobe subpleural lobular consolidation *⊡*, centrilobular micronodules 🖂, and thickening of the bronchovascular bundles 🔁 The prototypical lobar pneumonia seen Streptococcus pneumoniae infection is not common in M. pneumoniae pneumonia.





(Left) PA chest radiograph of a 28-year-old patient with M. pneumoniae pneumonia shows ill-defined left upper lobe heterogeneous air-space opacities 🔁. (Right) Coronal NECT of the same patient shows bilateral upper lobe predominant patchy groundglass opacities 🔁. Given frequent imaging findings of pulmonary micronodules and ground-glass opacities, it is common for M. pneumoniae pneumonia to lack conspicuous abnormalities on chest radiography, often interpreted as normal.





Definitions

• Pulmonary infection caused by Mycoplasma pneumoniae

IMAGING

General Features

- Best diagnostic clue
 - Basilar predominant ground-glass opacities &/or consolidation, centrilobular nodules, thickened bronchovascular bundles

Radiographic Findings

- Air-space opacification (86%)
 Lower lung zone predominance (67%)
- Nodules (50%)
 - o 3-10 mm (71%)
 - Lower lung zone predominance (57%)
- Bronchovascular thickening (18%)
- Linear opacities (10%)
- Lymphadenopathy (10%)
- Pleural effusion (7%)

CT Findings

- Ground-glass opacities (86%)
- Consolidation (79%)
 - Lobular distribution (59%)
 - Subpleural &/or peribronchovascular
 - Unilateral or bilateral
- Nodules (89%)
 - o Centrilobular > peribronchovascular distributiono Lower lung zone predominance
- Thickening of bronchovascular bundles (82%)
- Interlobular septal thickening (21%)

Imaging Recommendations

- Best imaging tool
 - Chest radiography: Imaging study of choice in patients with suspected pneumonia
 - CT: Patients with high clinical suspicion for pneumonia and normal or equivocal radiographic findings

DIFFERENTIAL DIAGNOSIS

Viral Pneumonia

- Imaging manifestations may be similar to those seen in mycoplasma pneumonia
- Proportion of centrilobular nodules and bronchovascular bundle thickening varies according to type of virus

Other Bacterial Pneumonia

- Similar imaging manifestations in pneumonias caused by a variety of bacteria
- Greater frequency of centrilobular nodules and thickened bronchovascular bundles in patients with *M. pneumoniae* pneumonia

Organizing Pneumonia Pattern

- Basilar predominant peribronchovascular or peripheral ground-glass opacities &/or consolidations
- Subacute or chronic clinical course

PATHOLOGY

General Features

- Etiology
 - *Mycoplasma pneumoniae:* Bacterium of family Mycoplasmataceae, class Mollicutes
 - Intracellular pathogen characterized by lack of cell wall
 - Smaller free-living bacteria with capacity for autonomous division
 - Mucosal pathogen with parasitic existence on host epithelial surfaces

Microscopic Features

- Acute cellular bronchiolitis with ulceration and destruction of bronchial and bronchiolar ciliated epithelium
- Peribronchial and perivascular interstitial infiltration by lymphocytes, plasma cells, and macrophages

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough (initially nonproductive)
 - Sore throat
 - o Fever
 - o Headache
- Other signs/symptoms
 - Extrapulmonary manifestations
 - Central nervous system (CNS) complications
 - □ Encephalitis, optic neuritis, cerebellar syndrome, aseptic meningitis
 - Skin complications
 - Erythematous maculopapular vesicular rashes and Stevens-Johnson syndrome
 - Bullous myringitis
 - Exacerbation of asthma or chronic bronchitis

Demographics

- Age
 - Children and young adults
 - Sex
 - Females > males
 - Epidemiology
 - 3-10% of patients with *M. pneumoniae* infection develop pneumonia
 - o 15-40% of all pneumonias in general population
 - 10% of pneumonias requiring hospitalization

Natural History & Prognosis

- Spreads person to person through respiratory droplets
- Long incubation period (2-3 weeks)
- *M. pneumoniae* pneumonia usually has good prognosis
- Severe course in 6% of pneumonia due to *M. pneumoniae* pneumonias
- Risk factors for severe pneumonia: Asplenia, sickle cell disease, and hypogammaglobulinemia

- Franquet T: Imaging of community-acquired pneumonia. J Thorac Imaging. 33(5):282-94, 2018
- Parrott GL et al: A compendium for Mycoplasma pneumoniae. Front Microbiol. 7:513, 2016

Viral Pneumonia

KEY FACTS

TERMINOLOGY

• Viruses typically affect respiratory epithelium

IMAGING

• Radiography

- May be normal at presentation (20%)
 Focal or multifocal consolidation
- CT/HRCT
 - Mosaic attenuation and expiratory air-trapping
 - Ground-glass opacity and consolidation
 - Nodules, micronodules, and tree-in-bud opacities
- Interlobular septal thickening
- Bronchial &/or bronchiolar wall thickening

TOP DIFFERENTIAL DIAGNOSES

- Bacterial pneumonia
- Aspiration
- Diffuse alveolar hemorrhage
- Organizing pneumonia

CLINICAL ISSUES

- Cold: Upper respiratory tract symptoms (tonsillopharyngitis, pharyngitis, epiglottitis, sinusitis, otitis media, and conjunctivitis)
- Influenza syndrome: Abrupt fever, headache, myalgias, and malaise
- Acute bronchiolitis in infants and children: Wheezing with concomitant signs of respiratory viral infection
- High rate of viral infection in patients with communityacquired pneumonia (2-35%)

DIAGNOSTIC CHECKLIST

- Diagnosis relies on clinical suspicion: Host risk factors, presentation, and exposure history
- Lobar consolidation uncommon in viral pneumonia
- Nodules < 10 mm, may exhibit CT halo sign, and do not exhibit cavitation
- Branching or centrilobular nodules and mosaic perfusion common in viral bronchiolitis

(Left) Coronal HRCT of a patient with acute infectious bronchiolitis due to respiratory syncytial virus shows diffuse bilateral tree-in-bud nodules and upper lobe ground-glass opacities. Respiratory syncytial virus is a common cause of infectious bronchiolitis and has been linked to asthma in children. (Right) Coronal HRCT of a 52-year-old woman with rhinovirus pneumonia shows multifocal bilateral perilobular ground-glass opacities. Rhinoviruses are the predominant cause of the common cold but occasionally produce lung involvement.





(Left) Axial NECT of a 75-yearold man with herpes simplex virus pneumonia shows multifocal ground-glass opacities and consolidations. Herpes pneumonia is rare but may occur in the setting of burns, transplantation, pregnancy, malignancy, and human immunodeficiency virus infection. (Right) Axial CECT of a 71-year-old woman with human metapneumovirus pneumonia shows bilateral consolidations \supseteq and a small right pleural effusion 🔁 Human metapneumovirus is a common cause of viral pneumonia.





Definitions

• Pulmonary viral infection; affects respiratory epithelium from trachea to terminal bronchioles: Alveolar involvement less common; often severe and rapidly progressive

RNA Virus-Related Diseases

- Influenza
 - Seasonal community infections, endemic infections, and unpredictable pandemics
 - Influenza type A: Most important respiratory virus of general population regarding morbidity and mortality
 - Major cause of respiratory illness in immunocompromised hosts
- Avian influenza (H5N1)
 - Contact with infected birds; usually poultry
 - Overall case fatality rate exceeds 60%
- Swine influenza (H1N1)
 - 1st pandemic of 21st century, originally reported in Mexico (spring of 2009)
 - High transmission among humans, but virulence not greater than that observed with seasonal influenza
- Parainfluenza virus
 - Common cause of seasonal upper respiratory tract infection in adults and children
 - Parainfluenza virus type 3: Respiratory illness in immunocompromised hosts and solid organ transplant recipients
- Respiratory syncytial virus (RSV)
 - Ubiquitous cause of respiratory infection
 - Most frequent viral cause of lower respiratory tract infection in infants
- Human metapneumovirus (hMPV)
 - Implicated in 4-21% of infants with acute bronchiolitis – Symptoms indistinguishable from those of RSV
 - 4% of cases in patients with community-acquired pneumonia (CAP) or chronic obstructive pulmonary disease (COPD) exacerbations
- Measles
 - One of 3 major infectious diseases worldwide
 - 1.5 million childhood deaths per year
- Coxsackievirus, echovirus, enterovirus
 - Lower respiratory tract infection may occur sporadically, not always associated with pneumonia
- Human T-lymphotropic virus type 1 (HTLV-1)
 - Etiologic retrovirus of adult T-cell leukemia or lymphoma
 - Associations
 - Myelopathy
 - Sjögren syndrome
 - Lymphoid interstitial pneumonia
- Hantavirus
 - Rodent-borne zoonotic disease
 - Hantavirus pulmonary syndrome: Severe acute respiratory distress syndrome (ARDS), rapid clinical progression, and high mortality
- Severe acute respiratory syndrome (SARS)
 - Atypical pneumonia caused by newly discovered SARSassociated coronavirus (SARS-CoV) in 2012 (Guangdong, China)
 - o COVID-19 pandemic (2019)

- Middle East respiratory syndrome (MERS)
 - Acute viral respiratory disease caused by novel virus currently named MERS coronavirus (MERS-CoV)

DNA Viruses

- Adenovirus
 - 5-10% of acute respiratory infections in infants and children, < 1% of respiratory illnesses in adults
 - Swyer-James-MacLeod syndrome: Acquired constrictive bronchiolitis due to childhood Adenovirus infection
- Varicella virus
 - Common contagious infection in childhood; increasing frequency in adults
 - Varicella pneumonia: 1 of every 400 cases of adult chickenpox infection
- Cytomegalovirus (CMV)
 - CMV infection: > 70% of hematopoietic stem cell transplant (HSCT) recipients; ~ 1/3 develop CMV pneumonia
 - Infection during postengraftment period (30-100 days after transplantation)
- Epstein-Barr virus (EBV)
 - Primary infection manifests as infectious mononucleosis
 - EBV pneumonia: Rare in immunocompetent or immunocompromised subjects
 - Associated with development of Burkitt lymphoma, Hodgkin lymphoma, nasopharyngeal carcinoma

IMAGING

Radiographic Findings

- Variable and overlapping appearance
 - Normal at presentation (20%)
- Tracheobronchitis
 - Bronchial wall thickening
 - Atelectasis: Discoid to segmental (mucus plugs)
- Pneumonia
 - Consolidation: Peripheral, mid, and lower lung zones (40%)
 - Unilateral or patchy bilateral consolidations
 - Diffuse consolidation
- Complications
 - Bacterial superinfection: Sudden worsening, cavitation, enlarging pleural effusion
- Uncommon findings
 - Hilar or mediastinal lymphadenopathy: Measles and infectious mononucleosis
 - Splenomegaly: Infectious mononucleosis
- Cardiac enlargement (pericardial effusion): Hantavirus
- Pleural effusion
 - o Rare except for Adenovirus, measles, hantavirus, HSV-1

CT Findings

- Alterations of parenchymal attenuation
 - Patchy heterogeneous lung attenuation (mosaic attenuation)
 - Bronchiolar obstruction (inflammation or cicatricial scarring) and secondary vasoconstriction
 - Inspiratory/expiratory CT: Differentiation of bronchiolar from pulmonary vascular disease

- Infection
- Bronchiolar disease (air-trapping): Decreased attenuation on inspiration, accentuated on expiration
- Vascular disease: Little increase in attenuation or decrease in volume
- Ground-glass opacity and consolidation
 - Coexistence of interstitial thickening and partial airspace filling
 - Consolidation: Patchy and poorly-defined (bronchopneumonia) vs. focal and well-defined (lobar pneumonia)
 - Opacities may be due to concomitant acute lung injury (ALI) in severe cases; perilobular distribution
- Nodules, micronodules, and tree-in-bud opacities
 - Nodules 1-10 mm in diameter common in viral infections
 - Centrilobular nodules
 Inflammation, infiltration, or fibrosis of adjacent interstitium and alveoli
 - Tree-in-bud opacities: Indicative of small airways disease
 - Dilatation of centrilobular bronchioles with mucus, fluid, or pus impacted lumina
 - Branching or centrilobular nodules and mosaic perfusion: Common in viral bronchiolitis
 - Miliary nodules
 - Nearly any organism; typically tuberculosis, fungi, varicella-zoster virus
- Interlobular septal thickening: Widespread with ARDS
- Bronchial &/or bronchiolar wall thickening
 - Inflammatory exudates and bronchiolar wall thickening from edema and smooth muscle hyperplasia

DIFFERENTIAL DIAGNOSIS

Bacterial Pneumonia

- Consolidation, cellular bronchiolitis
- May exhibit cavitation

Aspiration

- Basilar predominant cellular bronchiolitis
- Esophageal abnormalities, neurological, and deglutition disorders

Diffuse Alveolar Hemorrhage

- Ground-glass opacities ± interlobular septal thickening (crazy-paving pattern)
- No signs and symptoms of infection

Organizing Pneumonia

- May coexist with viral infection (e.g., COVID-19 and influenza)
- Peripheral or peribronchial consolidation; perilobular
- Migratory pulmonary opacities
- Reversed halo sign

PATHOLOGY

Microscopic Features

- Nodules contain infected cells with cytoplasmic inclusions: CMV, Adenovirus, herpesvirus
- Necrotizing bronchitis &/or bronchiolitis and diffuse alveolar damage (DAD): Influenza, RSV, parainfluenza viruses

- Bronchiolitis and bronchiectasis: Adenovirus
- Necrotizing bronchopneumonia, multicentric hemorrhage (centered on airways): Herpes simplex virus
- Acute interstitial pneumonia: Diffuse alveolar thickening by edema and mononuclear cells, airspace fibrinous exudate &/or hyaline membranes
 - CMV, hantaviruses (hantavirus pulmonary syndrome), SARS, MERS, COVID-19
- Endothelial damage to small vessels (focal hemorrhagic necrosis, mononuclear infiltration of alveolar walls, and alveolar fibrinous exudates): Varicella-zoster virus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Clinical syndromes
 - Cold: Upper respiratory tract symptoms (tonsillopharyngitis, pharyngitis, epiglottitis, sinusitis, otitis media, conjunctivitis)
 - Influenza syndrome: Abrupt fever, headache, myalgias, malaise
 - Acute bronchiolitis in infants and children: Wheezing with concomitant signs of respiratory viral infection
 - RSV (most common), Adenovirus, influenza, parainfluenza
 - CAP: Cough, sputum, dyspnea, fever, physical exam abnormalities (rhonchi, rales)
 - Influenza and RSV
 - Comorbidities or risk factors: Smoking, COPD, asthma, diabetes mellitus, malignancy, heart failure, neurologic diseases, narcotic and alcohol use, chronic liver disease
- Clinical profile
 - Role of biomarkers
 - Procalcitonin: ↓ or marginally elevated in viral infection, ↑ in bacterial infection

Demographics

- Increasingly frequent cause of pulmonary disease worldwide
- High rate of viral infection in CAP (2-35%)
 - Influenza, hMPV, and RSV: 2/3 of all viral pathogens in patients with CAP

Natural History & Prognosis

- Variable prognosis
 - Complete resolution in immunocompetent individuals

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Lobar consolidation uncommon in viral pneumonia
- Nodules < 10 mm, may exhibit CT halo sign; do not exhibit cavitation
- Branching or centrilobular nodules and mosaic perfusion/attenuation common in viral bronchiolitis
- Concomitant organizing pneumonia may occur as manifestation of ALI (perilobular distribution)

SELECTED REFERENCES

1. Koo HJ et al: Radiographic and CT features of viral pneumonia. Radiographics. 38(3):719-39, 2018

Viral Pneumonia





(Left) Axial HRCT of a bone marrow transplant recipient who developed parainfluenza virus 3 pneumonia shows scattered bilateral groundglass opacities 🔁. Influenza, respiratory syncytial virus, rhinovirus, and parainfluenza virus are the most common pathogens in this patient population. (Right) Axial CECT of a woman with influenza virus A pneumonia shows extensive, bilateral, peripheral ground-glass opacities and consolidations. The perilobular pattern is reminiscent of organizing pneumonia, which is often present histologically.





(Left) Axial NECT of a patient with cytomegalovirus pneumonia and a history of bilateral lung transplantation shows a left upper lobe nodule with surrounding groundglass opacity \square , the so-called CT halo sign, which often correlates with perilesional hemorrhage. (Right) Axial NECT of a hematopoietic stem cell transplant recipient with cytomegalovirus infection shows multiple random lung nodules that measure < 10 mm, with surrounding groundglass opacity 🔁. These findings are highly suggestive of a viral infection.





(Left) Axial CECT of a 28-yearold man with fever and a skin rash due to varicella-zoster virus infection shows profuse, miliary, 1- to 2-mm nodules scattered throughout the lung. (Right) Axial NECT of a patient with hantavirus pulmonary syndrome shows diffuse symmetric ground-glass opacities with superimposed linear and reticular opacities, the so-called crazy-paving pattern, and small bilateral pleural effusions 🔁. The findings were related to diffuse alveolar damage. (Courtesy A. S. Sousa, MD.)

KEY FACTS

TERMINOLOGY

- Human influenza: RNA virus, categorized as types A, B, C
- Influenza pneumonia: Lung inflammation/compromise due to direct viral infection of respiratory epithelium

IMAGING

- Radiography
 - o Interstitial opacities
 - Nodular or patchy ground-glass opacities
 - Extensive airspace disease from hemorrhagic edema
 - Acute pneumonia, rapid progression to acute respiratory distress syndrome
- CT
 - Mosaic attenuation
 - Ground-glass opacity and consolidation
 - o Nodules: Centrilobular, 1-10 mm
 - Tree-in-bud opacities
- HRCT: Expiratory air-trapping

TOP DIFFERENTIAL DIAGNOSES

- Other viral pneumonias
- Mycoplasma pneumonia, bacterial pneumonias

PATHOLOGY

• Airway epithelial necrosis, submucosal chronic inflammation

CLINICAL ISSUES

- Symptoms/signs
 - Often confined to upper respiratory tract
 - Dry cough, rhinorrhea, sore throat
 - Influenza syndrome: Abrupt fever, headache, myalgias, malaise
- Most viral pneumonias in immunocompetent adults
- Seasonal upper respiratory tract infections

DIAGNOSTIC CHECKLIST

• Imaging features cannot predict etiologic agent

(Left) AP chest radiograph of a 61-year-old man with chronic lymphocytic leukemia who presented with cough and dyspnea shows bilateral asymmetric patchy airspace and interstitial opacities more pronounced in the right lung. (Right) Axial CECT of the same patient shows tree-in-bud opacities 🛃, centrilobular nodules and a right lower lobe bilateral pleural effusions. The patient succumbed 1 week later to acute respiratory distress syndrome, as a complication of influenza A pneumonia.





(Left) Axial CECT of a 29-yearold woman with influenza A pneumonia (H1N1) shows centrally distributed peribronchovascular groundglass opacities with interlobular septal thickening 🔁 and small bilateral pleural effusions 🛃. (Right) Coronal CECT of the same patient shows bilateral pulmonary involvement and predominantly central distribution of the groundglass opacities 🔁 Note areas of perilobular distribution 🔁 of airspace disease, which can be seen in the context of organizing pneumonia.





Synonyms

• Influenza A: Avian flu H5N1, swine flu H1N1

Definitions

- Human influenza is RNA virus, categorized into types A, B and C, which can be subcategorized into several subtypes, e.g., influenza A: H1N1, H1N2, H2N1, H3N1, etc.; influenza B subtypes are B/Yamagata and B/Victoria lineages
- Influenza pneumonia results from lung inflammation and compromise caused by direct viral infection of respiratory epithelium

IMAGING

General Features

- Location
 - o Unilateral or bilateral, usually in lower lobes
- Size
 - Patchy areas of ground-glass &/or consolidation
- Morphology
 - Lobar consolidation uncommon

Radiographic Findings

- Radiography
 - Interstitial opacities
 - Nodular or patchy ground-glass opacities; bronchopneumonia pattern
 - Patchy consolidations (1-2 cm)
 - o Extensive airspace disease from hemorrhagic edema
 - Cavity formation suggests superinfection with *Staphylococcus* organisms
 - Small pleural effusions (rare); usually represent superimposed bacterial infection
 - Acute pneumonia with rapid progression to acute respiratory distress syndrome (ARDS)

CT Findings

- NECT
 - Mosaic attenuation: Patchy heterogeneous lung attenuation
 - Lobular ground-glass opacity and consolidation: Patchy, poorly-defined bronchopneumonia or focal well-defined lobar pneumonia
 - Perilobular distribution may be associated with acute organization
 - Nodules and tree-in-bud opacities: 1- to 10-mm, centrilobular, dense, or ground-glass nodules
 - Secondary bacterial pneumonia can occur
 - Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus
 - Denser lobar consolidation
 - Pleural effusion rare
- HRCT
 - Hypoperfused lung shows expiratory air-trapping

Imaging Recommendations

- Best imaging tool
 - Radiography: Disease detection, determination of extent of involvement, monitoring response to treatment

DIFFERENTIAL DIAGNOSIS

Mycoplasma Pneumonia

- Segmental peribronchial patchy opacities, similar to viral pneumonias; less symptomatic than expected for extent of radiographic disease
- Seasonal: Spring and fall

Other Viral Pneumonias

 Acute lung injury pattern in COVID-19 can be indistinguishable from involvement by Influenza

PATHOLOGY

General Features

• Diffuse epithelial infection

Microscopic Features

- Airway epithelial necrosis, submucosal chronic inflammation
- Necrotizing bronchitis &/or bronchiolitis
- Diffuse alveolar damage, hemorrhage

Laboratory Identification

- Single-stranded RNA viruses, Orthomyxoviridae family
- Viral culture results in 3-14 days
- Nucleic acid amplification tests, improved ability to detect viruses; reverse transcriptase PCR

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Often confined to upper respiratory tract
 - Dry cough, rhinorrhea, sore throat
 - Influenza syndrome: Abrupt fever, headache, myalgias, malaise
- Clinical profile
 - Biomarkers
 - Procalcitonin: Typically normal or marginally elevated; elevation often associated with concomitant bacterial infection

Demographics

- Epidemiology
 - Severe pneumonia may affect all ages

Natural History & Prognosis

- Influenza accounted for most viral pneumonias in immunocompetent adults (prior to COVID-19 pandemic)
- Seasonal upper respiratory tract infections, periodic and unpredictable pandemics
- Lower respiratory tract infections in 10% of cases
- H5N1 avian flu, 60% mortality

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Imaging features cannot predict etiologic agent

SELECTED REFERENCES

 Lin L et al: CT manifestations of coronavirus disease (COVID-19) pneumonia and influenza virus pneumonia: a comparative study. AJR Am J Roentgenol. 216(1):71-9, 2021

Cytomegalovirus Pneumonia

KEY FACTS

TERMINOLOGY

- Cytomegalovirus (CMV)
- CMV pneumonia is serious cause of mortality and morbidity in immunocompromised adults
- Severe viral community-acquired pneumonia in immunocompetent adults

IMAGING

- Radiography
 - Bilateral patchy or diffuse opacities
 - Small or large lung nodules
 - Pulmonary consolidation
 - Pleural effusion
- CT
 - Pulmonary consolidation
 - Patchy or diffuse ground-glass opacities
 - Small nodules in random distribution
 - Tree-in-bud opacities

TOP DIFFERENTIAL DIAGNOSES

- Pneumocystis jirovecii pneumonia
- Drug reaction
- Viral pneumonia
- Lung transplant rejection
- Organizing pneumonia

CLINICAL ISSUES

- Symptoms/signs
 - o Fever, dyspnea
- Treatment
 - o Ganciclovir, valganciclovir, foscarnet
 - o Correction of underlying immunosuppression
- Mortality > 50% in immunocompromised host
- Good prognosis in immunocompetent host

DIAGNOSTIC CHECKLIST

• Consider CMV pneumonia in immunocompromised patients with diffuse pulmonary abnormalities

(Left) AP chest radiograph of a patient with acute myeloid leukemia and neutropenic fever shows bilateral symmetric reticulonodular opacities, later confirmed to represent cytomegalovirus pneumonia. (Right) Axial CECT of the same patient shows bilateral patchy ground-glass and nodular 🔁 opacities and small bilateral pleural effusions. Cytomegalovirus pneumonia usually affects immunocompromised patients, but may also cause severe community-acquired pneumonia in immunocompetent adults.











- Abbreviations
- Cytomegalovirus (CMV)

Synonyms

• Formerly known as human herpesvirus 5 (HHV-5)

Definitions

- CMV
 - Member of herpesvirus family
 - Variety of disease manifestations
- CMV pneumonia is serious cause of mortality and morbidity in immunocompromised adults
 - Patients with acquired immunodeficiency syndrome (AIDS)
 - Allogeneic stem cell transplant recipients
 - Solid organ transplant recipients
- CMV pneumonia
 - Severe viral community-acquired pneumonia in immunocompetent adults
- Proven CMV pneumonia requires clinical symptoms &/or signs of pneumonia
 - e.g., new airspace disease on imaging, hypoxia, tachypnea, &/or dyspnea
 - CMV documented in lung tissue
 - Virus isolation
 - Rapid culture
 - Histopathology
 - Immunohistochemistry
 - DNA hybridization techniques

IMAGING

General Features

- Location
- Diffuse or lower lung zone predominance

Radiographic Findings

- Bilateral patchy or diffuse opacities
 o Ground-glass &/or reticular patterns
- Small or large lung nodules
- Bronchial wall thickening
- Pulmonary consolidation
 - Segmental or lobar
 - Peribronchovascular
 - Sub-pleural sparing may occur
- Pleural effusion
- Progressive volume loss

CT Findings

- Pulmonary consolidation
 May be mass-like
- Ground-glass opacities
 - o Patchy
 - o Diffuse
- Nodules
 - o < 10 mm
 - Random or subpleural distribution
 - ± ground-glass opacity halo
 - o Bilateral, symmetric, diffuse

- Tree-in-bud opacities
- Interlobular septal thickening
- Bronchial wall thickening
- Traction bronchiectasis
- Pleural effusion

Imaging Recommendations

- Best imaging tool
 - Chest radiograph for initial evaluation
 - CT indicated if radiograph is negative, particularly in evaluation of immunocompromised patients
 - Guides bronchoscopic or surgical biopsy

DIFFERENTIAL DIAGNOSIS

Pneumocystis jirovecii Pneumonia (PCP)

- CMV present in lungs of approximately 75% of patients with human immunodeficiency virus (HIV) and PCP
- Presence of CMV in patients with HIV infection and PCP does not indicate causal role of CMV in pneumonia
- If PCP is treated, respiratory symptoms usually resolve without anti-CMV therapy
- CMV more likely if nodules or masses present on CT

Drug Reaction

• Diffuse or patchy ground-glass opacities

Acute Exacerbation of Interstitial Lung Disease (ILD)

- New ground-glass opacities in patients with ILD
 Exacerbation of ILD
 - Pulmonary infection
- Interval development/worsening of traction bronchiectasis
- Difficult differentiation from infection, edema, and alveolar hemorrhage; may require bronchoscopy

Viral Pneumonia

- Influenza, Adenovirus, COVID-19, and CMV may exhibit similar clinical and imaging findings
- CMV, unlike influenza, is not seasonal

Lung Transplant Rejection

- CMV and lung transplant rejection have similar clinical presentation
 - Low-grade fever
 - o Dyspnea
 - o Cough
- Time course of symptoms is helpful
 - Acute rejection more likely < 2 weeks after transplantation
 - CMV pneumonia usually occurs in first 3 months after discontinuation of CMV prophylaxis

Organizing Pneumonia

- Patchy multifocal opacities; may wax and wane on serial imaging
- Perilobular pattern (i.e., arcades)
- Reversed halo sign

Eosinophilic Pneumonia

- Eosinophilia
- Peripheral ground-glass opacities; ± photographic negative of pulmonary edema

PATHOLOGY

Microscopic Features

- Interstitial mononuclear infiltrate with foci of necrosis
- Enlarged infected cells with intranuclear and cytoplasmic inclusion bodies
- ± associated organizing pneumonia or diffuse alveolar damage

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Mild flu-like symptoms in immunocompetent patients – Cough, fever
 - Life-threatening pulmonary infection in immunocompromised patients
 - Dyspnea
 - Tachypnea
 - Malaise
 - Fatigue
- Other signs/symptoms
 - Elevated lactate dehydrogenase (LDH)
 - o Leukopenia
 - Atypical lymphocytes
 - Thrombocytopenia
 - o Hypoxemia

Demographics

- Epidemiology
 - 50-100% of adults have serum anti-CMV antibodies, suggesting exposure
 - Virus remains latent within leukocytes in seropositive asymptomatic individuals
- CMV pneumonia in immunocompromised hosts
 - Recipients of solid organ transplant
 - CMV from seropositive donors or de novo infection more serious than reactivation of latent infection
 - CMV status match between donor and recipient to avoid combination of seronegative recipient and seropositive donor
 - Associated with acute rejection in lung, renal, and liver transplant
 - Lung transplant
 - 1-12 months post lung transplant, peak at 1-3 months
 - 2nd most common infection in lung transplant recipients, after bacterial pneumonia
 - □ Associated with acute and chronic rejection
 - Recipients of allogeneic stem cell transplant
 - Immunosuppression + graft-vs.-host disease
 - Usually reactivation of latent CMV
 - Occurs 30-100 days after transplantation
 - AIDS
 - CMV: Most common viral pulmonary pathogen
 May also cause retinitis, acalculous cholecystitis, esophagitis, colitis, encephalitis
 - Infection by sexual partners or reactivation of latent infection
 - CMV pneumonitis usually when CD4 < 100 cells/mm³

- Incidence reduced by effective anti-retroviral medications (HAART)
- Systemic lupus erythematosus (SLE)
 - CMV has immunomodulatory effects and may cause SLE flare
 - SLE flare with mildly elevated serum transaminases and pneumonitis, likely caused by CMV
- Other causes of immunosuppression
 - Steroid therapy for connective tissue or inflammatory bowel disease
 - Chemotherapy
- CMV pneumonia in immunocompetent hosts
 - Uncommon cause of severe community-acquired viral pneumonia

Natural History & Prognosis

- Routes of transmission
 - o Transplacental
 - Cervical or vaginal secretions at birth
 - o Breast milk
 - o Saliva
 - Respiratory secretions
 - Venereal transmission
 - o latrogenic
 - Organ transplants
 - Transfusion of blood products
- Accounts for 4% of deaths in 1st year after lung transplant
- Suppresses T-cell-mediated immunity
 - Associated pathogens
 - Pneumocystis jirovecii
 - Aspergillus spp.
 - Cryptococcus neoformans
- Good prognosis in immunocompetent host
- Mortality > 50% in immunocompromised patient despite therapy

Treatment

- Ganciclovir (intravenous) or valganciclovir (oral)
 Also used as prophylaxis
- Foscarnet
 - Used in patients who cannot tolerate ganciclovir
 - Treatment of ganciclovir-resistant CMV infection
- Anti-CMV immunoglobulin
 - Prophylaxis when seronegative host receives solid organ or stem cell transplant from seropositive donor
- Correction of underlying immunosuppression
 - Decrease in dose of immunosuppressant in transplant patients

DIAGNOSTIC CHECKLIST

Consider

• CMV pneumonia in immunocompromised patients with diffuse pulmonary abnormalities, particularly transplant recipients

- Kose A et al: Cytomegalovirus associated severe pneumonia in three liver transplant recipients. J Infect Dev Ctries. 14(11):1338-43, 2020
- Kunihiro Y et al: Differential diagnosis of pulmonary infections in immunocompromised patients using high-resolution computed tomography. Eur Radiol. 29(11):6089-99, 2019

Cytomegalovirus Pneumonia





(Left) PA chest radiograph of a patient undergoing chemotherapy for pancreatic cancer shows bilateral patchy airspace opacities. (Right) Coronal CECT of the same patient shows bilateral patchy ground-glass opacities with a peribronchovascular and subpleural distribution. Cytomegalovirus infection was confirmed by bronchoalveolar lavage. Bronchoalveolar lavage is important in the diagnostic work-up of *immunocompromised patients* with nonspecific CT findings, such as ground-glass opacity.





(Left) Axial NECT of a patient with acute myeloid leukemia, respiratory distress, and confirmed cytomegalovirus pneumonia shows patchy ground-glass and reticular opacities and thickening of the superior aspect of the major fissure. (Right) Axial NECT of the same patient shows patchy ground-glass and reticular opacities involving the right lower lobe. Differential considerations include other viral pneumonias, Pneumocystis jirovecii pneumonia, drug reaction, and pulmonary hemorrhage.





(Left) Axial NECT of a patient with acquired immunodeficiency syndrome, 34 days post stem cell transplantation for non-Hodgkin lymphoma, shows cytomegalovirus pneumonia manifesting as subtle bilateral tree-in-bud opacities \blacksquare . (Right) Axial NECT of a left lung transplant recipient with dyspnea shows mild patchy ground-glass opacities in the transplanted lung. CT findings of cytomegalovirus pneumonia can be quite subtle, and the radiologist must have a high index of suspicion in the appropriate clinical setting.

COVID-19

KEY FACTS

TERMINOLOGY

- SARS-CoV-2
- Beta coronavirus first reported in Wuhan, China in 2019
- Reverse transcriptase polymerase chain reaction (RT-PCR)

IMAGING

- **Radiography**: Patchy peripheral (subpleural) predominant hazy opacities ± consolidations
- CT
 - Early (~ 7-14 days after onset of symptoms)
 - Bilateral peribronchovascular and peripheral
 - predominant ground-glass opacities ± consolidations • ARDS (late phase; > 14 days)
 - Diffuse consolidations &/or ground-glass opacities
- Complications: Bacterial pneumonia, pneumothorax, pneumomediastinum, acute pulmonary thromboembolic disease
- Sequela: Peribronchovascular fibrosis with reticulation and traction bronchiectasis, constrictive bronchiolitis

TOP DIFFERENTIAL DIAGNOSES

- Other viral pneumonias
- Organizing pneumonia
- E- cigarette or vaping product use-associated lung injury

PATHOLOGY

- Organizing pneumonia
- Acute fibrinous and organizing pneumonia
- Diffuse alveolar damage

CLINICAL ISSUES

- Fever, chills, cough, shortness of breath, fatigue, muscle/body aches, headache, loss of taste/smell, sore throat, congestion, runny nose, nausea, vomiting, diarrhea
- Transmission: Person to person via respiratory droplets
- Diagnosis: RT-PCR in nasopharyngeal swab or other respiratory secretions
- Treatment: Prone ventilation, corticosteroids, convalescent serum, tocilizumab, remdesivir

(Left) AP chest radiograph of a 58-year-old patient with PCRproven COVID-19 who presented with cough, fever, and chills shows bilateral illdefined, peripheral, predominant opacities 🔁 (ferritin: 551 ng/mL, C-reactive protein: 193 mg/L.). (Right) Axial CECT of the same patient shows peripheral, subpleural, well-demarcated ground-glass opacities with central areas of spared lung. Early pathologic reports have shown some features suggestive of acute fibrinous organizing pneumonia (AFOP).





(Left) Coronal CECT of the same patient shows bilateral well-demarcated, peripheral, subpleural ground-glass opacities $\overline{\rightarrow}$, which are reminiscent of areas of organizing pneumonia. (Right) Axial CECT of a patient with COVID-19 shows extensive bilateral ground-glass opacities with peribronchial and subpleural distribution and a spontaneous pneumomediastinum 🖂 Pneumomediastinum and pneumothorax may occur in the context of the disease itself or as a consequence of barotrauma.





Abbreviations

- Human coronavirus (HCoV)
- Organizing pneumonia (OP)
- Acute fibrinous and organizing pneumonia (AFOP)
- Diffuse alveolar damage (DAD)
- Acute respiratory distress syndrome (ARDS)
- Reverse transcriptase polymerase chain reaction (RT-PCR)

Synonyms

• SARS-CoV-2

Definitions

- Coronavirus
 - RNA virus initially described in 1960s
 - COVID-19: Beta coronavirus first reported in Wuhan, China in 2019

IMAGING

General Features

- Best diagnostic clue
 - Bilateral peripheral predominant opacities

Radiographic Findings

- May be normal
- Patchy peripheral (subpleural) predominant hazy opacities ± consolidations
- Diffuse lung opacities ± reticular opacities
 - o Severe/advanced disease
 - May be indistinguishable from ARDS from other etiologies

CT Findings

- Early findings (~ 7-14 days after onset of symptoms)
 Bilateral peribronchovascular and peripheral
 - predominant ground-glass opacities ± consolidations
 - Often sharply demarcated from spared lung
 - "Crazy paving": Interlobular septal thickening and intralobular lines within areas of ground-glass opacities
 - Perilobar distribution
 - Bowed or polygonal opacities, surrounded by or surrounding aerated lung
 - Bronchial or bronchiolar &/or peripheral vascular dilation in affected areas
 - Reversed halo sign
 - Peripheral subpleural consolidation surrounding central ground-glass opacity
 - Small rounded or ill-defined scattered ground-glass opacities
- ARDS (late phase; > 14 days)
- Diffuse consolidations &/or ground-glass opacities
- Complications
 - o Bacterial pneumonia (rare)
 - Pneumothorax (rare)
 - May occur in absence of mechanical ventilation
 - Pneumomediastinum (rare); spontaneous or associated with barotrauma
 - Pneumatoceles ± pneumothorax

- Acute pulmonary thromboembolic disease (controversial whether incidence is increased)
- Chronic findings (after resolution)
 - Still early in pandemic to establish with certainty
 - Peribronchovascular fibrosis with reticulation and traction bronchiectasis described in some patients
 - Mosaic attenuation and air-trapping suggestive of constrictive bronchiolitis described in some patients

Imaging Recommendations

- Best imaging tool
 - CT superior to radiography for detection of pulmonary abnormalities, but not required for diagnosis, does not replace RT-PCR as diagnostic gold standard
 - CT not required for diagnosis, should be reserved to evaluate complications

DIFFERENTIAL DIAGNOSIS

Viral Pneumonia

• Various viral infections may exhibit imaging abnormalities similar to those of COVID-19, e.g., influenza

Organizing Pneumonia

- Typically subacute or chronic course
- AFOP
 - Histologic variant of OP with overlapping features of DAD
 - May be acute or subacute
 - Acute AFOP often has clinical presentation similar to that of typical ARDS/DAD
- OP and AFOP may be idiopathic or secondary (e.g., infection, connective tissue disease, autoimmunity, drug toxicity, etc.); often exhibit imaging findings similar to those seen in COVID-19

E-Cigarette or Vaping Product Use-Associated Lung Injury (EVALI)

- Various pathologic patterns: DAD, OP, hypersensitivity pneumonitis, acute eosinophilic pneumonia, chronic eosinophilic pneumonia, lipoid pneumonia
- Diffuse ground-glass opacities ± consolidations, centrilobular ground-glass micronodules

Desquamative Interstitial Pneumonia

- Within spectrum of smoking-related pulmonary diseases
- Multifocal subpleural ground-glass opacities &/or consolidations
- Often coexists with emphysema &/or other smokingrelated disease

PATHOLOGY

Microscopic Features

- AFOP
 - Subtype of OP
 - Predominant pattern of acute lung injury
 - Extensive intraalveolar fibrin deposition (a.k.a. fibrin balls) rather than hyaline membranes
 - Intraluminal loose connective tissue within alveolar ducts and bronchioles
 - Fibroblastic bodies and fibroblasts surrounding intraalveolar fibrin

- Moderate interstitial T-cell lymphocytic and plasma cells infiltrate and type 2 pneumocyte hyperplasia with cytologic atypia
- Vascular injury: Endothelial injury with cytoplasmic vacuolization and cell detachment in small to mediumsized pulmonary arteries
- Histological overlap with DAD
 - Different from DAD: Predominant feature is organizing intraalveolar fibrin

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Fever or chills, cough, shortness of breath, fatigue, muscle/body aches, headache, loss of taste/smell, sore throat, congestion, runny nose, nausea, vomiting, diarrhea
 - o 2 clinical phenotypes
 - Type L: 70-80%
 - Low: Elastance (near normal compliance), ventilation:perfusion (VA/Q) ratio, lung weight, lung recruitability
 - Type H (ARDS): 20-30%
 - High: Elastance (abnormal compliance), right-to-left shunt, lung weight, lung recruitability
 - o Children
 - Most asymptomatic or with mild symptoms; may spread disease even if asymptomatic
 - Some may develop severe illness
 - Mortality rare
 - Multisystem inflammatory syndrome in children (MIS-C)
 - □ Symptoms: Fever, abdominal pain, vomiting, diarrhea, neck pain, rash, red eyes, asthenia
 - May involve heart, lungs, kidneys, brain, skin, eyes, gastrointestinal organs
- Other signs/symptoms
 - RT-PCR in nasopharyngeal swab or other respiratory secretions
 - Laboratory
 - Lymphopenia
 - Thrombocytopenia
 - − ↑ liver enzymes
 - − ↑ lactate dehydrogenase (LDH)
 - ↑ inflammatory markers [e.g., C-reactive protein (CRP), ferritin], inflammatory cytokines [i.e., interleukin 6 (IL-6) and tumor necrosis factor (TNF)-alpha]
 - − ↑ D-dimer (> 1 mcg/mL)
 - − ↑ prothrombin time (PT)
 - − ↑ troponin
 - ↑ creatine phosphokinase (CPK)
 - Acute kidney injury
 - Procalcitonin is usually normal or mildly elevated; marked elevation suggests bacterial coinfection
- Clinical profile
 - Incubation period
 - 4-5 days; may be as long as 14 days
 - Protective factors: Prior BCG vaccination

Demographics

- Sex
 - o Males have reported higher mortality rate
- Ethnicity
 - Black, Hispanic, and South Asian subjects more likely to develop disease and have higher mortality rates
- Epidemiology
 - o > 55 million cases worldwide
 - o Transmission
 - Airborne via respiratory droplets (most common)
 - Contaminated surfaces
 - Low risk of transmission 7-10 days following symptom onset
- Risk factors for severe illness
 - o Cancer
 - Chronic kidney disease
 - Chronic obstructive pulmonary disease (COPD)
 - Heart conditions (e.g., heart failure, coronary artery disease, cardiomyopathy)
 - Immunocompromised state (weakened immune system) from solid organ transplant
 - Severe obesity (BMI \ge 40 kg/m²)
 - o Pregnancy
 - o Sickle cell disease
 - o Smoking
 - Type 2 diabetes mellitus
 - A+ ABO blood group
- Mortality
 - Increases with age
 - Crude mortality 2-3%; improved after corticosteroids and other measurements implemented
 - o > 4.5 million deaths (> 645,000 in USA)

Natural History & Prognosis

- Complications
 - o ARDS
 - 8 days after symptom onset in 20% of patients with severe disease
 - 12-24% require intubation
 - o Cardiovascular
 - Cardiomyopathy: 1/3 of patients admitted to ICU
 - Arrhythmia
 - Acute thromboembolic disease
 - o Secondary hemophagocytic lymphohistiocytosis
 - Hyperinflammatory syndrome with fulminant and fatal hypercytokinemia with multiorgan failure
 - Features: Unremitting fever, cytopenia, 1 ferritin; pulmonary involvement in ~ 50% (including ARDS)

Treatment

- Prone ventilation (whether patient intubated or not)
- Corticosteroids
- Convalescent serum
- Remdesivir, tocilizumab

- Copin MC et al: Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection. Intensive Care Med. 46(6):1124-6, 2020
- Gattinoni L et al: COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 46(6):1099-102, 2020

COVID-19





(Left) Axial CECT of a patient with COVID-19 and pulmonary involvement shows bilateral patchy ground-glass opacities. Note arc-like opacities \square , the so-called perilobular pattern (a.k.a. the atoll sign), a characteristic pattern seen in organizing pneumonia. (Right) Axial CECT of a patient with COVID-19 shows multifocal bilateral ground-glass opacities, including a right lower lobe nodule that exhibits the reversed halo sign 🔁 (i.e., denser peripheral opacities surrounding central ground-glass opacities), typical of organizing pneumonia.





(Left) Axial NECT of a patient with pulmonary involvement secondary to COVID-19 shows bilateral subpleural groundglass opacities that exhibit intrinsic mild bronchial dilatation \square , a finding that has been described in the context of organizing pneumonia. (Right) Axial NECT of a patient who recovered from a COVID-19 infection but remained short of breath shows bilateral scattered areas of mosaic attenuation \square , consistent with small airways disease, presumably constrictive bronchiolitis.





(Left) Coronal CECT of a patient with pulmonary involvement due to COVID-19 shows diffuse bilateral patchy ground-glass opacities secondary to organizing pneumonia. (Right) Coronal CECT of the same patient obtained 2 months later shows interval development of decreased lung volume and diffuse reticular opacities with extensive traction bronchiectasis 🔁 and $bronchiolectasis \ge$ secondary to postinflammatory fibrosis. The pulmonary sequela of COVID-19 infection are still not well established.

Histoplasmosis

KEY FACTS

TERMINOLOGY

• Infection with Histoplasma capsulatum

IMAGING

- Histoplasmoma: Lung nodule ± calcification
- Acute histoplasmosis: Solitary or multiple lower lobe airspace disease ± lymphadenopathy
- Disseminated histoplasmosis: Miliary or diffuse airspace disease; cavitation
- Hilar/mediastinal lymphadenopathy
- Broncholith: Calcified lymph node erodes into bronchus
- Fibrosing mediastinitis: Soft tissue infiltration of
- mediastinum, encasement and stenosis of airways, veins, arteries, esophagus
- Middle lobe syndrome: Bronchial obstruction by lymphadenopathy, chronic lobar collapse
- Chronic histoplasmosis: Progressive upper lobe volume loss, fibrosis, bullae

TOP DIFFERENTIAL DIAGNOSES

- Tuberculosis
- Lung cancer
- Other fungal infection

PATHOLOGY

• Inhalation of airborne spores

CLINICAL ISSUES

- Symptoms/signs
 - Immunocompetent: Asymptomatic
 - Immunosuppressed: Symptomatic
- Diagnosis: Smears and culture of bronchoscopic specimens, lymph nodes, bone marrow, radioimmunoassay of antigen in urine or serum
- Treatment
 - o Immunocompetent: Resolves without treatment
 - Immunosuppressed or large inoculum: Antifungals

(Left) Coned-down PA chest radiograph of a patient with a history of massive inhalational histoplasmosis shows profuse tiny calcified lung nodules \supseteq that represent the residua of remote granulomatous fungal infection. (Right) Axial NECT of a patient with histoplasmosis shows clustered Histoplasma granulomas manifesting with a dominant solid soft tissue nodule 🛃 and smaller satellite nodules. These imaging findings are virtually diagnosis of remote histoplasmosis in endemic areas.

(Left) Coronal NECT of a patient with chronic active histoplasmosis shows bilateral upper lobe volume loss, architectural distortion, and thick-walled cavitary lesions ➡. These abnormalities mimic those produced by active tuberculosis. (Right) Composite image with axial CECT in lung (left) and soft tissue (right) window shows a small right lower lobe solid nodule 🔁 secondary to focal Histoplasma pneumonitis with associated ipsilateral right hilar lymphadenopathy ₽. The appearance is typical of acute histoplasmosis.









Definitions

- Infection with dimorphic fungus Histoplasma capsulatum
- Disease manifestations
 - Histoplasmoma
 - Acute, massive inhalational histoplasmosis
 - Acute disseminated histoplasmosis
 - Chronic pulmonary or mediastinal histoplasmosis
 - Fibrosing mediastinitis

IMAGING

General Features

- Best diagnostic clue
 - Lung nodule with central, laminated, or diffuse calcification: Virtually diagnostic of histoplasmoma
- Location
- Lung and mediastinum most commonly affected
- Size
 - In endemic areas > 90% of lung nodules < 2 cm are granulomas
- Morphology
 - o Variable

Radiographic Findings

- Acute histoplasmosis
 - Airspace disease in any lobe, solitary or multiple; usually lower lungs
 - o Ipsilateral hilar/mediastinal lymphadenopathy (common)
 - Pleural or pericardial effusion + cavitation (uncommon)

• Massive inhalational histoplasmosis

- o Multilobar pneumonitis, hilar lymphadenopathy
- Complete resolution or evolution to tiny calcified or noncalcified nodules
- Disseminated histoplasmosis
 - Miliary or diffuse airspace disease ± cavitation
 - Chest radiograph may be normal
- Hilar/mediastinal lymphadenopathy ± calcification
- **Middle lobe syndrome**: Chronic middle lobe collapse from bronchial compression
- Mediastinal involvement
 - Mediastinal granuloma
 - Partially calcified mediastinal mass especially in upper mediastinum; unilateral or bilateral
 - Fibrosing mediastinitis
 - Encasement/stenosis of airways, systemic veins, pulmonary arteries, esophagus
- **Broncholithiasis**: Erosion of calcified lymph node into bronchus
 - Postobstructive pneumonia, interstitial opacities, atelectasis, oligemia, pleural effusion
- Chronic histoplasmosis
 - Progressive upper lobe patchy opacities, volume loss, fibrosis, bullae, honeycombing (20%)
 - o Emphysema, unilateral or bilateral
 - Opacities on background of emphysema; mimics thick- or thin-walled cavities
 - o Mycetomas may develop in upper lobe emphysema
 - Apical pleural thickening; no pleural effusion or lymphadenopathy

Fluoroscopic Findings

• **Barium swallow**: Assessment of esophageal stenosis, fistula, diverticula, downhill varices

CT Findings

- NECT
 - Thin-section CT to characterize lung nodules
 Histoplasmoma: Well-defined nodule, usually < 2 cm
 - (range: 0.5-3 cm)
 - □ Single or multiple
 - □ May enlarge slowly (2 mm/year)
 - □ Satellite nodules around dominant nodule
 - □ Smooth or lobular margins, sometimes irregular
 - □ Calcification (50%): Central, laminated, diffuse
 - Ipsilateral hilar/mediastinal lymph nodes with mulberry-like calcification (common); mimics tuberculous Ranke complex
 - Nodule cavitation uncommon
 - Thin-section CT and multiplanar reformations to show endobronchial location of broncholith
 - Calcified hepatic and splenic granulomas
- CECT
 - Lymph nodes with central low attenuation from caseous necrosis
 - Mediastinal granuloma
 - Enlarged mediastinal coalescent lymph nodes; may impinge on adjacent mediastinal structures
 Does not progress to fibrosing mediastinitis
 - Fibrosing mediastinitis
 - Soft tissue infiltration of mediastinal fat; encasement, stenosis, and obliteration of airways, veins, arteries, esophagus
 - Superior vena cava (SVC) syndrome: Stenotic or obstructed veins + collateral venous pathways

• Middle lobe syndrome: Bronchial

compression/obstruction by lymphadenopathy and chronic lobar collapse

- Exclusion of endoluminal obstructing neoplasm
- HRCT
 - Disseminated disease: Miliary nodules, 1-3 mm, random distribution

MR Findings

• Decreased signal in lymph nodes may represent calcification

Imaging Recommendations

- Best imaging tool
 - Radiography usually sufficient to demonstrate manifestations of thoracic histoplasmosis
- Protocol advice
 - NECT: 1- to 3-mm thick sections to identify and assess calcification in nodules
 - CECT for assessment of fibrosing mediastinitis

DIFFERENTIAL DIAGNOSIS

Consolidation With Lymphadenopathy

- Tuberculosis
- Infectious mononucleosis
- Bacterial pneumonia in children
- Other fungal infection

- Tuberculosis
- Drug reaction (methysergide)
- Radiation-induced lung disease

Solitary Pulmonary Nodule

- Malignant
- Lung cancer
- o Carcinoid
- Solitary metastasis
- Benign
 - Fungal: Blastomycosis, coccidioidomycosis
 - o Hamartoma
 - Intrapulmonary lymph node

PATHOLOGY

General Features

- Etiology
 - Soil-dwelling dimorphic fungus transmitted via airborne route
 - Septate mycelium in soil; temperate zones
 - Inhalation of airborne spores from soil infected by bird excreta and feathers, infected bats
 - Yeast form in human tissues

Gross Pathologic & Surgical Features

• Benign extrapulmonary spread in most infections, liver/spleen calcified granulomas

Microscopic Features

- Yeast forms in tissues; granulomas with caseous necrosis; fibrous capsule, calcification
- Progressive disseminated disease: Bone marrow involvement
- Usually not isolated from mediastinal fibrosis, pleural or pericardial effusions

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Malaise, fever, headache, muscle pain, nonproductive cough, wheezing, dysphagia, oropharyngeal ulcers, hemoptysis, chest pain
 - Lymphadenopathy, hepatosplenomegaly
 - Erythema nodosum, erythema multiforme
 - o Pericarditis
 - Acute respiratory distress syndrome: Immunosuppression or large inoculum
 - Progressive disseminated disease
 - Abnormal T-cell immunity, acquired immune deficiency syndrome (AIDS), chemotherapy, steroids, organ transplants, lymphoma
 - May result in adrenal regurgitation
 - Symptoms influenced by immune status
 - Immunocompetent
 - Asymptomatic or minimal symptomsSelf-limited disease
 - Immunosuppressed, patients with emphysema:
 Symptomatic

Demographics

- Age
 - Any age; symptomatic form more common in infants and older adults
- Epidemiology
 - Reported worldwide. Endemic in North, Central, and South America
 - o USA: Ohio and Mississippi River Valleys
 - o > 80% in endemic areas infected

Diagnosis

- Smears and culture of bronchoscopic specimens, lymph nodes, bone marrow
- Antibody detection
- Biomarkers
 - **Fungitell**: Elevated in fungal diseases, including histoplasmosis (not elevated in mucormycosis)
 - **Procalcitonin**: Typically not elevated; helps differentiate from bacterial infection

Natural History & Prognosis

- Pulmonary and lymph node abnormalities may resolve completely
- Late sequelae
- o Histoplasmoma
 - Calcified granulomas in healed disease; 3 months to years for foci to calcify
- Chronic hilar and mediastinal lymphadenopathy
- Calcific or constrictive pericarditis: Residual from *Histoplasma* pericarditis
- Broncholithiasis: Erosion of calcified lymph nodes into mainstem, lobar, segmental bronchi
 - Airway obstruction: Atelectasis, postobstructive pneumonia, mucoid impaction, bronchiectasis, expiratory air-trapping
- Death from respiratory failure (rare); cor pulmonale with fibrosing mediastinitis

Treatment

- Depends on immune status, age, and disease location and severity
- Itraconazole, amphotericin B
- Fibrosing mediastinitis: Does not respond to drug treatment; surgery often dangerous and unsuccessful
 Vascular and airway stents for treatment of stenoses

DIAGNOSTIC CHECKLIST

Consider

• Histoplasmosis in patients from endemic areas with pulmonary &/or mediastinal abnormalities

- 1. Baker J et al: Chronic pulmonary histoplasmosis-a scoping literature review. Open Forum Infect Dis. 7(5):ofaa119, 2020
- Di Mango AL et al: Endemic pulmonary fungal diseases in immunocompetent patients: an emphasis on thoracic imaging. Expert Rev Respir Med. 13(3):263-77, 2019
- Semionov A et al: Many faces of thoracic histoplasmosis-pictorial essay. Can Assoc Radiol J. 70(3):273-81, 2019
- Salzer HJF et al: Diagnosis and management of systemic endemic mycoses causing pulmonary disease. Respiration. 96(3):283-301, 2018
- Richmond BW et al: Histoplasmomas of uncommon size. Chest. 143(6):1795-8, 2013

Histoplasmosis





(Left) AP chest radiograph of a 27-year-old critically-ill pregnant woman with acute histoplasmosis shows bilateral lower lobe airspace disease, moderate right and small left pleural effusions, and marked unilateral mediastinal lymphadenopathy ➡. (Right) Axial CECT of a patient with fibrosing mediastinitis shows right paratracheal lymphadenopathy that produces superior vena cava \blacksquare stenosis and impending occlusion. Note mediastinal 🖂 and chest wall \triangleright vascular collaterals.





(Left) PA chest radiograph of a patient with remote granulomatous infection related to histoplasmosis shows middle lobe atelectasis ➡ that was stable from prior radiographs (not shown). (Right) Axial CECT of the same patient shows a large calcified mediastinal lymph node 🔁 that has eroded into the bronchus intermedius. The middle lobe bronchus was occluded by adjacent lymphadenopathy (not shown). The findings were secondary to broncholithiasis and resulted in right middle lobe syndrome.





(Left) PA chest radiograph of an asymptomatic 39-year-old woman shows a large mediastinal mass $\overline{ rad s}$ with a large intrinsic ovoid calcification. (Right) Composite image with axial NECT in soft tissue (left) and bone (right) window shows typical features of mediastinal granuloma with a large densely calcified mass 🔁 in the left prevascular mediastinum in an asymptomatic patient. Note the small calcified pulmonary granuloma 🖂, consistent with remote histoplasmosis infection.

Coccidioidomycosis

KEY FACTS

TERMINOLOGY

- Fungal infection with *Coccidioides immitis* or *Coccidioides posadasii*
- Inhalation of fungal arthrospores

IMAGING

- Radiography
 - Solitary or multifocal segmental or lobar consolidation (75%)
 - Solitary or multiple lung nodules; may cavitate with thick or thin ("grape-skin") walls
 - o Hilar lymphadenopathy (20-40%)
 - o Pleural effusion (20%)
 - Mediastinal lymphadenopathy typical of disseminated disease
- CT
 - o Airspace disease, nodules, cavities
 - Thoracic lymphadenopathy
 - Assessment of affected immunocompromised patients

TOP DIFFERENTIAL DIAGNOSES

- Bacterial pneumonia
- Fungal pneumonia
- Mycobacterial pneumonia
- Lung cancer

CLINICAL ISSUES

- Endemic to arid regions of Western hemisphere
- Signs/symptoms: Asymptomatic, mild flu-like symptoms, severe infection in immunocompromised
- Most infections resolve
- Chronic lung disease 5%; disseminated disease < 1%
- Exogenous reinfection may occur in endemic areas
- Reactivation of latent disease in immune impaired hosts

DIAGNOSTIC CHECKLIST

• Consider coccidioidomycosis in patients from endemic areas with nonresolving consolidations

(Left) PA chest radiograph of a patient with cough, fever, and a history of recent travel to Arizona shows a left lower lobe consolidation that did not respond to antibiotics. Serologic and skin tests were positive for coccidioidomycosis. This infection may mimic community-acquired pneumonia. (Right) PA chest radiograph of the same patient obtained 4 months later shows resolution of the consolidation with a residual thin-walled "grape-skin" cavity ► Coccidioidomycosis may take months to resolve.





(Left) Axial NECT of a 45-yearold man status post heart transplantation shows a left upper lobe consolidation 🔁, left hilar lymphadenopathy \blacksquare , and multiple small nodules \square . Coccidioides spherules were recovered from the sputum. The patient was originally from Arizona and likely developed reactivation of disease secondary to immunocompromise. (Right) Axial CECT of a patient with coccidioidomycosis shows a right upper lobe cavitary consolidation 🛃 and mediastinal \triangleright and hilar \triangleright lymphadenopathy.





Synonyms

• Valley fever

Definitions

- Fungal infection with *Coccidioides immitis* or *Coccidioides posadasii*
- Inhalation of fungal arthrospores

IMAGING

General Features

- Best diagnostic clue
- Cavitary consolidation in patient from endemic areaLocation
 - Primary form limited to lungs, thoracic lymph nodes
 Disseminated form involves nearly any tissue
- Size
 - Range: Lung nodule to disseminated disease
- Morphology
 - Foci of consolidation may evolve into nodule(s) or thinwalled ("grape-skin") cysts

Radiographic Findings

- Solitary or multifocal segmental or lobar consolidation (75%)
- Solitary or multiple lung nodules
 - Nodules may cavitate with thick or thin ("grape-skin") walls
- Hilar lymphadenopathy in 20-40%
- Pleural effusion in 20%
- Mediastinal lymphadenopathy typical of disseminated disease

CT Findings

- Focal airspace disease, lung nodules, cavitary lesions
- Hilar &/or mediastinal lymphadenopathy
- Assessment of affected immunocompromised patients

Imaging Recommendations

- Best imaging tool
 - Chest radiographs for disease detection and follow-up
- Protocol advice
 - Consider chest CT for assessment and characterization of lung and mediastinal involvement, particularly in immunocompromised patient

DIFFERENTIAL DIAGNOSIS

Bacterial Pneumonia

- Typically symptomatic with fever and cough
- Parenchymal consolidation

Fungal Pneumonia

• Nodules, consolidation, cavitation, lymphadenopathy

Mycobacterial Pneumonia

- Cavitary consolidation, chronic fibrocavitary disease
- Miliary nodules with disseminated disease

Lung Cancer

• Persistent cavity or granuloma; may mimic lung cancer

PATHOLOGY

General Features

• Etiology: Inhalation of arthroconidia of Coccidioides species

Gross Pathologic & Surgical Features

• Consolidation may evolve to granuloma

Microscopic Features

- Endemic dimorphic fungus: Virulent, resistant to drying • Soil: Mycelium, produces 2- to 5-µm arthrospores
 - Host (humans and animals): Arthrospore inhalation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Asymptomatic acute infection
 - Asymptomatic acute infection
 - Mild flu-like symptoms in some patients
 Immune compromised at risk for severe infection
- Other signs/symptoms
 - Valley fever: Syndrome of fever, rash, arthralgias – Erythema nodosum and erythema multiforme
- Clinical profile
 - Large mature spherules with endospores found in sputum, gastric contents, pus, skin lesions
 - Serologic and skin tests become positive within 3 weeks after exposure

Demographics

- Epidemiology
 - Endemic to arid regions of Western hemisphere
 - California and northern Mexico: Coccidioides immitis
 - Arizona, Utah, Nevada, Texas, and Latin America: Coccidioides posadasii
 - Persons with high dust exposure at risk
 - o 100,000 new cases/year in USA
- Incidence increases with age, most > 40 years
- Males and females similarly affected

Natural History & Prognosis

- Incubation period of 1-4 weeks
- Most infections resolve
- Chronic lung disease 5%; disseminated disease < 1%
- Exogenous reinfection may occur in endemic areas
- Reactivation of latent disease in immune impaired

Treatment

• Fluconazole (3-6 months)

DIAGNOSTIC CHECKLIST

Consider

 Coccidioidomycosis in patients from endemic areas with nonresolving consolidations

- Kimes KE et al: Pulmonary coccidioidomycosis. Semin Respir Crit Care Med. 41(1):42-52, 2020
- Torres PPTES et al: Tomographic assessment of thoracic fungal diseases: a pattern and signs approach. Radiol Bras. 51(5):313-21, 2018
- 3. Jude CM et al: Pulmonary coccidioidomycosis: pictorial review of chest radiographic and CT findings. Radiographics. 34(4):912-25, 2014

Blastomycosis

KEY FACTS

TERMINOLOGY

- Synonym: North American blastomycosis
- Fungal infection with *Blastomyces dermatitidis*
- Dimorphic fungus: Disease caused by inhalation of airborne spores

IMAGING

- Radiography
 - Acute patchy consolidation, may be mass-like
 - Lung nodules of variable size, may be miliary
 - Any lobe can be affected
 - o Cavitation in 15-35%
 - Pleural thickening common, pleural effusion 20%
 - Lymph node enlargement in 10-35%
- CT
 - Characterization of airspace disease
 - Evaluation of mass-like consolidations, cavitation, complications

TOP DIFFERENTIAL DIAGNOSES

- Lung cancer
- Bacterial pneumonia
- Mycobacterial or fungal infection
- Rounded atelectasis

PATHOLOGY

- Inhalation of conidia of *B. dermatitidis*
- Endemic to Southeastern USA, Great Lakes region

CLINICAL ISSUES

- Asymptomatic or flu-like illness
- Skin lesions common, draining sinus tract
- Young to middle-aged outdoorsmen

DIAGNOSTIC CHECKLIST

• Consider culture of lung biopsy specimens for *Blastomyces* in endemic areas

(Left) PA chest radiograph of a 38-year-old man with blastomycosis who presented with fever shows extensive right lung consolidation and multifocal small lung nodules. (Right) Axial CECT of the same patient shows extensive right lower lobe consolidation and centrilobular left lower lobe nodules and patchy lobular consolidations. The imaging findings are nonspecific and mimic those of bacterial pneumonia. The diagnosis of blastomycosis was established on bronchial washings.





(Left) PA chest radiograph shows blastomycosis manifesting as a left lower lobe mass-like consolidation ➡. This characteristic imaging manifestation often mimics lung cancer. (Right) Composite image with axial CECT in lung (left) and soft tissue (right) window of a 39-year-old man with cough and fever shows right lower lobe consolidation \mathbf{E} and centrilobular nodules adjacent to a lobulated soft tissue mass that encases the right inferior pulmonary vein ▶ and the adjacent left atrium. Blastomycosis may mimic lung cancer.





Synonyms

- North American blastomycosis
- Chicago disease
- Gilchrist disease

Definitions

- Fungal infection with Blastomyces dermatitidis
- Dimorphic fungus: Disease caused by inhalation of airborne spores
- Found in dead, decaying, or moist material
- Pulmonary and disseminated forms

IMAGING

General Features

- Best diagnostic clue
 - Consolidation or mass in outdoorsmen from endemic area
- Location
 - o Unilateral (75%) more common than bilateral (25%)o Any lobe can be affected
- Size
- Range: Tiny nodules to lobar or multilobar consolidation
- Morphology
 - o Consolidation is most common manifestation

Radiographic Findings

- Acute patchy consolidation (70-90%)
 - Nonsegmental, segmental, lobar, or multilobarMass-like consolidation
 - Lung nodules of variable size, may be miliary
- Any lobe can be affected
- Cavitation (15-35%)
- Pleural thickening common, pleural effusion (20%)
- Lymph node enlargement (10-35%)
- Chronic blastomycosis: Upper lung fibrocavitary disease

CT Findings

- Characterization of airspace disease
- Evaluation of mass-like consolidations, cavitation, complications
- Identification of lymph node involvement

Imaging Recommendations

- Best imaging tool
 - Radiography usually suffices for detection and follow-up

DIFFERENTIAL DIAGNOSIS

Lung Cancer

- Indeterminate nodule or mass ± pleural thickening
- Fungal osteomyelitis may mimic metastasis

Pneumonia

- Bacterial
 - Patchy, segmental, or lobar consolidation
- Mycobacterial or fungal
 - o Consolidation, nodules, cavitation, miliary nodules
 - Lymphadenopathy

PATHOLOGY

General Features

- Etiology
 - Inhalation of conidia of *B. dermatitidis*Exposure typically occurs in heavily wooded areas
- Associated abnormalities
 Ulcerative skin, bone, genitourinary infections

Microscopic Features

- Bronchopneumonia evolves into noncaseating granulomas with central microabscesses
- Pyogranulomas
- Thermally dimorphic fungus
 - Source (soil): Mycelial form (room temperature)
 - Host (humans and animals): Inhalation of spores
 - Forms 8- to 15-μm round budding yeast (37°C)
- Characteristic yeast form found in sputum, pus, tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic or flu-like illness
 - Skin lesions common, draining sinus tract
- Other signs/symptoms
 - o Dissemination to skin, bone, genitourinary system
 - Hematogenous spread from lung infection
 - Osteomyelitis of vertebral body, pelvis, sacrum
- Clinical profile
 - Young to middle-aged outdoorsmen
 - Incubation period of ~ 6 weeks after exposure
 - o Severity varies with inoculum size and immune status
 - Immune-impaired host at increased risk

Demographics

- Age
- Most patients are adults, uncommon in children
- Epidemiology
 - Endemic to Southeastern USA, Great Lakes region, Central and South America, Africa

Natural History & Prognosis

- Mortality of untreated blastomycosis nearly 60%
- May develop progressive or disseminated disease

Diagnosis

• No reliable skin or serologic tests

Treatment

• Itraconazole

DIAGNOSTIC CHECKLIST

Consider

• Culture of lung biopsy specimens for *Blastomyces* in endemic areas

- Benedict K et al: Blastomycosis surveillance in 5 states, United States, 1987-2018. Emerg Infect Dis. 27(4), 2021
- 2. Maini R et al: Pulmonary blastomycosis: a case series and review of unique radiological findings. Med Mycol Case Rep. 28:49-54, 2020

Cryptococcosis

KEY FACTS

TERMINOLOGY

Infection of respiratory system by Cryptococcus neoformans

IMAGING

- Radiography
 - Multiple pulmonary nodules
 - Less commonly pulmonary masses
 - Patchy airspace consolidation
 - Lesions may exhibit cavitation
- CT
 - Pulmonary nodules or masses
 - Cavitation, more common in immunocompromised patients
 - Ground-glass opacity; CT halo sign
 - Mediastinal lymphadenopathy
 - Air-fluid levels in abscesses
 - o Pleural effusions

TOP DIFFERENTIAL DIAGNOSES

- Squamous cell carcinoma
- Pulmonary metastases
- Septic emboli
- Granulomatosis with polyangiitis

CLINICAL ISSUES

- Symptoms/signs
 - Cough, fever, chest pain, dyspnea, headache
- Serum cryptococcal antigen (sCRAG) used for diagnosis and monitoring
- Immunocompromised patients with more aggressive disease may have higher sCRAG titers
- Treatment: Oral and intravenous antifungals

DIAGNOSTIC CHECKLIST

• Consider cryptococcosis in immunocompromised patients with 1 or more lung nodules or masses

(Left) Axial NECT of a patient with cryptococcosis demonstrates clustered lobulated nodules \square in the left lower lobe. A cluster of nodules is one of the most common imaging manifestations of pulmonary cryptococcosis. (Right) Axial NECT shows consolidation \square , nodules 🔁, and interlobular septal thickening \bowtie in the right lower lobe. These findings persisted after treatment, leading to subsequent biopsy, which revealed pulmonary cryptococcosis.





(Left) Axial NECT of an asymptomatic patient shows a solitary pulmonary nodule → in the left upper lobe. (Right) Fused axial FDG PET/CT of the same patient demonstrates increased FDG uptake → in the left upper lobe nodule. Biopsy revealed cryptococcosis. Lung nodules due to infection or inflammation may result in increased uptake on FDG PET/CT examinations and may mimic primary lung cancer.





Definitions

• Infection of respiratory system by Cryptococcus neoformans

IMAGING

General Features

- Best diagnostic clue
 - Multiple pulmonary nodules that may cavitate
- Location
 - Peripheral > central lung
- Size
 - o Most 7-20 mm
 - May exceed 30 mm
- Morphology
 - Poorly-circumscribed margins
 - Clustered nodules most common
 - Solitary and scattered nodules less common

Radiographic Findings

- Pulmonary nodule(s) or mass(es)
- Patchy airspace consolidation
- May exhibit cavitation

CT Findings

- Pulmonary nodules
- Pulmonary masses less common
- Cavitation
 - More common in immunocompromised patients
 Air-fluid levels in abscesses
- Patchy airspace consolidation
- Ground-glass opacity
 - CT halo sign
- Mediastinal lymphadenopathy
 May exhibit central low attenuation
- Pleural effusions

Nuclear Medicine Findings

- PET/CT
 - FDG uptake variable
 - FDG-avid nodules or masses may mimic lung cancer and metastatic disease

Imaging Recommendations

- Best imaging tool
 - CT for assessment of lung nodules, masses, consolidations

DIFFERENTIAL DIAGNOSIS

Squamous Cell Carcinoma

- Most common lung cancer to cavitate
 Cavitation in 15% of cases
- Strongly associated with cigarette smoking

Pulmonary Metastases

- Well-defined pulmonary nodules or masses
- Hemorrhagic metastases may exhibit irregular margins and surrounding ground-glass opacity
 Renal cell cancer, melanoma, choriocarcinoma
- Squamous cell carcinomas and sarcomas may cavitate

Septic Emboli

- Poorly-defined pulmonary nodules or masses
- Varying degrees of cavitation

Granulomatosis With Polyangiitis

- Multiple cavitary pulmonary nodules or masses
- Consolidation and ground-glass opacity less common

PATHOLOGY

General Features

Etiology

- C. neoformans
 - Fungus typically affects respiratory system
 - Immunocompromised > immunocompetent

Microscopic Features

- Macrophages and proteinaceous fluid within airspaces
 - Correlate with ground-glass opacity surrounding pulmonary lesions

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Cough, fever
- Other signs/symptoms
 - Chest pain, shortness of breath, headache
- Clinical profile
 - Serum cryptococcal antigen (sCRAG) used for diagnosis and monitoring
 - Immunocompromised patients with more aggressive disease may have higher sCRAG titers

Natural History & Prognosis

- Immunocompromised patients
 - Radiographic abnormalities may improve, stabilize, or progress over time
 - Imaging abnormalities improve more slowly
 - o sCRAG titers decrease more slowly or fluctuate
- Immunocompetent patients
 - Radiographs improve and sCRAG titers decrease more rapidly over time in most

Treatment

- Antifungals
- Oral: Fluconazole
- o Intravenous: Amphotericin B

DIAGNOSTIC CHECKLIST

Consider

• Cryptococcosis in immunocompromised patients with 1 or more lung nodule(s) or mass(es)

- Wu HH et al: Clinicopathological features of isolated pulmonary cryptococcosis in HIV-negative patients. J Int Med Res. 48(6):300060520927877, 2020
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- Gazzoni FF et al: Fungal diseases mimicking primary lung cancer: radiologicpathologic correlation. Mycoses. 57(4):197-208, 2014

Paracoccidioidomycosis

KEY FACTS

TERMINOLOGY

- Paracoccidioidomycosis (PCM)
- Systemic mycosis endemic to Latin America secondary to fungi of genus *Paracoccidioides*, order Onygenales

IMAGING

- Acute PCM
 - Similar to primary tuberculosis complex
 - Hilar lymphadenopathy
 - o Pleural effusion
- Chronic PCM
 - Ground-glass opacities (58.4%)
 - o Nodules (45.5%)
 - o Emphysema (47.8%)
 - o Interlobular septal thickening (43.5%)
 - o Cavitation (39.1%)
 - o Consolidation (26.1%)
 - Reversed halo sign

TOP DIFFERENTIAL DIAGNOSES

- Tuberculosis
 - Upper lobe predominance
- Chronic histoplasmosis
 - Upper lobe predominance

CLINICAL ISSUES

- Acute/subacute (juvenile) 20%
 - Fever, lymphadenopathy, and hepatosplenomegaly
- Chronic (adult) 90%
 - Chronic cough, dyspnea, hemoptysis, and chest painExtrapulmonary foci
 - Oropharyngeal mucous membrane lesions and skin lesions
 - Adrenal, genital, or neurologic involvement
 - o M:F = 15:1-22:1
 - Protective effect of estradiol; inhibits transformation from mycelium to yeast

(Left) AP chest radiograph of a patient with

paracoccidioidomycosis shows bilateral subpleural predominant nodular and mass-like consolidations 2. (Right) Axial CECT of the same patient shows right upper lobe subpleural and peribronchovascular lobulated soft tissue nodules and masses 2 with intrinsic air bronchograms. Nodules are a

common but nonspecific finding in paracoccidioidomycosis.

Infection should be suspected in people who live in or come from endemic areas.









(Left) *AP* chest radiograph of a patient with

paracoccidioidomycosis shows multilobar bilateral basilar predominant nodular, linear, and reticular opacities. (Right) Axial NECT of the same patient shows reticular and nodular opacities 🖂, solid nodules of variable size \bowtie , and a left lower lobe cavitary mass 🔁. As with other fungal and mycobacterial infections, cavitation is a common finding. Unfortunately, there are no diagnostic imaging findings, and a high index of clinical suspicion is required to suggest the diagnosis.

Abbreviations

• Paracoccidioidomycosis (PCM)

Synonyms

• South American blastomycosis

Definitions

• Systemic mycosis endemic to Latin America due to fungus of genus *Paracoccidioides*

IMAGING

Radiographic Findings

- Acute
 - Similar to primary tuberculosis complex
 - o Hilar lymphadenopathy
 - o Pleural effusion
- Chronic (90%)
 - Reticular and linear opacities
 - o Nodules
 - o Consolidation
 - o Cavitation
 - Fibrosis-related findings
 - Architectural distortion, paracicatricial emphysema, bronchiectasis
 - Parenchymal alterations are bilateral; involve > 1/3 of lungs

CT Findings

- Ground-glass opacities (58.4%)
 - Focal, multifocal, or diffuse
- Nodules (45.5%)
 - Variable size and contours
- Emphysema (47.8%)
- Interlobular septal thickening (43.5%)
- Cavitation (39.1%)
- Pulmonary architectural distortion (30.4%)
- Consolidation (26.1%)
- Other findings
 - Reversed halo sign
 - o Cysts
- Tracheal involvement
 - o Irregular and circumferential wall thickening

DIFFERENTIAL DIAGNOSIS

Tuberculosis

- Upper lobe predominance
- Tree-in-bud opacities
- Pleural involvement more common

Chronic Histoplasmosis

- Upper lobe predominance
- Common pleural thickening adjacent to pulmonary lesions

Coccidioidomycosis

- Endemic areas different from those of tuberculosis
- Upper lobe predominance (chronic disease)

PATHOLOGY

General Features

Etiology

- Dimorphic fungi of genus *Paracoccidioides*, order Onygenales
- By molecular taxonomy, 2 species of *Paracoccidioides* (*P. brasiliensis* and *P. lutzi*); 4 recognized variants of *P. brasiliensis* (S1, PS3, PS2, and PS4)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Acute /subacute (juvenile) 20%
 - Incubation period: 2 weeks to 3 months
 - Fever, lymphadenopathy, hepatosplenomegaly
 - o Chronic (adult) 90%
 - Reactivation of latent foci
 - Chronic cough, dyspnea, hemoptysis, and chest pain
 - Fever, anorexia, and weight loss
 - Extrapulmonary foci
 - Oropharyngeal mucous membrane lesions and skin lesions
 - Adrenal, genital, or neurologic involvement
- Diagnosis: Identification of fungus in tissue or clinical specimens

Demographics

- Age
 - Acute/subacute (< 30 years)
- Chronic (> 30 years)
- Sex
 - Acute: M:F = 1:1
 - Chronic: M:F = 15:1-22:1
 - Protective effect of estradiol; inhibits transformation from mycelium to yeast
- Epidemiology
 - Central and South American countries
 - Higher frequency in Brazil, Colombia, and Venezuela
 - Travelers from nonendemic affected after visiting natural *Paracoccidioides* reservoirs (even years later)
 - Variable incidence: 1-4 cases/100,000 persons/year in endemic areas; 9.4 cases/100,000 persons/year in hyperendemic areas
 - Major risk factor for PCM infection is exposure to rural areas
 - o Smoking
 - 90% of patients with chronic PCM are smokers
 - Risk of PCM in smokers is 14x higher

DIAGNOSTIC CHECKLIST

Consider

• PCM in individuals from endemic areas with ground-glass opacities, nodules, and cavitation

SELECTED REFERENCES

1. Queiroz-Telles FV et al: New insights on pulmonary paracoccidioidomycosis. Semin Respir Crit Care Med. 41(1):53-68, 2020

Aspergillosis

KEY FACTS

TERMINOLOGY

- Aspergillosis: Fungal infection caused by organisms of genus *Aspergillus*
- Most mycetomas are aspergillomas: Terms often used interchangeably

IMAGING

- Aspergilloma
- Nodule or mass within preexisting cavity
- Semi-invasive aspergillosis
 Slow-growing apical nodule or consolidation
- Airway invasive aspergillosis
- All way invasive asper gillosis
 Control pin way wall thicken in
 - Central airway wall thickening ± ulceration and bronchocentric nodules/bronchopneumonia
- Angioinvasive aspergillosis
 - Rapidly progressive lung nodules or consolidations, air crescent sign
 - CT halo sign suggests diagnosis in febrile neutropenic patient

TOP DIFFERENTIAL DIAGNOSES

- Bacterial pneumonia, mycobacterial infection
- Other fungal infections
- Pulmonary emboli
- Primary lung cancer

PATHOLOGY

• Most Aspergillus infections caused by A. fumigatus

CLINICAL ISSUES

- Aspergilloma: Immunocompetent
- Invasive aspergillosis: Severely immunocompromised
- Voriconazole is treatment of choice
- Bronchial artery embolization or surgery may be needed in patients with hemoptysis

DIAGNOSTIC CHECKLIST

• Consider angioinvasive aspergillosis in febrile neutropenic patients with new lung nodules or consolidations

(Left) AP chest radiograph of a 73-year-old man with neutropenic fever in the setting of previously resected pancreatic cancer and adjuvant Nivolumab shows multiple bilateral nodular $consolidations \supseteq$ with intrinsic central lucency. (Right) Coronal CECT of the same patient shows bilateral upper lobe cavitary lesions with heterogeneous intracavitary material 🖂, air crescents, and a small amount of surrounding ground-glass opacity, the so-called CT halo sign.





(Left) Fused axial dual-energy CECT iodine lung perfusion blood volume image of the same patient shows absence of perfusion 🔁 in the intracavitary devitalized lung and a faint increase in blood volume surrounding the lesions attributed to inflammation and hemorrhage. (Right) Graphic illustrates typical features of invasive aspergillosis, characterized by multifocal cavitary lesions containing devitalized lung 🔁 surrounded by air crescents and peripheral halos of hemorrhage 🔁.





Synonyms

 Mycetoma, aspergilloma: Most mycetomas are aspergillomas; terms often used interchangeably

Definitions

- Aspergillosis: Fungal infection caused by organisms of genus *Aspergillus* (> 100 species)
- **Saprophytic aspergillosis (aspergilloma)**: Fungus ball that develops in preexisting cavity
- Semi-invasive aspergillosis: Chronic necrotizing pulmonary aspergillosis
 - Subacute disease in patient with mildly depressed immune function or chronic underlying lung disease
- Invasive aspergillosis: Fungal infection that affects severely immunocompromised patients
 - Airway invasive aspergillosis: Central invasive airway infection
 - **Angioinvasive aspergillosis**: Rapidly progressive angioinvasive infection

IMAGING

General Features

- Best diagnostic clue
 - **Aspergilloma**: Dependent spherical or ovoid nodule that develops in preexisting cavity or cystic space
 - Angioinvasive aspergillosis: CT halo sign
 Nodule, mass, consolidation surrounded by groundglass opacity related to hemorrhage
- Location
 - Aspergillomas: Most within upper lobe preexisting cavities
- Size
 - Bronchocentric or miliary nodules to multifocal coalescent consolidations

Radiographic Findings

- Saprophytic aspergillosis (aspergilloma)
 - Intracavitary, dependent, nodule or mass with surrounding gas
 - May not be visible on radiography
- Semi-invasive aspergillosis
 - o Slow-growing nodule or upper lung consolidation
 - May coexist with aspergilloma(s)
 - Underlying chronic lung disease common
- Angioinvasive aspergillosis
 - Chest radiography may initially be normal
 - Rapid progression of lung nodules/consolidations
 - Air crescent sign
 - Crescent-shaped gas collection within nodule, mass, or consolidation
 - Consistent with invasive aspergillosis in appropriate setting
 - Indicates recovery of white blood cell function; associated with favorable outcome
 - May progress to extensive cavitation and necrosis
 - Pleural invasion: Pleural effusion, empyema, pneumothorax

CT Findings

Aspergilloma

- Heterogeneous nodule/mass within cavity: May fill entire cavity or move dependently
- May exhibit air crescent sign; Monod sign
- Semi-invasive aspergillosis
 - o Nodule, mass, consolidation + apical thickening
 - Cavitary disease

• Angioinvasive aspergillosis

- Multifocal peribronchial or lobar consolidation, centrilobular nodules, ground-glass opacities
- Peripheral wedge-shaped consolidation may mimic pulmonary infarct
- CT halo sign
 - Peri-lesional hemorrhage
 - Highly suggestive of invasive aspergillosis in appropriate setting
 - Consistent early finding of angioinvasive aspergillosis
 - May be seen in other invasive fungal infections or noninfectious entities
- Air crescent sign, suggests invasive aspergillosis
 - < 1/2 of affected patients, often after start of therapy
 Antifungal therapy and immune recovery:
 "Shrinking" of necrotic lung and development of curvilinear gas-filled void

• Airway invasive aspergillosis

- Tracheal and central bronchial wall thickening ± ulcerations
- Bilateral centrilobular and tree-in-bud nodules → bronchopneumonia
- May be seen in profound neutropenia or AIDS

Imaging Recommendations

- Best imaging tool
 - CT: Assessment of lung abnormalities and features of angioinvasive fungal disease

DIFFERENTIAL DIAGNOSIS

Bacterial Pneumonia

 Lung abscess with cavitation may mimic angioinvasive aspergillosis

Other Fungal Infections

- *Mucormycosis, Cryptococcus,* and *Candida* species
- May produce angioinvasive disease with halo sign and cavitation

Mycobacterial Infection

- May exhibit consolidation, halo sign, and cavitation
- Cavitary tuberculosis may mimic mycetoma

Pulmonary Emboli

- Bland or septic emboli
- Resultant lung infarcts may appear similar
 Peripheral nodule or consolidation ± halo sign

Non-Small Cell Lung Cancer

- Cavitary lung cancer may mimic mycetoma
- Tumor-related vascular invasion and infarction
PATHOLOGY

General Features

- Etiology
 - Ubiquitous environmental fungus found in soil and decaying organic material (leaves, grain)
 - Most infections caused by *Aspergillus fumigatus; A. flavus* and *A. niger* less common

Gross Pathologic & Surgical Features

- Angioinvasive aspergillosis: Hyphae invade blood vessels
 - Vascular invasion results in infarct, hemorrhage, and systemic dissemination
 - Devitalized lung within cavitary invasive aspergillosis mimics aspergilloma
- Airway invasive aspergillosis: Infection deep to airway basement membrane

Microscopic Features

- Dimorphic fungus: Conidial and hyphal forms, 45° angle branching
- Aspergilloma: Mass containing hyphae, fibrin, and mucus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Cough, fever, chills, dyspnea, chest pain
- Clinical profile
 - Aspergillomas affect immunocompetent patients
 - Underlying lung disease with preexisting cavity
 - □ Bullae, prior mycobacterial/fungal infection
 - Upper lung disease: Sarcoidosis, cystic fibrosis
 - Semi-invasive aspergillosis affects mildly immunocompromised patients
 - Chronic illness; prolonged corticosteroid use
 Malignancy, diabetes mellitus, alcoholism, malnutrition
 - □ Underlying chronic lung disease (emphysema)
 - Airway and angioinvasive aspergillosis affect severely immunocompromised patients
 - Bone marrow and solid organ transplants (up to 25%)
 - Acute leukemia (up to 20%)
 - Chemotherapy-induced immune deficiency (up to 20%)
 - No preexisting lung abnormality

Demographics

- Age
 - Advanced age more susceptible; any age group may be affected
- Epidemiology
 - o Estimated 200,000 cases annually, worldwide
 - Nearly 15,000 hospitalizations in USA in 2014
 - Most cases sporadic; nosocomial outbreaks do occur
 - Associated with hospital construction or renovation with resultant increased airborne fungus
 - Most common type of fungal infection among stem cell transplant recipients
 - Second most common among solid organ transplants
 - One of top four most common diagnoses leading to death in ICU autopsy studies

- Secondary fungal infection may affect mechanically ventilated patients with acute lung injury
 - COVID-19-associated pulmonary aspergillosis (CAPA)
 - o Influenza-associated pulmonary aspergillosis (IAPA)

Diagnostic Options

- Sputum culture, bronchoalveolar lavage, transthoracic/open lung biopsy
- Elevated serum galactomannan and Fungitell levels
- Serum Aspergillus precipitin test

Natural History & Prognosis

- Aspergilloma may remain stable for years
 - Prognosis generally good
 - Hemoptysis in 40%; may be life threatening
- Semi-invasive aspergillosis progresses over weeks to years
 Prognosis often good, reports of up to 40% mortality
- Angioinvasive aspergillosis progresses over days to weeks
 Poor prognosis, high mortality
- Increased incidence of antifungal resistant infection
 - Prior exposure or environmental factors
 - Up to 7% of Aspergillus specimens in transplant patients
 - Agricultural use of azole fungicides may lead to regional growth of resistant strains

Treatment

- First line: Azole antifungal agents
 - o Aspergilloma
 - Oral itraconazole
 - Intracavitary amphotericin B
 - o Semi-invasive and invasive aspergillosis
 - Voriconazole is treatment of choice
 - Amphotericin B and caspofungin also effective
- Prophylaxis for severely immunocompromised
- Bronchial artery embolization or surgical excision for massive or recurrent hemoptysis

DIAGNOSTIC CHECKLIST

Consider

• Angioinvasive aspergillosis in febrile, neutropenic patient with new lung nodules or consolidations

Image Interpretation Pearls

- Aspergillomas develop in preexisting cavities
 - Pleural thickening adjacent to cavity may suggest aspergilloma
 - Cavities should be examined for aspergillomas and monitored closely over time
- Invasive aspergillosis develops in previously normal lungs of patients with neutropenia

Reporting Tips

• Imaging findings suggestive of angioinvasive aspergillosis warrant prompt initiation of antifungal therapy; prior to tissue confirmation or speciation if necessary

SELECTED REFERENCES

1. Webb BJ et al: Epidemiology and clinical features of invasive fungal infection in a US health care network. Open Forum Infect Dis. 5(8):ofy187, 2018

Aspergillosis





(Left) AP chest radiograph of a 75-year-old man with acute myelogenous leukemia and neutropenic fever shows a focal right upper lobe masslike opacity 🛃. (Right) Axial NECT of the same patient confirms a 5-cm right upper lobe mass 🔁 with intrinsic air bronchograms. CT-guided biopsy demonstrated invasive aspergillosis. While the halo sign is helpful in suggesting angioinvasive fungal disease, its absence does not exclude the diagnosis. The diagnosis should be suspected in patients with neutropenic fever.





(Left) AP chest radiograph of a 62-year-old woman with hemoptysis shows biapical parenchymal scarring and a right upper lobe mass-like opacity with linear peripheral lucencies 🔁 and adjacent heterogeneous consolidations ► (Right) Axial CECT of the same patient shows a right upper lobe mass 🔁 with adjacent cystic lucencies \square , consistent with bronchiectasis and cavitation. Peripheral lucencies 🔁 suggest a process within an existing cavity. Note adjacent consolidation \blacksquare and ground-glass opacity.





(Left) Fused axial dual-energy CECT iodine lung perfusion blood volume image of the same patient shows absent perfusion ➡ in the mass and reduced perfusion \supseteq in the thickened cavity wall. (Right) PA DSA image of the same patient during bronchial artery embolization demonstrates a markedly enlarged right bronchial artery \square with foci of contrast blush 🖂 surrounding the lesion. Embolization temporized the patient's hemoptysis. Resection was performed, and diagnosis of aspergilloma was confirmed.

Aspergillosis

(Left) AP chest radiograph of a 51-year-old woman with neutropenic fever in the setting of myelodysplastic syndrome receiving Decitabine shows multiple irregular opacities in the right upper lobe \supseteq and left perihilar region 🖂. (Right) Sagittal CECT of the same patient shows a lingular mass-like consolidation with an area of central hypoattenuation 🛃 reflective of necrosis or hypoattenuating fungal elements. Note an additional small nodule 🔁 in the apicoposterior left upper lobe.





(Left) Axial CECT of the same patient shows bilateral small irregular nodules ⊇ and a right upper lobe mass-like consolidation ⊇ surrounded by subtle faint ground-glass attenuation. (Right) Axial CECT of the same patient shows the

peribronchovascular location of the dominant lesion, which displaces adjacent blood vessels and central hypoattenuation 2. Typical imaging findings of angioinvasive aspergillosis should prompt urgent initiation of antifungal therapy.





(Left) Axial CECT of a 38-yearold woman with end-stage sarcoidosis and new hemoptysis shows a left upper lobe thick-walled cavitary mass with intrinsic heterogeneous content *→* and an air crescent sign *⊡*. The findings are typical of mycetoma, and aspergilloma was diagnosed on surgical resection. (Right) Coronal NECT of a 40-year-old woman shows chronic thin-walled lung cavities 🔁 with intrinsic soft tissue nodules, consistent with mycetomas or saprophytic aspergillosis.





Aspergillosis





(Left) Axial NECT of a 76-year old man with acute myelogenous leukemia and neutropenic fever shows a nonspecific left upper lobe consolidation with a small amount of adjacent groundglass opacity. (Right) Axial CECT of the same patient obtained 6 days later because of radiographic disease progression shows the rapid progressive nature of angioinvasive aspergillosis with a significantly increased left upper lobe consolidation and new clustered nodules in the left lower lobe.





(Left) Axial CECT of a 40-yearold man with prior tuberculosis shows an aspergilloma manifesting as an intracavitary, partially calcified nodule in the dependent aspect of the right upper lobe cavity. (Courtesy S. Digumarthy, MD.) (Right) Axial prone CECT of the same , patient shows that the aspergilloma moves to the dependent aspect of the cavity. Repeat low-dose CT in the prone position may help demonstrate intracavitary mobility of an aspergilloma. (Courtesy S. Digumarthy, MD.)





(Left) High-power photomicrograph (H&E stain) shows fungal hyphae branching at 45° angles ➡, typical of Aspergillus species. (Right) Axial NECT of a 54year-old man with acute myelogenous leukemia and invasive aspergillosis shows multifocal cavitary nodules, some with air crescents ➡, around devitalized lung tissue and surrounding ground-glass opacity halos ➡. The findings are characteristic of angioinvasive fungal infection.

Zygomycosis

KEY FACTS

TERMINOLOGY

- Synonym: Mucormycosis
- Opportunistic infection caused by fungi belonging to *Zygomycetes* class
 - Rhizopus and Mucor are most common

IMAGING

- Radiography
 - Unilateral or bilateral mass-like consolidation
 - Solitary or multiple nodules or masses
 - Small pleural effusion
 - Hilar lymphadenopathy
- CT
 - o Nodule(s) and mass(es)
 - Ground-glass halo related to hemorrhage
 - Reversed halo sign
 - o Cavitation
 - o Consolidation; may be mass-like or wedge-shaped

TOP DIFFERENTIAL DIAGNOSES

- Aspergillosis
- Bacterial pneumonia

PATHOLOGY

• Distinctive hyphae: Branching at 90° angles, rare septations

CLINICAL ISSUES

- Fever, cough, dyspnea, chest pain
- Risk factors: Diabetic ketoacidosis, hematologic malignancy, steroids, solid organ or hematopoietic stem cell transplant
- Treatment: Excision of localized disease, amphotericin B
- High mortality: > 60%

DIAGNOSTIC CHECKLIST

• Consider zygomycosis in immunocompromised patients with fever and consolidation, but particularly in patients with poorly-controlled diabetes or hematologic malignancies

(Left) PA chest radiograph of a 39-year-old woman with acute myeloid leukemia, fever, and cough secondary to zygomycosis shows bilateral nodular opacities 🔁. (Right) Coronal CECT of the same patient shows a right upper upper lobe nodule 🔁 and a left upper lobe mass-like consolidation \square , both of which exhibit with internal lucencies that suggest cavitation. Zygomycosis is a relatively uncommon infection that manifests as consolidation(s), nodule(s), or mass(es) and mostly affects immunocompromised hosts.











Synonyms

• Mucormycosis

Definitions

• Opportunistic infection caused by fungi belonging to *Zygomycetes* class, which includes *Rhizopus, Mucor*, and *Lichtheimia*

IMAGING

Radiographic Findings

- Predominantly peripheral distribution
- Solitary or multiple nodules or masses
- Unilateral or bilateral consolidation(s), may be mass-like
- Small pleural effusion
- Hilar lymphadenopathy

CT Findings

- Nodule(s) and mass(es)
 - Ground-glass halo related to hemorrhage
 - Ground-glass halo may be larger than solid component
 - Usually present at initial CT
 - Reversed halo sign, ground-glass opacity surrounded by peripheral consolidation
 - Most common cause of reversed halo in immunocompromised host
 - Air crescent sign, central cavitation
 - Cavitation usually absent on initial imaging
 - Necrosis and cavitation usually manifest after development of halo or reversed halo signs
 - Concurs with resolution of neutropenia
- Consolidation
 - May be wedge-shaped
 - May exhibit internal air bronchograms
- Endocarditis
 - Filling defects in pulmonary arteries
- Pulmonary artery pseudoaneurysm (infrequent)
- Direct extension into adjacent mediastinum, heart, diaphragm
- Hypoattenuating hepatic, splenic or renal lesions from hematogenous spread

Imaging Recommendations

- Best imaging tool
 - CECT allows further characterization of radiographic abnormalities
 - Transbronchial or CT-guided needle biopsy helpful in identifying organism

DIFFERENTIAL DIAGNOSIS

Aspergillosis

- Difficult to distinguish from zygomycosis clinically and radiologically
- Factors that favor zygomycosis over aspergillosis
 Concomitant sinusitis
 - > 10 pulmonary nodules on CT
 - o Pleural effusion
 - Prior voriconazole prophylaxis

Bacterial Pneumonia

• Lack of response to empiric antibiotic therapy should raise suspicion for atypical organisms

PATHOLOGY

Microscopic Features

- Distinctive hyphae
 - ο Broad (5-15 μm in diameter)
 - o Irregular branching pattern, branches at 90° angles
 - Rare septations
- Vascular invasion: Resultant necrosis, infarction, aneurysm

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Fever, cough, dyspnea, chest pain
 - Other signs/symptoms
 - o Hemoptysis

Demographics

- Epidemiology
 - 3rd most common invasive fungal infection, after aspergillosis and candidiasis
 - 8.3-13.0% of all fungal infections in autopsies of patients with hematologic malignancies
 - Pulmonary involvement caused by inhalation of spores or hematogenous spread
 - Ubiquitous in nature: Decaying vegetation and soil
 - Risk factors
 - Diabetes, particularly ketoacidosis
 - Leukemia, lymphoma
 - Steroid treatment
 - Solid organ and hematopoietic stem cell transplant
 - Intravenous drug user
 - Deferoxamine therapy
 - Neutropenia

Natural History & Prognosis

- Rapid progression and tissue destruction
- Mortality 60-100% in immunocompromised patients

Treatment

- Surgical resection: Lobectomy for localized disease
- Antibiotics
 - Intravenous amphotericin B
 - o Oral posaconazole
 - After response to amphotericin B
 - 2nd-line therapy for patients who do not tolerate or respond to amphotericin B

DIAGNOSTIC CHECKLIST

Consider

• Zygomycosis in immunocompromised patients with fever and consolidation, but particularly in patients with poorlycontrolled diabetes or hematologic malignancies

SELECTED REFERENCES

 Lin CY et al: Comparison of clinical manifestation, diagnosis, and outcomes of invasive pulmonary aspergillosis and pulmonary mucormycosis. Microorganisms. 7(11), 2019

KEY FACTS

TERMINOLOGY

- Pneumocystis pneumonia (PCP); Pneumocystis jirovecii pneumonia (PJP)
- Opportunistic fungal infection that affects individuals with T-cell immunodeficiency

IMAGING

- Radiography
 - Normal, diffuse bilateral heterogeneous opacities
 - Spontaneous pneumothorax in HIV(+) patient is nearly diagnostic of PCP
- CT
 - Ground-glass opacities are dominant finding
 - o Crazy-paving pattern, less common
 - Variable-sized cysts, variable wall thickness
 - Atypical patterns: Multiple small nodules, lobar consolidation, masses
 - Lymphadenopathy uncommon (10%)
 - o Pleural effusion rare

TOP DIFFERENTIAL DIAGNOSES

- Cytomegalovirus pneumonia
- Diffuse alveolar hemorrhage
- Lymphoid interstitial pneumonia
- Hypersensitivity pneumonitis
- Pulmonary alveolar proteinosis

CLINICAL ISSUES

- Most prevalent opportunistic infection in AIDS
- HIV(+) patients: Subacute fever, cough, dyspnea
- Non-HIV patients: Fulminant respiratory failure, fever, cough
- Diagnosis: Bronchoscopy with bronchoalveolar lavage
- Treatment: Trimethoprim-sulfamethoxazole, IV pentamidine

DIAGNOSTIC CHECKLIST

• Consider PCP in immunocompromised patient with diffuse bilateral ground-glass opacities

(Left) AP chest radiograph of a 41-year-old woman with HIV/AIDS who presented with subacute cough, fever, and dyspnea shows typical radiographic findings of pneumocystis pneumonia characterized by diffuse bilateral hazy pulmonary opacities. (Right) Axial CECT of the same patient demonstrates diffuse bilateral ground-glass opacities, with a few scattered foci of lobular sparing 🔁. Diffuse groundalass opacities are the most common CT manifestation of Pneumocystis jirovecii pneumonia.





(Left) AP chest radiograph of a 47-year-old man with HIV/AIDS and pneumocystis pneumonia shows diffuse bilateral opacities, ill-defined heterogeneous consolidations, and scattered cystic spaces 🖂 Note small right apical pneumothorax 🗁 and right pleural catheter in place. (Right) Coronal NECT of the same patient shows diffuse bilateral ground-glass opacities, scattered lobular and confluent consolidations \blacksquare , and cysts \blacksquare . The small right pneumothorax is secondary to cyst rupture into the adjacent pleural space.





Abbreviations

- Pneumocystis pneumonia (PCP)
- Pneumocystis jirovecii pneumonia (PJP)

Definitions

• Opportunistic fungal infection that often affects individuals with T-cell immunodeficiency

IMAGING

General Features

- Best diagnostic clue
 - Diffuse symmetric or patchy ground-glass opacities on CT in hypoxic immunocompromised patient
- Location
 - Diffuse lung involvement, relative central predominance
 - Less commonly upper lobe predominant disease with thin-walled cysts
- Morphology
 - Ground-glass opacities ± interlobular septal thickening, consolidations, cysts

Radiographic Findings

- Chest radiograph may be normal
- Diffuse or central predominant hazy and reticular opacities ± patchy consolidations
- Patient with AIDS and spontaneous pneumothorax: Highly suggestive of PCP

CT Findings

- HRCT
 - **Ground-glass opacities** are dominant finding (92%)
 - Most commonly central with relative subpleural sparing (41%), heterogeneous with mosaic attenuation (29%), or diffuse (24%)
 - ± superimposed interlobular septal thickening and intralobular lines (crazy-paving pattern)
 - Upper lobe distribution may be associated with aerosolized pentamidine prophylaxis

• Cysts (10-34%)

- Variable size and wall thickness; usually thin-walled
- Upper lobe predominant
- Resolution within several months with successful treatment
- Rarely described in patients without HIV/AIDS

Consolidations

- Lobular, confluent, patchy, diffuse
- Suggest severe/progressive disease or additional superimposed infection/aspiration

$\circ~$ Spontaneous pneumothorax

Associated with rupture of subpleural cysts/pneumatoceles

$\circ~$ Less common findings

- Multiple small nodules (1-10 mm) related to granuloma formation (± cavitation); miliary pattern
- Segmental or lobar consolidation
- Mass(es)
- Mediastinal &/or hilar lymphadenopathy
- Pleural effusion (rare)
- Punctate subpleural calcification

• Chronic PCP findings

- Linear and reticular opacities, bronchiectasis, architectural distortion
- Large nodules > 10 mm
- Confident diagnosis in 95% of patients with AIDS

Imaging Recommendations

Best imaging tool
 HRCT

DIFFERENTIAL DIAGNOSIS

Cytomegalovirus (CMV) Pneumonia

- Affects similar immunocompromised patient population: Most common co-associated infection
- Most frequent finding: Bilateral diffuse ground-glass opacities ± consolidation
- Centrilobular nodules (± ground-glass opacities) more common than in PCP

Diffuse Alveolar Hemorrhage (DAH)

- Diffuse bilateral ground-glass opacities with crazy-paving pattern and consolidations
- Clinical history, tissue sampling, and laboratory investigation required to differentiate various etiologies of DAH

Lymphoid Interstitial Pneumonia (LIP)

- Increased frequency in patients with HIV/AIDS, especially children
- Thin-walled cysts, ground-glass opacities ± small lobular consolidations, centrilobular nodules
- Lymphadenopathy more common than in PCP

Hypersensitivity Pneumonitis

- Diffuse heterogeneous ground-glass opacities, most common imaging manifestation
- Ill-defined centrilobular nodules more common than in PCP
- Air-trapping common at expiratory CT, uncommon with PCP

Noncardiogenic Edema

- Frequent predisposing etiology: Sepsis, toxic fume inhalation, surgery, aspiration
- Gradient of findings: Normal nondependent lung to ground-glass opacities to consolidated dependent lung
- Severely hypoxic patients

Pulmonary Alveolar Proteinosis

- Indolent symptoms (often over months), except rare patients with hematologic malignancy
- Fever and severe hypoxia uncommon (33% asymptomatic)
- Ground-glass opacities with interlobular septal thickening and intralobular lines
 - Crazy-paving pattern less common in PCP

PATHOLOGY

General Features

- Etiology
- Patients with impaired cell-mediated immunity predisposed to PCP
 - HIV/AIDS, specifically in patients with CD4 counts that are < 200/mm³

- Long-term corticosteroid therapy, particularly during tapering phase
- Organ transplantation, bone marrow transplantation, chemotherapy, immunotherapy
- Congenital immunodeficiency
- Prematurity and malnutrition

Gross Pathologic & Surgical Features

- Opportunistic fungal infection caused by *P. jirovecii*
- Organism difficult to culture

Microscopic Features

- Intraalveolar foamy exudate, fungus usually seen in tiny bubble-like areas
- Radiologic-pathologic correlation
 - Ground-glass opacities: Alveolar filling by foamy exudates (surfactant, fibrin, cellular debris) containing pneumocystis organisms
 - Interlobular septal thickening and intralobular lines: Interstitial space expansion by edema or cellular infiltration
 - Nodules: Granuloma, inflammation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - HIV/AIDS patients
 - Younger patients
 - Subacute clinical course: Fever, cough, dyspnea; often gradual worsening over 2-6 weeks
 - Non-HIV/AIDS patients
 - Older patients
 - Risk factors: Lymphopenia, chronic corticosteroids, combination immunosuppressive agents, and concomitant lung disease
 - Severe/fulminant presentation: Abrupt onset respiratory failure with fever and cough usually developing over 4-10 days
- Other signs/symptoms
 - Hypoxia on room air: Common and important clinical feature
 - Absence of hypoxia favors entities other than PCP
 - White blood cell count usually not elevated
 - Patients with AIDS usually develop infection when CD4 count < 200/mm³
 - 90% have elevated LDH
 - Rising LDH despite therapy predicts poor outcome

Demographics

- Age
 - Any age, dependent on risk factors
- Epidemiology
 - Organism found in normal lungs, without associated disease
 - Airborne transmission
 - Even with highly active antiretroviral therapy (HAART), PCP remains most prevalent opportunistic infection in AIDS
 - Up to 15% patients after bone marrow or solid organ transplant (without prophylaxis)

Natural History & Prognosis

- Prophylaxis in patients with AIDS indicated when CD4 count < 200/mm³
 - Patients with CD4 < 200/mm³ not on prophylaxis, 9x more likely to develop infection
 - Consider in patients on prolonged corticosteroid therapy or immunosuppressive monoclonal antibodies
 - Main prophylactic medications: Oral trimethoprimsulfamethoxazole, dapsone, atovaquone, aerosolized pentamidine
- Diagnosis
 - Bronchoscopy with bronchoalveolar lavage (BAL) is procedure of choice
 - Sputum induction with hypertonic saline can be used: 50-90% diagnostic yield
 - PCR: Greater sensitivity and specificity than conventional or histochemical stains and immunofluorescence for diagnosis
 - Serum β-D-glucan testing (Fungitell) may enable diagnosis
 - Easier to diagnose in patients with HIV/AIDS: Reported sensitivities of up to 98%
 - Non-HIV/AIDS patients: PCP more difficult to diagnose
 - Less fungal load, greater inflammatory component
 - Delayed diagnosis: Negative sputum &/or BAL may lead to consider other diagnoses
 - High clinical suspicion required
 - Transbronchial biopsy may be needed for diagnosis
- Mortality rate: Affected patients with HIV/AIDS (1-15%); non-AIDS patients (30-45%)

Treatment

- Appropriately treated PCP has a very good prognosis
 - Trimethoprim-sulfamethoxazole most commonly used medication (numerous other options available)
 - Frequent progression of radiographic abnormalities in early course of therapy as large amount of IV fluid required for drug administration
 - Anti-pneumocystic medication often used with concomitant steroids to minimize inflammation
 - PCP and severe hypoxia: Early adjuvant corticosteroid therapy with significantly decreased rate of respiratory failure
 - After treatment initiation, clinical improvement in 80% of cases (mean: 5 days)
 - Radiographic improvement lags by approximately 5 days

DIAGNOSTIC CHECKLIST

Consider

• PCP in immunocompromised patient with diffuse bilateral ground-glass opacities

SELECTED REFERENCES

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- Hsu JM et al: Radiographic features in investigated for Pneumocystis jirovecii pneumonia: a nested case-control study. BMC Infect Dis. 20(1):492, 2020





(Left) AP chest radiograph of a 34-year-old woman with HIV/AIDS who presented with subacute chest pain and fever shows pneumocystis pneumonia manifesting as bilateral ill-defined diffuse hazy pulmonary opacities. (Right) Axial CECT of the same patient shows diffuse bilateral ground-glass opacities and a few tiny thin-walled pulmonary cysts []. These are typical CT manifestations of P. jirovecii pneumonia.





(Left) Axial CECT of a 72-yearold man who was receiving chemotherapy for lymphoma and presented with cough and fever shows multifocal geographic areas of groundglass attenuation. P. jirovecii was detected on sputum analysis. (Right) Coronal CECT of a 53-year-old man with neutropenic fever and pneumocystis pneumonia shows bilateral ground-glass opacities and consolidations with intrinsic air bronchograms 🛃. Mediastinal $lymphadenopathy \supseteq was$ related to known lymphoma.





(Left) PA chest radiograph of a 40-year-old man with HIV infection noncompliant with highly active antiretroviral therapy (HAART) shows pneumocystis pneumonia manifesting with asymmetric right lung diffuse, hazy, and reticular opacities. (Right) Axial CECT of the same patient shows right lung ground-glass opacities, thickened peribronchovascular interstitium, and a small right lower lobe thin-walled cyst *⊡*. Asymmetric lung involvement is an atypical manifestation of pneumocystis pneumonia.

Dirofilariasis

KEY FACTS

TERMINOLOGY

- Dirofilaria immitis (dog "heartworm")
- Filarial nematode found commonly in heart of dogs and other mammals, (e.g., cats, foxes, muskrats, and wolves)
- Humans are accidental hosts that become infected by microfilaria transmitted by mosquitoes

IMAGING

- Solitary pulmonary nodule (90%)
- Non-calcified
- Peripheral location
- More common in lower lobes
- 1-3 cm in diameter
- Variable degree of metabolic activity on FDG PET/CT

TOP DIFFERENTIAL DIAGNOSES

- Fungal infection
 - o Histoplasmosis
 - o Coccidioidomycosis

- Tuberculosis
- Lung cancer

PATHOLOGY

- Round nodule surrounded by granulomatous zone of epithelial cells, plasma cells, lymphocytes, and fibrous capsule rich in eosinophils
- Calcification and caseous necrosis
- Dead parasite within thrombotic pulmonary artery
- Overlying pleura usually inflamed and fibrotic (75%)

CLINICAL ISSUES

- Typically asymptomatic
- Predominantly adults; average age: ~ 50 years
- M:F = 2:1 (USA)

DIAGNOSTIC CHECKLIST

• Consider dirofilariasis in patient with solitary pulmonary nodule in areas endemic for canine dirofilariasis

(Left) PA chest radiograph of an asymptomatic 14-year-old girl with dirofilariasis shows a noncalcified solitary lung nodule 🛃 in the right upper lobe. Histopathologic analysis demonstrated an infarcted peripheral vessel containing remnants of the parasite. Surgical excision is usually required for definitive diagnosis. (Right) Axial CECT of a patient with dirofilariasis shows a peripheral lung nodule with a surrounding air $crescent \blacksquare$. Such CT findings may mimic angioinvasive fungal infection. (Courtesy P. Boiselle, MD.)

(Left) PA chest radiograph of a patient with dirofilariasis shows a faint nodular opacity \blacksquare in the right middle lobe. (Right) Axial NECT of the same patient shows a solitary welldefined middle lobe nodule Primary lung cancer should be excluded, particularly if the patient is a smoker. Definitive diagnosis is usually made histologically or with needle aspiration of the nodule and demonstration of fragments of the parasite. (Courtesy N. Patz, MD.)









Synonyms

• Dirofilaria immitis (dog "heartworm")

Definitions

- Filarial nematode found commonly in hearts of dogs and other mammals (e.g., cats, foxes, muskrats, and wolves)
- Humans are accidental hosts
 Become infected by microfilaria transmitted by mosquitoes

IMAGING

General Features

- Best diagnostic clue
 - Solitary pulmonary nodule (90%)
- o Multiple or bilateral (10%)
- Location
 - Peripheral more common in lower lobes (67%)
- Morphology
- Spherical, wedge-shaped, non-calcified

Radiographic Findings

- Radiography
 - o Well-circumscribed, noncalcified lung nodule
 - o Typically subpleural (68%)
 - o Right lower lobe affected in 76% of cases
 - o 1-3 cm in diameter

CT Findings

- NECT
 - o Solitary/multiple lung nodules
 - Typically subpleural (68%)
 - Non-calcified; rare eccentric calcification
 - Air crescent sign (rare)
 - May exhibit feeding vessel
 - Pleural thickening or effusion

Nuclear Medicine Findings

• Variable degree of metabolic activity on FDG PET/CT

DIFFERENTIAL DIAGNOSIS

Fungal Infection

- Histoplasmosis
- Coccidioidomycosis

Lung Cancer

• May manifest as solid or subsolid lung nodule

Metastasis

- Typically multiple
- Solitary metastasis rare

PATHOLOGY

General Features

- Etiology
 - o D. immitis (dog "heartworm")

Gross Pathologic & Surgical Features

- Solitary nodule (90%)
- Multiple nodules (10%)

• Lung nodule

- End-stage lesion resulting from death of parasite in pulmonary vascular bed
- o Well-circumscribed, grayish-yellow rounded nodule

Microscopic Features

- Nodule with fibrous capsule rich in eosinophils
- Nodule surrounded by granulomatous zone of epithelial cells, plasma cells, and lymphocytes
- Peripheral fibrosis
- Calcification and caseous necrosis
- Dead parasite within thrombotic pulmonary artery
- Overlying pleura usually inflamed and fibrotic (75%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Usually asymptomatic
 - Subcutaneous or lung parenchymal nodule(s)
- Other signs/symptoms
 Cough and hemoptysis
 - Blood eosinophilia (< 10%)

DemographicsAge

- Predominantly adults; average age: ~ 50 years
- Sex
 - M:F = 2:1 (USA)
- Epidemiology
 - Related to prevalence of canine dirofilariasis and suitable mosquito vectors
 - Temperate climates: East Coast and Southern USA; sporadic cases worldwide
 - Should be included in differential diagnosis of solitary pulmonary nodule, especially in endemic areas

Natural History & Prognosis

- Usually infects dogs
- Disease transferred to humans by mosquito bites
 - Pulmonary embolization: Granulomatous reaction and infarct
- Dirofilaria stop developing at temperatures below 14°C
 Predominant occurrence in warmer climates

DIAGNOSTIC CHECKLIST

Consider

- Dirofilariasis in patient with solitary pulmonary nodule in areas endemic for canine dirofilariasis
 - Often incidental finding on imaging exams for unrelated or nonspecific symptoms

Image Interpretation Pearls

• No distinctive imaging features that allow differentiation from other conditions that manifest as solitary pulmonary nodules

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- Atsumi E et al: Thirteen cases of pulmonary dirofilariasis in a single institution in Okinawa Island. Virchows Arch. 475(3):335-40, 2019
- 2. Jacob S et al: Human pulmonary dirofilariasis masquerading as a mass. Asian Cardiovasc Thorac Ann. 24(7):722-5, 2016

Hydatidosis

KEY FACTS

TERMINOLOGY

- Parasitic disease caused by larval stage (metacestode) of cestodes (tapeworms) of genus *Echinococcus*
- Four species known to infect humans: *E. granulosus, E. multilocularis, E. vogeli, E. oligarthrus*

IMAGING

• Radiography

- Solitary or multiple spherical or ovoid masses with welldefined borders
- Variable size (1 cm to > 20 cm)
- o Tracheobronchial communication (rupture): Meniscus/crescent or water lily/camalote sign
 o Pleural effusion; hydropneumothorax
- CT
 - Spherical or ovoid fluid-filled cyst
 - Cyst wall enhancement
 - May involve mediastinum, heart, chest wall, pulmonary artery, diaphragm

TOP DIFFERENTIAL DIAGNOSES

- Benign cystic lesion
 - Foregut duplication cyst (bronchogenic cyst)
 - Congenital pulmonary airway malformation
- Malignancy
 - Primary sarcoma
 - Lung cancer
 - o Metastasis

CLINICAL ISSUES

- Usually asymptomatic: Incidental imaging finding
- Compression of adjacent structures
- Cyst rupture (tracheobronchial tree or pleura)
- Serologic test: ELISA AgB (antigen B-rich fraction)

DIAGNOSTIC CHECKLIST

• Consider hydatid cyst in patient from endemic sheepraising areas with solitary or multiple, well-defined pulmonary nodule(s) or mass(es)

(Left) PA chest radiograph of a 54-year-old man with pulmonary hydatid disease shows a large, sharply marginated lobular mass in the left upper lung zone. (Right) Axial CECT of the same patient shows a mass of homogeneous fluid attenuation surrounded by an enhancing peripheral soft tissue rim **➡**. E. granulosus was identified at pathologic analysis. In endemic areas, a large solitary spherical or ovoid fluid-filled cystic lung mass with well-marginated borders is characteristic of hydatid disease.









Synonyms

- Hydatid disease, hydatidosis
- Echinococcosis

Definitions

- Parasitic disease caused by larval stage (metacestode) of cestodes (tapeworms) of genus *Echinococcus*
 - Four species are known to infect humans
 - Echinococcus granulosus (E. granulosus): Cystic echinococcosis.
 - More common, wide distribution, endemic in sheep-raising areas (Australia, Mediterranean region, South America, Middle East, New Zealand)
 - Echinococcus multilocularis (E. multilocularis): Alveolar echinococcosis
 - Rare; most cases in Europe, some in China
 - Echinococcus vogeli (E. vogeli): Polycystic echinococcosis; Central and South America
 - *Echinococcus oligarthrus (E. oligarthrus*): Polycystic echinococcosis; South America

IMAGING

Radiographic Findings

- Radiography
 - Solitary or multiple spherical or ovoid masses; welldefined borders
 - Multiple (30%), bilateral (20%), lower lobe (60%)
 - Variable size (1 cm to > 20 cm)
 - Complications
 - Tracheobronchial communication (rupture)
 - Meniscus or crescent sign: Cyst communication with bronchus (air between pericyst and exocyst)
 - Water lily or camalote sign: Undulating cyst membranes floating in fluid
 - Hydatid pneumonitis: Aspiration of hydatid material (vomica)
 - Pleural effusion; hydropneumothorax

CT Findings

- NECT
 - Spherical or ovoid fluid-filled cyst (~ 0 HU); smooth, thin walls
 - Calcification extremely rare (0.7%)
- CECT
 - Cyst wall enhancement
 - May involve mediastinum, heart, chest wall, pulmonary artery, diaphragm
 - Complications: Acute hydatid pulmonary embolism (rare) from invasion of cardiovascular system
 - ± hepatic involvement

DIFFERENTIAL DIAGNOSIS

Benign Cystic Lesion

- Foregut duplication cyst (bronchogenic cyst)
- Congenital pulmonary airway malformation (CPAM)

Malignancy

• Primary sarcoma

- Lung cancer
- Metastasis

PATHOLOGY

Gross Pathologic & Surgical Features

- 3 layers
 - Pericyst: Dense and fibrous host reaction to parasite
 - **Exocyst** (outer laminated cyst membrane): Acellular portion of parasite, permits passage of nutrients
 - **Endocyst** (inner membrane): Germinal layer, produces larval scolices

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Usually asymptomatic: Incidental imaging finding
 - Compression of adjacent structures: Chest pain, cough, hemoptysis
 - Cyst rupture (tracheobronchial tree or pleura)
 - Expectoration of cyst fluid, membranes, scolices ("hydatid vomica")
 - Aspiration pneumonitis
 - Hypersensitivity reaction (antigenic material released by cyst): Fever, wheezing, urticaria; anaphylaxis (rare)
 - Chest pain: Pleural effusion, pneumothorax
- Other signs/symptoms
 - o Laboratory
 - Serologic test: ELISA AgB (antigen B-rich fraction)

Natural History & Prognosis

- Dog: Definitive host for *E. granulosus* (harbors adult worm in intestine)
 - Eggs shed in dog feces: Viable for weeks, contaminate food sources of intermediate hosts (sheep, cattle, horses)
- Humans (accidental intermediate hosts): Food contaminated with eggs; eggs migrate from gastrointestinal tract to circulation to reach liver (primarily affected organ)
 - Hydatid cysts develop over several months or years
- Secondary involvement by hematogenous dissemination may affect almost any anatomic location

DIAGNOSTIC CHECKLIST

Consider

 Hydatid cyst in patient from endemic sheep-raising areas with solitary or multiple, well-defined pulmonary nodule(s) or mass(es)

Image Interpretation Pearls

• Signs of complicated hydatid cyst: Meniscus or crescent sign, water lily or camalote sign

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- Saeedan MB et al: Thoracic hydatid disease: a radiologic review of unusual cases. World J Clin Cases. 8(7):1203-12, 2020
- 3. Sarkar M et al: Cystic pulmonary hydatidosis. Lung India. 33(2):179-91, 2016

KEY FACTS

TERMINOLOGY

• Infection by Strongyloides stercoralis

IMAGING

- Autoinfection
 - Diffuse reticular opacities and miliary nodules
 - Bronchopneumonia and patchy airspace opacities
 - Serial radiography may show migratory disease
- Hyperinfection syndrome
 - Diffuse bilateral airspace opacities
 - o Diffuse alveolar hemorrhage
- Imaging findings of acute respiratory distress syndrome
- Pleural effusions
- Cardiac enlargement (pericardium involvement)
- Secondary infection and abscess formation
 - Enteric bacteria (*Klebsiella pneumoniae, Escherichia coli,* etc.)
 - Cavitation and air-fluid levels

TOP DIFFERENTIAL DIAGNOSES

- Bronchopneumonia
- Diffuse alveolar hemorrhage
- Acute respiratory distress syndrome
- Chronic eosinophilic pneumonia

PATHOLOGY

- Autoinfection: Cycle of endogenous reinfection
- Hyperinfection syndrome: High worm burden
- Disseminated strongyloidiasis: Spread to organs outside of normal migration pattern
- Identification of larvae in stool, sputum, ± skin

CLINICAL ISSUES

- Consider strongyloidiasis in patients with focal or diffuse airspace disease in endemic locations
- Hyperinfection syndrome in immunosuppressed patients (corticosteroids, transplant, HIV, malnutrition, etc.)

(Left) AP chest radiograph of a patient with strongyloidiasis shows diffuse bilateral miliary micronodules. Autoinfection may manifest as miliary disease or diffuse reticular opacities. (Right) Composite image with CECT in lung (left) and soft tissue (right) window shows a right upper lobe $abscess \implies$ with an intrinsic air-fluid level and adjacent airspace disease 🔁. Note smaller right lower lobe abscess $\overline{ \Rightarrow}$. Mortality of patients with strongyloidiasis complicated by secondary infection approaches 80%.





(Left) Axial NECT of a patient with autoinfection shows a left lower lobe mass-like $consolidation \implies$ with intrinsic air bronchograms. In these patients, coalescent airspace opacities and consolidations indicate progression of disease burden. (Right) AP chest radiograph of an intubated patient demonstrates diffuse bilateral airspace opacities. Washings from bronchoalveolar lavage revealed Strongyloides stercoralis organisms in this patient with hyperinfection syndrome.





Definitions

• Infection by *Strongyloides stercoralis*

IMAGING

Radiographic Findings

Autoinfection

- o Migration of larvae from capillary bed into alveoli
 - Diffuse reticular opacities
 - Miliary nodules
- Progression of disease burden
 - Bronchopneumonia
 - Patchy airspace opacities; may coalesce
 - Migratory involvement on serial radiography

• Hyperinfection syndrome

- Diffuse bilateral airspace opacities
- Diffuse alveolar hemorrhage
- Acute respiratory distress syndrome (ARDS)
 - Bilateral airspace opacities and consolidations
- Pleural effusions
- Cardiac enlargement
 - Migration of larvae into pericardiumPericarditis and pericardial effusion

CT Findings

• Assessment for secondary infection, abscess formation • Cavitation, air-fluid levels

Imaging Recommendations

- Best imaging tool
 - Chest radiography for monitoring disease course/progression
 - CT used as problem-solving tool

DIFFERENTIAL DIAGNOSIS

Bronchopneumonia

- Parenchymal abnormality in patient with fever
- Ranges from consolidation to interstitial thickening; focal or diffuse/multifocal (multilobar)

Diffuse Alveolar Hemorrhage

- Diffuse bilateral airspace opacities
- Normal heart size

Acute Respiratory Distress Syndrome

- Radiologic and pathologic findings typically categorized in terms of hours, days, weeks, months
- Days: Bilateral airspace opacities and consolidations
- Weeks: Decreased consolidations; patchy airspace or reticular opacities
- Months: Subpleural reticular opacities ± honeycomb lung

Chronic Eosinophilic Pneumonia

- Persistent peripheral upper lobe consolidations
 Peripheral distribution (outer 2/3)
- Migratory consolidations: Waxing and waning; simultaneous involvement of different lung regions

PATHOLOGY

General Features

• Etiology

- o S. stercoralis: Small nematode
 - Autoinfection
 - □ Cycle of endogenous reinfection within host is unique to *S. stercoralis*
 - □ May lead to chronic infection ~ 50+ years
 - Hyperinfection syndrome
 - □ Acceleration of nematode life cycle
 - High worm burden; normal migration pattern
 - Affected patients usually immunocompromised
 - Disseminated strongyloidiasis
 - Spread to extraintestinal organs outside normal migration pattern (central nervous system, heart, urinary tract)
- Infection: Contact with soil contaminated with free-living larvae

Microscopic Features

• Identification of larvae in stool, sputum, ± skin

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Hyperinfection syndrome
 - Acute respiratory failure and ARDS
- Other signs/symptoms
 - Gastrointestinal involvement
 - Nausea, vomiting, diarrhea, and abdominal pain
 - Skin involvement: Urticaria and macular rashes
 - Eosinophilia common in chronic infection

Demographics

• Epidemiology

- Tropical and subtropical climates
- USA: Southeast and Puerto Rico
- o > 100 million persons with chronic infection worldwide

Natural History & Prognosis

- Mortality from hyperinfection or dissemination: 70%
 - Complicated by secondary infection: 80% (enteric bacteria: *Klebsiella pneumoniae, Escherichia coli*, etc.)

Treatment

• Thiabendazole or mebendazole

DIAGNOSTIC CHECKLIST

Consider

- Strongyloidiasis in patients with focal or diffuse airspace disease in endemic locations
 - Hyperinfection syndrome in immunosuppressed patients (corticosteroids, transplant recipients, human immunodeficiency virus infection, malnutrition)

SELECTED REFERENCES

 Vasquez-Rios G et al: Strongyloides stercoralis hyperinfection syndrome: a deeper understanding of a neglected disease. J Parasit Dis. 43(2):167-75, 2019

Amebiasis

KEY FACTS

TERMINOLOGY

• Parasitic disease caused by infection with protozoan *Entamoeba histolytica*

IMAGING

- Pleural &/or pulmonary disease associated with liver abscess
 - Most pleuropulmonary complications from amebic liver abscess affect right hemithorax
 - Elevated right hemidiaphragm
 - Atelectasis and reactive pleural effusion without pleuropulmonary infection
 - Hydropneumothorax due to bronchopleural fistula
 - Left-sided amebic liver abscesses at higher risk of pericardial involvement
 - Diaphragmatic disruption by "hourglass" abscess located above and below affected hemidiaphragm

TOP DIFFERENTIAL DIAGNOSES

- Pyogenic liver abscess
- Echinococcal cyst
- Necrotic hepatic tumor

CLINICAL ISSUES

- Right pleuritic chest pain &/or shoulder pain
- Right upper quadrant abdominal pain
- Fever, respiratory symptoms

DIAGNOSTIC CHECKLIST

- Focal liver lesion with diaphragmatic disruption is highly suggestive of amebic liver abscess
- Loculation and septations rare in amebic empyema

SCANNING TIPS

- CECT is imaging modality of choice; should include upper abdomen and entire liver
- Ultrasound for assessment of diaphragmatic integrity

(Left) PA chest radiograph of a patient with amebic liver abscess, which drained into the right hemithorax shows a loculated right hydropneumothorax with an air-fluid level 🔁 and elevation of the right hemidiaphragm [2]. (Right) Lateral chest radiograph of the same patient shows the large loculated hydropneumothorax \square Pleural involvement is the most common thoracic manifestation of amebiasis and often results from direct extension (i.e., rupture) of a hepatic abscess into the adjacent pleural cavity.











Synonyms

- Amoebiasis
- Amoebic dysentery
- Amebic dysentery

Definitions

• Parasitic disease caused by infection with protozoan *Entamoeba histolytica*

IMAGING

General Features

- Best diagnostic clue
 - Pleural &/or pulmonary disease associated with liver abscess
 - Elevated right hemidiaphragm
- Location
 - Right lower lobe &/or middle lobe
 - Right pleural space
 - Right hemidiaphragm
- Morphology
 - Triangular consolidation with base against diaphragm and apex directed toward ipsilateral hilum (65%)
- Pleural involvement
 - Pleural effusion in 2/3
 - Pleural effusion of variable size: Small, moderate, or large

Radiographic Findings

- Elevated right hemidiaphragm
- Right lower lobe &/or middle lobe consolidation(s)
- Right pleural effusion
- Hydropneumothorax in cases complicated by bronchopleural fistula

CT Findings

- Pleuropulmonary involvement
 - Pleural effusion may be aseptic (reactive) or infected (empyema); differentiation not reliable on imaging and requires sampling
 - Pleural effusion
 - Pleural thickening
 - Pulmonary opacity
 - Thick or irregular diaphragm
- Liver abscess
 - Typically hypodense, unilocular, solitary; near hepatic capsule
 - Rim enhancement is common
 - o Target sign with double or triple layer appearance

MR Findings

- MR is useful for evaluation of liver abscesses
- Amebic liver abscess is more often single than multiple
- Imaging characteristics of amebic liver abscess
 - o Low signal intensity on T1WI
 - High signal intensity on T2WI
 - o Perilesional edema
 - Peripheral rim of variable signal intensity
- MR is good imaging modality for diaphragmatic evaluation

• Transdiaphragmatic extension is optimally identified on sagittal &/or coronal images

Ultrasonographic Findings

- Right pleural effusion more common than left pleural effusion
- Loculations and septations rare in amebic empyema
- Typically unilocular intrahepatic fluid collection without perceptible wall
- Diaphragmatic disruption may be identified with demonstration rupture site of liver abscess into thoracic cavity
- Focal liver lesion with diaphragmatic disruption is highly suggestive of amebic liver abscess

Imaging Recommendations

- Best imaging tool
 - Contrast-enhanced chest CT
 - Abdominal CT should also be obtained to assess liver if clinical suspicion is high
- Protocol advice
 - Chest CT should include upper abdomen, including entire liver

DIFFERENTIAL DIAGNOSIS

Pyogenic Liver Abscess

• Clinical and imaging manifestations and pleuropulmonary complications may be identical to those of amebic abscess

Echinococcal Cyst

- Typically multiple clustered fluid collections or septated cysts
- May also result in pleuropulmonary involvement
- Septic clinical presentation is less common

Necrotic Hepatic Tumor

- Necrotic liver tumors may be primary or metastatic
- Less likely to show peripheral rim enhancement
- Pleuropulmonary involvement with diaphragmatic disruption is rare
- Septic clinical presentation is uncommon
- Typically hypermetabolic on FDG PET/CT

PATHOLOGY

General Features

- Amebic liver abscess is most common extra-intestinal manifestation of amebiasis
 - Dissemination of trophozoites from colon to liver via portal circulation
- Pleuropulmonary disease is second most common extraintestinal complication of amebiasis
 - Liver abscess may produce right lung atelectasis and reactive sterile pleural effusion in absence of pleuropulmonary infection
 - Pleuropulmonary infection may occur secondary to liverabscess rupture through diaphragm (7-20%)
- Rupture into pericardium is less common but may occur
 - Left hepatic lobe abscesses have higher risk of rupture into pericardium
- Hematogenous spread from liver abscess may result in brain, lung, or skin abscess

• Bacterial coinfection may occur

Gross Pathologic & Surgical Features

- Liver abscess with tissue necrosis: Necrotic hepatocytes, liquefied cells, and cellular debris
- Connective tissue rim: Inflammatory cells and amebic trophozoites
- Aspiration: Chocolate-colored fluid or "anchovy paste" fluid consistent of necrotic hepatocytes

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Pleuritic chest pain Right upper quadrant abdominal pain
 - Ipsilateral shoulder pain &/or scapular pain
 - Hepatomegaly
 - 95% of pleuropulmonary complications from amebic liver abscess affect right hemithorax
 - Only approximately 1/3 of patients with amebic liver abscess with or without pleuropulmonary amebiasis have history of amebic dysentery
- Other signs/symptoms
 - Cough and respiratory symptoms (90%)
 - Fever (> 80%)
 - o Hemoptysis
 - Expectoration of "anchovy sauce-like" pus should indicate liver origin
 - Expectoration of bile indicates coexistent bilio-bronchial fistula
 - Hiccups associated with diaphragmatic involvement
 - o Liver enzymes usually remain normal
 - o Peripheral leukocytosis: Neutrophilia, no eosinophilia

Demographics

- Age
 - Peak presentation: 20-40 years
 - Amebic liver abscess is rare in children
- Sex
 - Amebic liver abscess and its complication are 10x more common in men than in women
- Epidemiology
 - USA cases more common in
 - Immigrants from developing countries
 - Travelers returning from endemic areas
 - Fecal-oral transmission is rare in USA
 - Most cases occur in developing countries
 - Amebiasis is third most common cause of death from parasitic disease after malaria and schistosomiasis
 - More common in tropical and subtropical regionsAreas with poor sanitary conditions
 - Amebic liver abscess occurs in 3-9% of patients with amebic enterocolitis
 - Between 6 and 40% of patients with amebic liver abscess develop pleuropulmonary involvement
 - Amebiasis is responsible for up to 18% of all empyemas
 - 85% on right
 - 13% on left
 - 2% bilateral

• Higher incidence of pulmonary amebiasis is seen in patients with atrial septal defect (ASD)

Natural History & Prognosis

- Pleuropulmonary amebiasis is serious disease with significant mortality (5-16%)
- Mortality is higher in patients with poor health, malnutrition, delayed diagnosis, or inadequate treatment
- Intraperitoneal rupture of amebic liver abscess is rare
- Intrapericardial rupture is rare (< 2%) but is associated with higher mortality
- Lung involvement remote from diaphragm may occur via lymphatic dissemination

Treatment

- Two types of antibiotics are needed
 - Amebicidal tissue agent
 - Metronidazole
 - Tinidazole
 - Luminal cysticidal agent
 - Aminoglycoside paromomycin
- Percutaneous drainage recommended in cases of impending abscess rupture
 - Definition of impending rupture
 - Abscess cavity > 5 cm in diameter
 - Left hepatic lobe abscess
- Drainage or aspiration of liver abscess and pleural fluid collection may be required

DIAGNOSTIC CHECKLIST

Consider

- Amebiasis in patients with pleuropulmonary disease
 Endemic areas
 - Immigrants or travelers
- Pleural &/or pulmonary disease with peripheral and subcapsular liver fluid collection should suggest transdiaphragmatic extension of liver abscess

Image Interpretation Pearls

- Focal liver lesion with diaphragmatic disruption is highly suggestive of amebic liver abscess
- May manifest with "hourglass" abscess morphology and involvement both above and below diaphragm

Reporting Tips

 Always report exact location of suspected amebic abscess and distance of any liver abscess from liver capsule and diaphragm

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Amebiasis





(Left) Axial CECT of a patient with a subcapsular amebic liver abscess shows an ovoid low-attenuation fluid collection 🛃 that abuts the liver capsule and the medial aspect of the right hemidiaphragm 🛃. (Right) Sagittal CECT of the same patient shows the close , relationship between the hepatic abscess \blacksquare , the liver capsule, and the diaphragm \supseteq . Liver abscess is the most common extraintestinal manifestation of amebiasis and the most common source of pleural disease secondary to rupture.





(Left) Axial NECT of a patient with an amebic liver abscess shows a large fluid collection in the posterior aspect of the right hepatic lobe 🛃 and associated small bilateral pleural effusions 🔁. Note hepatic edema that manifests as a lower attenuation rim 🔁 around the fluid collection. (Right) Parasagittal ultrasound of a patient with a right hepatic lobe amebic liver abscess shows rupture \blacksquare through the right hemidiaphragm, a diaphragmatic defect \boxtimes , and an associated right pleural effusion 🖂





(Left) Axial NECT of a patient with an amebic liver abscess shows a right subcapsular hepatic fluid collection \mathbf{E} , deformity of the liver capsule *■*, and a small amount of subcapsular fluid \blacksquare , which is indicative of tension and early rupture. (Right) Axial NECT of a patient with amebic liver abscess with pulmonary involvement shows a right upper lobe heterogeneous consolidation 🛃 with intrinsic irregular low-attenuation areas 🛃 secondary to necrosis.

Schistosomiasis

KEY FACTS

TERMINOLOGY

- Schistosomiasis = bilharziasis
- Disease caused by fluke worms of genus Schistosoma
- Pulmonary arterial hypertension (PAH)

IMAGING

- Acute schistosomiasis
 - Small pulmonary nodules ± halo sign
 - Interlobular septal thickening
 - Ground-glass opacities
- Chronic pulmonary schistosomiasis: Findings of PAH

TOP DIFFERENTIAL DIAGNOSES

- Acute schistosomiasis
- Broad differential diagnosis includes numerous diseases that manifest with small nodules (e.g., infection, metastatic disease, vasculitis, etc.)
- Chronic pulmonary schistosomiasis
 Primary pulmonary hypertension

- o Secondary pulmonary hypertension
 - Pulmonary veno-occlusive disease/pulmonary capillary hemangiomatosis
 - Chronic thromboembolic disease
 - Cor pulmonale

PATHOLOGY

- Ectopic migration of eggs to pulmonary vasculature from portosystemic shunt due to portal hypertension
- Intravascular pulmonary eggs induce granulomatous inflammation and necrotizing and obliterative endarteritis with resultant pulmonary hypertension

CLINICAL ISSUES

• Schistosomiasis responsible for significant number of cases of PAH in endemic areas (> 30%)

DIAGNOSTIC CHECKLIST

• Consider schistosomiasis in patients with PAH, fibrotic liver disease, &/or portal hypertension in endemic areas

(Left) Axial NECT of a young patient with acute pulmonary schistosomiasis shows several small lung nodules ≥, some of which demonstrate an illdefined peripheral groundglass opacity halo, which while nonspecific can be frequently seen in acute schistosomiasis. (Right) Axial NECT of the same patient shows numerous additional pulmonary nodules \square , many of which exhibit predominant ground-glass opacity or a peripheral ground-glass opacity halo.





(Left) Axial CECT of a patient with chronic schistosomiasis manifesting with liver disease and pulmonary arterial hypertension shows an enlarged pulmonary trunk 🔁 and right pulmonary artery. Note esophageal wall thickening 🛃 and a prominent azygos vein 🖂. (Right) Axial CECT of the same patient shows extensive collateral circulation in the mediastinum and chest wall, large paraesophageal varices \blacksquare , and a dilated and tortuous azygos vein 🔁.





Abbreviations

• Pulmonary arterial hypertension (PAH)

Synonyms

- Bilharziasis
- Katayama fever (acute schistosomiasis)

Definitions

- Tropical parasitic disease caused by trematode fluke worms of genus *Schistosoma*
 - o Two main clinical forms: Genitourinary, gastrointestinal
- Three main schistosomes infect humans
 - o S. mansoni: Africa, Arabian peninsula, South America
 - o *S. haematobium:* Africa, Eastern Mediterranean region, and Arabian peninsula
 - o S. japonicum: China, Philippines, and Indonesia

IMAGING

General Features

- Best diagnostic clue
 - Acute schistosomiasis
 - Pulmonary nodules (2-15 mm) ± halo sign
 - Interlobular septal thickening
 - Ground-glass opacities
 - Chronic pulmonary schistosomiasis
 - Imaging findings of PAH
 - No significant concomitant pulmonary parenchymal disease

Radiographic Findings

- Cardiomegaly, right ventricular enlargement
- Enlarged pulmonary trunk and central pulmonary arteries

CT Findings

- Cardiomegaly, right ventricular enlargement
- Enlarged pulmonary trunk and central pulmonary arteries
- No pulmonary parenchymal disease (fibrosis, emphysema, interstitial lung disease, etc.)
- No obvious cardiovascular abnormality (e.g., intracardiac shunt or chronic thromboembolism)
- Thoracic manifestations of chronic liver disease: Paraesophageal varices

Ultrasonographic Findings

• Transthoracic or transesophageal echocardiography for demonstration of PAH

DIFFERENTIAL DIAGNOSIS

Metastatic Disease

- May be indistinguishable from acute schistosomiasis
- History of malignancy

Vasculitis

- May be indistinguishable from acute schistosomiasis
- Cavitation common in granulomatosis and polyangiitis

Infection

- May be indistinguishable from acute schistosomiasis
- Acute infectious symptoms more common

Chronic Pulmonary Hypertension

• May be indistinguishable from acute schistosomiasis

PATHOLOGY

General Features

- Infection occurs in fresh water containing larval forms (cercariae)
- Snails infected by eggs excreted in human feces or urine
- Larvae develop in water snails (intermediate host)
- Cercariae penetrate skin of individual in contact with water
- Parasite migrates in blood via lungs to liver where they transform into young worms

Staging, Grading, & Classification

- Acute schistosomiasis (Katayama fever)
- Chronic schistosomiasis

Gross Pathologic & Surgical Features

- Chronic infection: Parasites trapped in tissue induce granulomatous inflammation and fibrosis
 - o Urinary and gastrointestinal tract, liver, etc.
 - Ectopic migration of eggs to pulmonary vasculature induces necrotizing and obliterative endarteritis, fibrosis, and PAH
- PAH in 10% to 20% of patients with schistosomiasis
- > 30% of all cases of PAH occur in endemic areas

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Acute: Febrile syndrome with cough, fever, and eosinophilia
 - Chronic: Nonspecific symptoms (heart murmur, PAH)

Other signs/symptoms Hepatosplenomegaly and signs of portal hypertension

Demographics

- High mortality due to parasites, schistosomiasis second only to malaria
- > 230 million infected worldwide (most in Africa)

Treatment

• Praziquantel active against all schistosome species

DIAGNOSTIC CHECKLIST

Consider

- Schistosomiasis in patients with small pulmonary nodules and exposure to fresh water in endemic areas
- Chronic pulmonary schistosomiasis in patients with PAH in endemic regions

Image Interpretation Pearls

• Look for imaging signs of PAH in patients with fibrotic liver disease &/or portal hypertension and no imaging signs of pulmonary (fibrosis, emphysema) or cardiovascular disease (intracardiac shunt, chronic thromboembolism)

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SECTION 5 Pulmonary Neoplasms

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Introduction

Pulmonary neoplasms are a heterogeneous group of lesions with variable morphologic and imaging features. The most common lung neoplasm is metastatic disease, and the most common primary lung neoplasm is lung cancer. Other primary malignant neoplasms are rare. Benign lung neoplasms are also rare, but establishing a prospective diagnosis of benignity in a lung lesion precludes unnecessary invasive procedures. The radiologist plays a critical role in the detection, diagnosis, staging, and management of lung neoplasms. A major challenge is the prospective distinction of various tumor-like infectious and inflammatory conditions from pulmonary neoplasia.

Pulmonary Metastases

Pulmonary metastases typically manifest with multifocal lung nodules or masses that exhibit spherical shapes, well-defined borders, and a peripheral and basilar distribution. Hemorrhagic metastases may demonstrate ill-defined borders due to surrounding alveolar hemorrhage. Atypical manifestations of metastatic disease include: A solitary nodule, cavitation, calcification, and lymphangitic carcinomatosis. Lung metastases characteristically disseminate via hematogenous routes, but lymphatic and tracheobronchial dissemination and direct lung invasion also occur.

Lung Cancer

Lung cancer comprises several histologic cell types, including adenocarcinoma, squamous cell carcinoma, small cell carcinoma, large cell carcinoma, and neoplasms of mixed histology. These lesions exhibit variable morphologic features and biologic behaviors. Lung cancer is intimately associated with cigarette smoking, but 10-20% of cases affect never smokers. Inhaled carcinogens and indoor pollutants are also associated with lung cancer and include radon, arsenic, asbestos, beryllium, cadmium, chloromethyl ethers, chromium, nickel, silica, and vinyl chloride. Lung cancer is also associated with chronic diseases, such as chronic obstructive pulmonary disease (COPD), fibrosing lung disease, and human immunodeficiency virus (HIV) infection.

Epidemiology

Lung cancer is the leading cause of cancer mortality worldwide and in 2020 accounted for 2.2 million new cases and 1.8 million deaths. Although recent years have shown a decline in lung cancer incidence in the USA, it remains the leading cause of cancer mortality, and it is estimated that there will be over 235,000 new cases and over 131,000 deaths from lung cancer in 2021. In spite of major advances in diagnosis and treatment, the 5-year survival of lung cancer in the USA was 19.4% in 2019, and most (57%) lung cancers demonstrate metastatic disease at the time of diagnosis.

Clinical Presentation

Lung cancer is most common in patients over 70 years of age. Affected individuals characteristically present with symptoms, and only 10% of affected patients are asymptomatic and diagnosed incidentally. Symptomatic patients may present with symptoms related to the primary tumor, intra- and extrathoracic spread of the malignancy, or because of a paraneoplastic syndrome known to be associated with lung cancer. Presenting complaints are often nonspecific and include thoracic and constitutional symptoms. Central primary lung cancers are likely to produce symptoms related to bronchial obstruction and its secondary effects (atelectasis &/or postobstructive pneumonia) and may include cough, dyspnea, and hemoptysis. Chest pain or discomfort may also occur.

Advanced lung cancers with intrathoracic spread may produce similar symptoms. Dyspnea may be secondary to atelectasis from bronchial obstruction, pleural effusion, or lymphangitic carcinomatosis. Mediastinal invasion may produce superior vena cava syndrome, diaphragmatic paralysis from phrenic nerve involvement, hoarseness from recurrent laryngeal nerve involvement, and dysphagia from esophageal invasion. Involvement of the parietal pleura and adjacent chest wall may produce local pain. Patients with locally invasive superior sulcus lung cancers may develop Pancoast syndrome and may present with findings related to brachial plexus involvement &/or Horner syndrome.

Patients with lung cancer may also present with symptoms related to distant metastases. Frequently affected sites include bone, adrenal glands, liver, lymph nodes, and the central nervous system. Symptoms vary with the affected organ(s) and include anorexia, weight loss, and weakness, bone pain due to pathologic fracture, or headache, seizures, neurological deficits, &/or altered metal status due to brain metastases.

Finally, patients with lung cancer may present with paraneoplastic syndromes or systemic effects of the neoplasm unrelated to metastatic disease. These usually result from biogenic substances produced by the tumor and include hypercalcemia, syndrome of inappropriate secretion of antidiuretic hormone, and Cushing syndrome.

Imaging Features

Lung cancer exhibits a wide range of imaging findings. Peripheral lung cancer often manifests as a pulmonary nodule, mass, or consolidation. Such lesions may invade extrapulmonary structures, including the chest wall, diaphragm, and mediastinum. Central lung cancer often manifests as a hilar or perihilar mass, which may be obscured by surrounding pneumonia &/or atelectasis. Thus, unexplained atelectasis should be investigated, and consolidations in adults should be followed to complete resolution to exclude underlying malignancy. Some lung cancers, specifically adenocarcinomas, may manifest as consolidations or multifocal lung nodules or masses that mimic metastases. Advanced lung cancer may manifest with extensive intrathoracic lymphadenopathy and may mimic lymphoma and metastatic disease from extrathoracic malignancy. In some cases, patients with lung cancer are initially diagnosed because of imaging findings related to distant metastases to the abdomen, brain, skeleton, or extrathoracic lymph nodes.

Although radiologists are often the first health care providers to suggest the diagnosis of lung cancer, interpretation of chest radiographs is fraught with pitfalls related to superimposition of numerous structures of different size and radiographic density and to the poor conspicuity and small size of many lung cancers. Observer error, technical factors, failure to compare to prior imaging, and incomplete clinical information may further exacerbate the problem. In fact, missed lung cancer on radiography constitutes the second leading cause of malpractice actions against radiologists. Radiologists interpreting chest imaging studies must have indepth knowledge of normal imaging anatomy, evaluate imaging studies in a systematic manner, and consistently compare current to prior studies. When suspicious abnormalities are found, the radiologist must communicate unexpected findings to the referring clinician and outline management recommendations, which may include further imaging &/or tissue sampling.

Diagnosis

Although imaging features may be highly suggestive of lung cancer, microscopic analysis of tissue samples is required for a specific and definitive diagnosis. A careful evaluation of the anatomic location of the lesion &/or its metastases and identification of affected extrapulmonary structures allows the radiologist to suggest the most appropriate site and method of tissue sampling, including image-guided biopsy, bronchoscopy, or more invasive surgical procedures, such as mediastinoscopy, mediastinotomy, video-assisted thoracoscopic surgery, or thoracotomy. In some cases, the radiologist may both diagnose and stage lung cancer by performing image-guided biopsy of metastatic foci.

Histologic Classification

The most common cell type of lung cancer is adenocarcinoma, which is characterized by glandular differentiation and mucin production. Adenocarcinomas are typically peripheral lung neoplasms, may be multicentric, and usually grow slowly but metastasize early. Squamous cell carcinoma is characterized by flattened cells, intercellular bridges, and individual cell keratinization. It is typically a central neoplasm that manifests with an irregular polypoid endoluminal bronchial lesion. Squamous cell carcinoma exhibits rapid growth and has a strong association with cigarette smoking. Small cell carcinoma is a highly aggressive lung cancer that is almost universally metastatic at presentation. It is characterized by small cells with scant cytoplasm, granular nuclear chromatin, and numerous mitotic figures and forms part of the spectrum of neuroendocrine lung neoplasms. It has an irrefutable association with cigarette smoking, and affected patients have a very poor prognosis.

Staging

The eighth edition of the tumor-node-metastasis (TNM) system classification published jointly by the Union for International Cancer Control (UICC), the American Joint Committee on Cancer, and the International Association for the Study of Lung Cancer (IASLC) is used for staging lung cancer and other primary lung malignancies. Clinical staging of lung cancer is of crucial importance in therapeutic planning and is based on anatomic and metabolic imaging, endoscopy, and minimally invasive surgery. Surgical-pathologic staging allows informed prediction of prognosis and further management and therapeutic decisions.

Treatment

Treatment of lung cancer is based on cell type, stage at presentation, performance status, and general health of the affected patient. Complete tumor resection and lymph node dissection is ideally performed for localized nonsmall cell lung cancers. Patients who are not surgical candidates may undergo radiation therapy or ablative procedures. Multimodality therapy with chemotherapy, radiation &/or targeted treatments may be used in advanced disease.

Screening

The National Lung Screening Trial (NLST) published its results in 2011 and reported a 20% decrease in death from lung cancer in high-risk persons undergoing screening with lowdose chest CT (LDCT). In early 2014, lung cancer screening with LDCT was given a B commendation (which implies moderate certainty of at least moderate net benefit) by the United States Preventive Services Task Force (USPSTF). Since then, multiple national and international medical organizations have endorsed LDCT screening including the American Cancer Society, the American Lung Association, and the National Comprehensive Cancer Network. In early 2021 the USPSTF published a final recommendation statement on lung cancer screening in which yearly screening with LDCT was recommended for individuals between 50 and 80 years with a 20 pack-year history of smoking who are current smokers or quit smoking within the last 15 years. In spite of the data and the general availability of lung cancer screening, it is estimated that a very low percentage of eligible individuals currently undergo screening for lung cancer in the USA (4.6% in one study).

Uncommon Primary Pulmonary Neoplasms

The majority of pulmonary neoplasms are metastases and primary lung cancers. Other primary pulmonary neoplasms are rare. Bronchial carcinoid is an important lung malignancy with a favorable prognosis. Affected patients are generally younger than patients with lung cancer. Bronchial carcinoid typically manifests as a central lung nodule or mass that demonstrates a bronchial relationship and may exhibit intense contrast enhancement. Affected patients typically present with symptoms related to the endoluminal neoplasm, including wheezing, hemoptysis, recurrent pneumonia, &/or atelectasis.

Lymphoproliferative disorders may also affect the lung. While most thoracic lymphomas are lymph node malignancies that primarily affect the mediastinum, both Hodgkin and non-Hodgkin lymphomas can affect the lung with primary or secondary involvement. These lesions may manifest with lung nodules, masses, or consolidations and may exhibit a multifocal distribution mimicking lung cancer and metastatic disease. These tumors may also exhibit intrinsic air bronchograms and may simulate pulmonary infections and other nonneoplastic processes.

Pulmonary hamartoma is a rare benign lung neoplasm characterized by intrinsic heterogeneous tissues in varying proportions, including cartilage, fat, connective tissue, and smooth muscle. Most hamartomas are peripheral tumors, and affected patients are often asymptomatic and diagnosed because of the incidental discovery of an indeterminate pulmonary nodule. Imaging identification of fat &/or chondroid calcification within these lesions allows a confident prospective diagnosis of hamartoma. In these cases, excision is generally not warranted in the absence of symptoms.

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Approach to Pulmonary Neoplasms

Eighth Edition of the TNM Classification of Lung Cancer

T Descriptor	Features		
Tx	Tumor in sputum/bronchial washings; not assessed on imaging or bronchoscopy		
ТО	No evidence of tumor		
Tis	Carcinoma in situ		
T1	≤ 3 cm; surrounded by lung/visceral pleura; not involving mainstem bronchus		
T1a (mi)	Minimally invasive carcinoma		
T1a	≤1cm		
T1b	> 1 to ≤ 2 cm		
T1c	> 2 to ≤ 3 cm		
T2	> 3 to \leq 5 cm or involvement of mainstem bronchus (but not carina); visceral pleural invasion; atelectasis or postobstructive pneumonia that extends to hilum		
T2a	> 3 to ≤ 4 cm		
T2b	> 4 to ≤ 5 cm		
Τ3	> 5 to \leq 7 cm; tumor of any size with invasion of chest wall, pericardium, phrenic nerve; satellite nodules in same lobe		
T4	> 7 cm; tumor of any size with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine; separate tumor in different lobe of ipsilateral lung		
N Descriptor			
N1	Involved ipsilateral peribronchial &/or hilar and intrapulmonary lymph nodes		
N2	Involved ipsilateral mediastinal &/or subcarinal lymph nodes		
N3	Involved contralateral mediastinal or hilar; ipsilateral/contralateral scalene/supraclavicular lymph nodes		
M Descriptor			
M1	Distant metastases		
M1a	Tumor in contralateral lung or pleural/pericardial nodule/malignant effusion		
М1Ь	Single extrathoracic metastasis, including single non-regional lymph node		
M1c	Multiple extrathoracic metastases in 1 or more organs		

Eighth Edition of TNM Classification of Lung Cancer: Staging

		N0	N1	N2	N3		
T1/M0	T1a	IA1	IIB	IIIA	IIIB		
	T1b	IA2	IIB	IIIA	IIIB		
	T1c	IA3	IIB	IIIA	IIIB		
T2/M0	T2a	IB	IIB	IIIA	IIIB		
	T2b	IIA	IIB	IIIA	IIIB		
T3/M0	Т3	IIB	IIIA	IIIB	IIIC		
T4/M0	Т4	IIIA	IIIA	IIIB	IIIC		
TX/M1	M1a	IVA	IVA	IVA	IVA		
	M1b	IVA	IVA	IVA	IVA		
	M1c	IVB	IVB	IVB	IVB		
T_{V} NMM - occult carcinoma: Tis NMM - stage 0: T1a(mi)NMM - stage 1A1: Note: TY stands for any T							

TxN0M0 = occult carcinoma; TisN0M0 = stage 0; T1a(mi)N0M0 = stage IA1; Note: TX stands for any T.

Lung Cancer: Nodule





(Left) PA chest radiograph of an asymptomatic 45-year-old man with an incidentally discovered radiographic abnormality shows a subtle right upper lobe indeterminate lung nodule 🛃 (Right) Axial CECT of the same patient shows a right upper lobe partsolid nodule with a dominant solid component, intrinsic air bronchograms, and pleural tags. Such features are highly concerning for primary lung cancer. Invasive adenocarcinoma was diagnosed at surgery.

Lung Cancer: Mass





Lung Cancer: Mass

(Left) PA chest radiograph of a 60-year-old woman who presented with hemoptysis shows a large right upper lobe pulmonary mass that is highly suspicious for primary lung cancer. (Right) Axial CECT of the same patient shows the large lobulated right upper lobe mass, which involves the lumen of the right upper lobe anterior segmental bronchus ⊇. Endoluminal involvement by the neoplasm likely contributed to hemoptysis. Note adjacent paraseptal and centrilobular emphysema.

Lung Cancer: Atelectasis



Lung Cancer: Atelectasis



(Left) PA chest radiograph of a smoker who presented with weight loss and hemoptysis shows marked middle and right lower lobe volume loss with associated inferior displacement of the minor fissure 🔁 secondary to a right hilar mass 🛃. (Right) Axial CECT of the same patient shows complete right lower lobe atelectasis \blacksquare and medial displacement of the minor fissure 🛃 from marked middle lobe volume loss secondary to a central obstructing tumor. Small cell lung cancer was diagnosed at bronchoscopy.

Pulmonary Neoplasms

(Left) PA chest radiograph of a patient with squamous cell carcinoma who presented with cough and hemoptysis shows a left apical mass with intrinsic cavitation 🔁. Cavitation is a common feature of primary lung squamous cell carcinomas. (Right) Coronal CECT of the same patient shows that the radiographic abnormality corresponds to a large, heterogeneous, necrotic and cavitary mass that directly invades the mediastinum and produces luminal obstruction ➡ of the left upper lobe apicoposterior segmental bronchus.

(Left) PA chest radiograph of a 52-year-old smoker who presented with advanced lung cancer shows a right upper lobe spiculated nodule ➡ and ipsilateral right hilar ➡ and mediastinal ➡ lymphadenopathy. (Right) Coronal CECT of the same patient shows nodular encasement and narrowing of the right tracheobronchial tree by metastatic coalescent mediastinal and hilar lymphadenopathy. · · · ·

Lung Cancer: Cavitary Mass



Lung Cancer: Cavitary Mass



Lung Cancer: Metastatic Lymphadenopathy





Lung Cancer: Hilar/Mediastinal Mass



Lung Cancer: Hilar/Mediastinal Mass



(Left) Axial CECT of a patient with advanced lung cancer shows a large right hilar mass with associated endoluminal tumor within the right mainstem bronchus. (Right)

with advanced lung cancer shows a large right hilar mass with associated endoluminal tumor within the right mainstem bronchus. (Right) Axial CECT of the same patient shows a large, heterogeneous right hilar/mediastinal mass that invades the mediastinum and the superior vena cava 🔼 Intrinsic low attenuation with peripheral enhancement represents extensive necrosis. Central lung cancer typically produces symptoms and may manifest as a hilar &/or mediastinal mass.

Pulmonary Metastases





(Left) PA chest radiograph of a patient with metastatic cancer shows bilateral well-defined lung nodules and masses and a right pleural effusion. The lesions are most numerous in the mid and lower lung zones, consistent with the normal dominant pulmonary blood flow. (Right) Coronal CECT MIP reformatted image of a patient with metastatic carcinoma of unknown primary shows multifocal welldefined solid nodules, some with an angiocentric distribution \square , consistent with hematogenous metastases.

Lymphangitic Carcinomatosis

Primary Pulmonary Lymphoma





(Left) PA chest radiograph of a patient with metastatic prostate carcinoma shows right greater than left interlobular septal thickening due to lymphangitic carcinomatosis, an unusual but well-recognized manifestation of metastatic disease. (Right) Axial NECT shows primary B-cell pulmonary non-Hodakin lymphoma manifesting as a right upper lobe mass-like consolidation with spiculated borders and intrinsic air bronchograms 🔁. Pulmonary lymphoma may mimic pulmonary infection.

Bronchial Carcinoid





Hamartoma

(Left) Axial CECT of a patient with hemoptysis shows bronchial carcinoid manifesting as a spherical, enhancing mass 🔁 that produces postobstructive right upper lobe atelectasis with intrinsic mucus-filled dilated bronchi 🔁 secondary to central bronchial obstruction. (Right) Axial NECT of an asymptomatic patient shows an incidentally discovered left lower lobe solid nodule that exhibits intrinsic macroscopic fat 🔁 and calcification 🔁. The imaging findings are pathognomonic for pulmonary hamartoma.

DIFFERENTIAL DIAGNOSIS

Common

- Granuloma
- Intrapulmonary Lymph Node
- Mucus Plug
- Lung Cancer
- Nodule Mimics

Less Common

- Atypical Adenomatous Hyperplasia
- Carcinoid
- Hamartoma
- Solitary Metastasis
- Infarct
- Laceration
- Abscess

Rare but Important

- Pulmonary Arteriovenous Malformation
- Amyloidoma
- Pulmonary Inflammatory Myofibroblastic Tumor

ESSENTIAL INFORMATION

Key Differential Diagnosis Issues

• Solitary pulmonary nodule (SPN)

- Single focal rounded or ovoid opacity, \leq 3 cm
- SPN detection
 - Radiography
 - SPN found in up to 2% of chest radiographs
 - Improved detection: Dual-energy radiography, bone suppression software, computer-aided detection
 - **CT**
 - Superior for SPN detection
 - Imaging study of choice for SPN characterization: Size, morphology, density (calcification, fat, air), attenuation (solid, subsolid), growth, enhancement, metabolic activity
 - Improved detection/characterization: Thin-section CT (1.0-1.5 mm), multiplanar reformations, maximum intensity projection (MIP), computer-aided detection
- General features
 - Size: 90% of nodules < 2 cm are benign
 - Spherical morphology is typical of benignity
 - o Growth
 - 2-year stability implies benignity; but indolent lung cancer occurs
 - Doubling time < 30 days or > 465 days favors benignity
- SPN imaging assessment
 - Benign: No follow-up required
 - Indeterminate: Follow-up per published guidelines
 - Documentation of stability
 - Detection of growth
 - Detection of morphologic and attenuation changes
 - Possibly malignant
 - Short-term imaging follow-up to document growth
 - FDG PET/CT for assessment of metabolic activity
 - Tissue sampling: Image-guided biopsy, bronchoscopic biopsy, surgical resection

Helpful Clues for Common Diagnoses

• Granuloma

- o Solid nodule, stable size, typically small
- Spherical, smooth or minimally lobular borders
- Frequent calcification
 - SPN < 9 mm on radiography likely calcified granuloma
 - Complete or diffuse Ca++
 - Central Ca++, > 10% of nodule on cross section
 - Laminar or concentric Ca++
- Satellite nodules
- o Histoplasmosis, coccidioidomycosis, tuberculosis
- Asymptomatic adult
- Intrapulmonary Lymph Node
 - Frequent incidental finding on thin-section CT
 20% prevalence in lung screening population
 - Fissural or perifissural, juxtapleural; no pleural retraction
 - Within 20 mm of pleural surface, caudal to level of carina
 - Small, < 6 mm; may exhibit growth
 - o Triangular or lentiform; smooth sharp margins
- Mucus Plug
 - May mimic SPN on axial CT; multiplanar reformatted images for differentiation
 - o Identification of proximal and distal patent airway
 - Associated bronchial wall thickening, mucus plugs

Lung Cancer

- Risk factors
 - Exposure to cigarette smoke or other carcinogens
 - History of malignancy (pulmonary or extrapulmonary)
 - Pulmonary fibrosis
 - Lung cancer in 1st-degree relative
- Most common in upper lobes
- Increased risk of cancer in SPN > 1 cm
- o Doubling time 1-18 months; average: 100 days
- o Morphology: Irregular, spiculated, lobulated
 - Spiculation: Highly suggestive of malignancy
 - Pleural tags in 60-80% of peripheral lung cancers
 - Lobulated borders
 Histologic heterogeneity
 - □ 40% of malignant nodules
- Density
 - Air bronchograms/bronchiolograms and bubbly lucencies more common in malignant nodules
 - Calcification in 13%; eccentric, stippled
 - Cavitation: Irregular walls > 16 mm thick suggest malignancy
- Attenuation
 - Solid (soft tissue): Most lung cancers, less likely to be malignant than part-solid or nonsolid nodules
 - Part-solid (soft tissue and ground-glass): 40-50% of part-solid SPNs < 1.5 cm are malignant; typically adenocarcinoma
 - Nonsolid (ground-glass): 34% malignant; particularly if
 > 1.5 cm; typically adenocarcinoma
- Metabolic activity: FDG PET/CT
 - 90% likelihood of malignancy for FDG-avid SPNs in patients > 60 years
 - False-negative FDG PET/CT
 - Indolent and low-grade lung cancer
 - □ Malignant SPN < 1 cm

• Nodule Mimic (Pseudonodule)

• Exclusion of underlying true SPN

• Nipple/skin lesion

- Nipples: Bilateral symmetric rounded opacities, mid to inferior hemithorax, midaxillary line, incomplete border sign
- Radiography with metallic (nipple) markers

• Osseous lesion

- Asymmetric 1st costochondral articulation
- Rib fracture, callus, bone island
- Dependent atelectasis
 - May mimic nodule on CT; posterior subpleural, resolves on prone or follow-up imaging

Helpful Clues for Less Common Diagnoses

• Atypical Adenomatous Hyperplasia

- Earliest preinvasive lesion of adenocarcinoma
- Frequent incidental finding with adenocarcinoma
- Pure ground-glass nodule, typically ≤ 5 mm

• Carcinoid

o Well-defined lobulated borders

o Bronchus sign

- Airway leads into or is associated with SPN; "iceberg" lesion, endoluminal component and dominant extraluminal SPN
- Postobstructive effects: Atelectasis, bronchiectasis, mucus plugs
- Contrast enhancement, tumor vascularity
- Multifocal punctate or coarse calcification in 38%
- More common in lesions adjacent to central airways
- Somatostatin receptor PET (SSTR-PET) with gallium-68 DOTATATE (somatostatin analogue) PET/CT
 - Increased sensitivity and specificity for detection of neuroendocrine tumors
- False-negative on FDG PET/CT; low metabolic activity
 Hamartoma
 - Slow-growing benign neoplasm, well-defined lobular or notched borders
 - Intralesional fat on CT in > 50%; -40 to -120 HU
 - Popcorn calcification on CT in 10-15%

Granuloma



• Solitary Metastasis

- o Most common: Melanoma, sarcoma, testicular cancer
- o Also: Breast, prostate, colon, and renal cancers
- Peripheral location

Infarct

- o Lower lobe, peripheral, subpleural, wedge-shaped
- Decreased contrast enhancement
- Central lucency, cavitation, halo sign
- o Slow resolution (months); may heal with scar
- o 10-15% of patients with pulmonary embolism

Laceration

- Traumatic disruption of lung parenchyma ± adjacent rib fractures
- Round or ovoid air-filled lesion on CT: Homogeneous or heterogeneous SPN when filled with blood &/or fluid
- Surrounding ground-glass opacity from adjacent contusion
- Slow resolution (months); may heal with scar

Abscess

- Spherical, thick-walled lesion with internal low attenuation or cavitation
- Frequent associated pleural effusion
- Signs and symptoms of infection, sequela of aspiration
- Mixed aerobic/anaerobic polymicrobial infection

Helpful Clues for Rare Diagnoses

• Pulmonary Arteriovenous Malformation

- Peripheral and lower lobe predominant
- Rounded, ovoid, 1- to 5-cm nidus; feeding and draining vessel(s)
- Single in 2/3 of cases
- Vascular enhancement
- Right-to-left shunt; risk of peripheral abscess or infarct
- Amyloidoma (Nodular Amyloidosis)
 - Solitary nodule; variable border characteristics
 - May exhibit calcification
 - Older patient, M:F = 3:2
- Inflammatory Myofibroblastic Tumor (Pseudotumor)
 - Lung nodule or mass; well-defined borders
 - Young patient or child

Granuloma



(Left) Coned-down PA chest radiograph of an asymptomatic 71-year-old man shows a well-defined calcified left lung nodule 🖂 and ipsilateral calcified nonenlarged left hilar lymph nodes 🔁 (Right) Axial NECT of the same patient shows a mildly lobulated left upper lobe nodule 🔁 that demonstrates diffuse calcification, a benign pattern of calcification. Note associated calcified left hilar lymph node 🖾. The findings are typical of remote aranulomatous disease secondary to histoplasmosis.

(Left) Coned-down PA chest radiograph of a 68-year-old woman shows a left mid lung zone nodule \bowtie that exhibits central calcification, consistent with a granuloma. Calcification involves > 10% of the nodule diameter. (Right) Composite image with axial CECT in lung (left) and soft tissue (right) window of a 70year-old woman shows a middle lobe granuloma with central calcification that involves > 10% of the cross section of this spherical nodule, a benign pattern of calcification for which no further imaging is warranted.

(Left) Coronal CECT (bone window) of a 63-year-old woman with chest pain shows a left lower lobe nodule with central and laminar calcifications, both benign patterns of calcification typical of granuloma. (Right) Composite image with axial CECT MIP reformatted images in lung (left) and soft tissue (right) window shows a centrally calcified right lower lobe nodule 🔁 with surrounding satellite $micronodules \supseteq$ and calcified right hilar lymph nodes $\overline{\mathbb{A}}$, characteristic of remote histoplasmosis infection.

(Left) Composite image with axial (left) and coronal (right) NECT shows an ovoid nodule \square adjacent to the minor fissure, which exhibits a lentiform morphology 🔁 on coronal imaging, typical of intrapulmonary lymph node. (Right) Composite image with axial (left) and sagittal (right) NECT shows a right lower lobe nodular lesion 🔁 and adjacent thick-walled bronchi *⊡*. The "nodule" corresponds to an endobronchial mucus $plug \supseteq$ on sagittal imaging. Obstructing mucus plugs may mimic lung nodules on axial thin-section CT.

Granuloma





Granuloma

Granuloma



Intrapulmonary Lymph Node



Mucus Plug



Lung Cancer



Lung Cancer



(Left) Axial NECT of a 74-yearold smoker shows a left upper lobe lung cancer that manifests as a spiculated solid nodule with pleural tags \supseteq Spiculation and pleural tags are CT features suggestive of malignancy. (Right) Axial CECT of a 58-year-old woman shows a moderately differentiated left upper lobe adenocarcinoma that manifests as a solid nodule with lobulated margins 🖾. Note right upper lobe groundglass nodule \supseteq that may represent atypical adenomatous hyperplasia, a preinvasive lesion.

Lung Cancer



Lung Cancer

(Left) Axial CECT of an asymptomatic 75-year-old man shows a moderately differentiated right upper lobe adenocarcinoma that manifests as a lobulated spiculated nodule \supseteq with intrinsic air bronchograms and small round "bubbly" lucencies. (Right) Axial NECT shows an asymptomatic 79year-old woman with a right lower lobe biopsy-proven minimally invasive adenocarcinoma that manifests as a right lower lobe ground-glass nodule 🔁 that abuts and mildly retracts the adjacent right major fissure.

Nodule Mimics





Nodule Mimics

(Left) Composite image with coned-down PA chest radiograph (left) and axial NECT (right) of a 63-year-old man shows an ill-defined left upper lung zone nodular $opacity \supseteq$ that corresponds to a bone island ≥ on CT. Osseous lesions may mimic lung nodules. (Right) Coneddown PA chest radiograph of an asymptomatic adult shows bilateral symmetric nodular lesions \supseteq projecting over the lower lungs, typical of nipple shadows. The nodular lesions exhibit the incomplete border sign, indicating that they are extrapulmonary.

(Left) Composite image with axial CECT of a 66-year-old woman with hemoptysis shows a right upper lobe solid nodule and a bronchus \supseteq that courses into the lesion, the socalled bronchus sign. Peripheral tubular opacities correspond to mucus plugs from bronchial obstruction. (Right) Composite image with axial NECT (left) and Gallium-68 DOTATATE PET/CT (right) of a 59-year-old woman shows a right upper lobe solid nodule rightarrow that exhibits gallium-68DOTATATE avidity, consistent with a neuroendocrine tumor, in this case, a carcinoid tumor.

Carcinoid





(Left) Axial NECT of a 52-yearold man with a radiographic abnormality shows a middle lobe solid nodule with a small focus of internal macroscopic fat, an imaging finding diagnostic of hamartoma for which no further management is required. (Right) Axial NECT of a 50-year-old woman smoker with breast cancer shows a new left upper lobe nodule found on surveillance imaging, concerning for lung cancer. Biopsy demonstrated metastatic breast cancer. Solitary metastases are rare, but important causes of solitary lung nodules.

(Left) Axial CECT of a 78-yearold man with chest pain secondary to pulmonary thromboembolism (not shown) shows a left lower lobe subpleural lobulated nodule with central lucency \square , characteristic of a pulmonary infarct. (Right) Composite image with axial CECT (left) and NECT obtained 8 months later (right) of a 63-year-old man with pulmonary thromboembolism (not shown) shows a lingular lung infarct that manifests as a solid lung nodule \supseteq . Months later, the infarct demonstrates healing with linear scar formation 🔁.

Hamartoma





Infarct



Infarct



Laceration



Abscess

(Left) Composite image with axial CECT in lung (left) and bone (right) window of a patient with chest trauma shows a heterogeneous right lower lobe subpleural nodule \square , characteristic of a pulmonary laceration. Note adjacent nondisplaced right rib fracture 🔁. (Right) Coronal NECT of a young man with fever, leukocytosis, and a peripheral right basilar nodule identified on radiography shows a right lower lobe subpleural nodule with cavitation \boxtimes and surrounding ground-glass opacity 🔁, consistent with a lung abscess.

Pulmonary Arteriovenous Malformation



(Left) Coned-down PA chest radiograph of an asymptomatic 38-year-old woman shows a well-defined right upper lobe nodule 🖂 Note the tubular opacity 🔁 that courses from the nodule toward the ipsilateral right hilum. (Right) Coronal oblique CECT (MIP image) of the same patient confirms that the nodule 🔁 represents a pulmonary arteriovenous malformation. Note the lesion's feeding artery ᠫ and draining vein 🔁. The latter was visible on radiography and suggested the correct prospective diagnosis.

Amyloidoma



Pulmonary Inflammatory Myofibroblastic Tumor



(Left) Composite image with axial CECT in lung (left) and soft tissue (right) window of a 68-year-old man with prostate cancer and a radiographic abnormality shows a spiculated nodule with coarse eccentric calcification \square Biopsy demonstrated an amyloidoma. (Right) Axial CECT of a 38-year-old man with an incidentally discovered radiographic abnormality shows a right upper lobe nodule *with internal low* attenuation suspicious for primary lung cancer. Biopsy demonstrated inflammatory myofibroblastic tumor.
KEY FACTS

TERMINOLOGY

- Most common histologic subtype of lung cancer
- Term bronchioloalveolar carcinoma no longer in use

IMAGING

- Adenocarcinoma in situ (AIS)
 o Ground-glass nodule (GGN) ≤ 3 cm
- Minimally invasive adenocarcinoma (MIA)
 GGN or part-solid nodule < 3 cm
- Invasive adenocarcinoma
 - Lepidic predominant adenocarcinoma (LPA)
 Usually part-solid; may be purely ground-glass
 - Acinar, papillary, micropapillary, or solid predominant with mucin production
 - Usually solid; may include ground-glass component
 - Invasive mucinous adenocarcinoma
 - Multifocal, multilobar, bilateral
 - Consolidation, air bronchogram

TOP DIFFERENTIAL DIAGNOSES

- Infection
 - Several infections, even if subclinical, can manifest with ground-glass opacity, part-solid or solid nodules

PATHOLOGY

- AIS
 - o Malignant but preinvasive
- MIA
 - Invasion ≤ 0.5 cm in any 1 focus
- Invasive adenocarcinoma
- Admixture of histologic subtypes

CLINICAL ISSUES

- Cigarette smoking is single most important risk factor
- Common symptoms/signs: Asymptomatic, cough, dyspnea, chest pain, weight loss, hemoptysis
- Treatment: Surgery, targeted therapy, chemotherapy, radiation, palliation

(Left) Coned-down sagittal NECT shows a ground-glass nodule 🔁 in the right lower lobe superior segment. Ground-glass opacity is characterized by absence of obscuration of underlying vascular structures, typical of solid nodules and consolidations. (Right) Photomicrograph (H&E stain, 100x) shows adenocarcinoma in situ manifesting with pure lepidic growth (along alveolar walls) of neoplastic cells without stromal, vascular, or pleural invasion. These lesions are typically pure ground-glass nodules that measure \leq 3 cm.





(Left) Axial NECT shows a minimally invasive adenocarcinoma that manifests as an ill-defined ground-glass nodule 🔁. These lesions are typically small ground-glass or part-solid nodules. For part-solid nodules, the solid component measures up to 0.5 cm. (Right) Photomicrograph (H&E stain, 40x) shows predominantly lepidic growth of tumor cells that exhibited a < 5-mm focus of invasion. Histologically, most adenocarcinomas in situ and minimally invasive adenocarcinomas are nonmucinous.





TERMINOLOGY

Definitions

- Most common subtype of lung cancer
- Lepidic: Neoplastic cell growth along alveolar walls
- Term bronchioloalveolar carcinoma (BAC) no longer used

IMAGING

Radiographic Findings

- Solitary nodule: Often inconspicuous; solid and large nodules more likely to be visible
- Peripheral or central mass
- Consolidation (may be multifocal)
- Band-like opacities resembling focal fibrosis/scarring
- Associated findings
 - Postobstructive atelectasis or pneumonia
 - Local invasion of mediastinum &/or chest wall
 - o Lymphadenopathy
 - o Pleural effusion

CT Findings

- Pulmonary nodule (≤ 3 cm)
 - Solid, part-solid, ground-glass
 - ± multifocal ground-glass nodules (GGN) in same or other lung lobes
- Pulmonary mass (> 3 cm)
 - Peripheral or central location
 - o Borders: Well- or ill-defined, lobular, spiculated
 - o May exhibit locally invasive behavior
 - CECT may distinguish tumor from adjacent atelectasis
- Focal or multifocal consolidations
- Bubbly appearance, pseudocavitation, or cystic airspaces with wall thickening/nodularity
- Associated findings
 - Local mediastinal or chest wall invasion
 - Hilar/mediastinal lymphadenopathy
 - Smooth or nodular interlobular septal thickening due to lymphangitic carcinomatosis
 - Miliary pattern of pulmonary metastases
 - May be seen in epidermal growth factor receptor (EGFR)-positive adenocarcinoma

CT/Pathologic Correlation

- Nodule (characterized on thin-section CT)
 - Atypical adenomatous hyperplasia (AAH)
 - Preinvasive
 - GGN ≤ 0.5 cm
 - Adenocarcinoma in situ (AIS)
 - Malignant and preinvasive
 - GGN \leq 3 cm
 - o Minimally invasive adenocarcinoma (MIA)
 - GGN or part-solid nodule ≤ 3 cm (i.e., coexistent ground-glass and solid components)
 - Solid component ≤ 0.5 cm
 - □ Correlates with invasive component at pathology
 - Often larger on imaging than on histology (adjacent atelectasis, inflammation, fibrosis)
 - Ground-glass component
 - Correlates with lepidic component
 - □ Invasive component can exist in GGN

- Nodule, mass, or mass-like consolidation
 - o Invasive adenocarcinoma
 - Lepidic-predominant adenocarcinoma (LPA)
 Part-solid or ground-glass nodule/mass
 - □ Solid component > 0.5 cm
 - Acinar, papillary, micropapillary, or solid predominant with mucin production
 - Usually solid; may include ground-glass component
 - Variants of invasive adenocarcinoma
 - Invasive mucinous adenocarcinoma
 - □ Variable appearance; focal or multifocal
 - Consolidations, air bronchograms (may simulate pneumonia)
 - □ GGN, part-sold, or solid nodules or masses
 - Other variants
 - □ Colloid adenocarcinoma: Peripheral, circumscribed, low-attenuation lesion

CT/Prognostic Correlation

- Part-solid nodule
 - Solid component more predictive of prognosis than total lesion size, including ground-glass component
 - Solid component < 2 cm: Higher disease-free survival
 - Extensive ground-glass component: Favorable prognostic sign
 - T descriptor (TNM) is determined by size of solid component
 - T1mi (≤ 0.5 cm), T1a (0.6-1 cm), T1b (1.1-2.0 cm), T1c (2.1-3.0 cm)
- Predictors of better outcome
 - Pure GGN
 - Intrinsic air bronchograms or lucencies
- Predictors of poor outcome
 - Morphology: Lobulated, spiculated, concave notch
 - o Cavitation
 - Fissural retraction
 - Solid lesions have increased likelihood to spread through airspaces, associated with early recurrence after sublobar resection

Nuclear Medicine Findings

- PET/CT
 - Initial staging and restaging
 - FDG uptake may correlate with lesion size and size of solid component
 - Multiple studies suggest optimal SUV of ~ 2.0 to differentiate MIA from invasive adenocarcinoma
 - Another study found SUV of 2.0 as optimal cutoff for invasiveness
 - FDG-avid GGN associated with foci of invasion

Imaging Recommendations

- Best imaging tool
 - o Thin-section CT, preferably ≤ 1.5-mm sections
- Reporting recommendations
 - Report size of entire nodule and size of solid component
 - Management of solid and subsolid nodules per Fleischner Society guidelines; use Lung-RADS for screening exams

DIFFERENTIAL DIAGNOSIS

Infection

- Nodule
 CON past calid a
- o GGN, part-solid nodule, or solid nodule
- Mass: Consolidation, pneumonia, lung abscess

Vasculitis

- Granulomatosis with polyangiitis (GPA)
 - Multifocal lung nodules; frequently part-solid, ± cavitation

PATHOLOGY

General Features

- Etiology
 - Cigarette smoking: Single most important risk factor
 Carcinogens: Asbestos, radon

Microscopic Features

- AAH (preinvasive)
 - Alveoli lined by cuboidal cells with atypical nuclei, scant cytoplasm, and minimal mitoses
- AIS (malignant but preinvasive)
 - o ≤3 cm
 - Purely lepidic growth
 - Along alveolar walls; no stromal, vascular, or pleural invasion
 - Usually nonmucinous
 - Diagnosis requires evaluation of entire lesion
- MIA
 - o ≤3 cm
 - Predominantly lepidic growth
 - Invasion ≤ 0.5 cm in any 1 focus
 - Absence of stromal, vascular, or pleural invasionUsually nonmucinous
- Invasive adenocarcinoma
 - Admixture of histologic subtypes; predominant subtypes reported in semiguantitative 5% increments
 - o LPA
 - Mostly lepidic, similar to AIS and MIA
 - Lymphatic, vascular, pleural invasion, or necrosis
 - Invasive component > 0.5 cm
 - Acinar predominant adenocarcinoma
 - Round to oval-shaped malignant glands invading fibrous stroma
 - Neoplastic cells and glandular spaces may contain mucin
 - Papillary predominant adenocarcinoma
 - Malignant cuboidal to columnar malignant cells growing along fibrovascular cores
 - o Micropapillary predominant adenocarcinoma
 - Small papillary clusters of glandular cells growing within alveoli; no fibrovascular cores
 - Implies worse prognosis compared to other cell types
 - Solid predominant adenocarcinoma with mucin production
 - Large component of polygonal cells forming sheets, without adenocarcinoma patterns
 - □ i.e., acinar, papillary, micropapillary, or lepidic

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Cough, dyspnea, chest pain (may be pleuritic)
 - o Hemoptysis, hoarseness, weight loss
 - Superior vena cava syndrome, Pancoast syndrome
 - o May be asymptomatic, discovered with screening
- Other signs/symptoms
 - Extrathoracic metastases: Variable signs and symptoms depending on affected organ
 - Skeletal metastases: Bone pain, pathologic fracture
 - Liver metastases: Altered liver function,
 - hepatomegaly, &/or jaundice
 - Paraneoplastic syndromes

Demographics

- Age
 - o Mean age: 64 years
- Sex
 - M > F; dramatic increase among women in last 3 decades
 Nonsmokers: More frequently women
- Ethnicity
 - Higher incidence in African Americans

Natural History & Prognosis

- Prognosis depends mostly on stage at presentation
- Molecular features
 - EGFR mutation
 - Commonly nonsmokers, women, and Asians
 - Implies better prognosis
 - Good response to EGFR tyrosine kinase inhibitors (e.g., erlotinib, gefitinib, afatinib)
 - Anaplastic lymphoma kinase (ALK) mutation
 - Typically younger age, nonsmokers and ex-smokers
 - Good response to ALK inhibitors (e.g., crizotinib)
 - KRAS, ROS1, BRAF, RET mutations
 - Also respond to various targeted therapies
 - o PD1/PD-L1 and CTLA-4
 - Immunotherapy checkpoint inhibitors (e.g., nivolumab, pembrolizumab)

Treatment

- Surgical resection
- Radiotherapy or ablation for poor surgical candidates
- Targeted therapies, chemotherapy, &/or radiation therapy
- Palliation

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(Left) Axial NECT of a patient with left upper lobe atypical adenomatous hyperplasia shows a 5-mm ground-glass nodule 🔼 Distinction between indolent malignancy and atypical adenomatous hyperplasia is not possible based on imaging. (Right) Photomicrograph (H&E stain, 40x) shows a small proliferation of atypical type II pneumocytes &/or Clara cells. Histologic differentiation between cellular atypical adenomatous hyperplasia and adenocarcinoma in situ may be impossible.





(Left) Axial NECT shows a left upper lobe part-solid spiculated mass with air bronchograms and pleural tags, consistent with invasive adenocarcinoma. Histology showed 60% acinar and 40% lepidic invasive adenocarcinoma. Air bronchograms are often associated with welldifferentiated neoplasms. (Right) Axial fused FDG PET/CT of the same patient shows FDG uptake in the solid component of the lesion. FDG uptake correlates with extent of invasive components in adenocarcinomas.





(Left) PA chest radiograph of a patient with lung adenocarcinoma shows a right lower lobe consolidation $\overline{\supseteq}$ (Right) Composite image with CECT and PET/CT of the same patient shows a right lower lobe consolidation 🔁 with peripheral ground-glass $opacities \supseteq$, which exhibits marked FDG uptake 🖾 Note that this imaging appearance mimics pneumonia, a reason to follow-up consolidations to resolution. Histology demonstrated papillary predominant adenocarcinoma with minor acinar and mucinous components.

(Left) Axial NECT shows a heterogeneous right upper lobe adenocarcinoma with intrinsic cystic lucencies (pseudocavitation), a finding that correlates with slowgrowing neoplasms. Air bronchograms and pure ground-glass opacity are also good prognostic indicators. (Right) Axial NECT of a patient with adenocarcinoma shows a solid right lower lobe mass 乏 with retraction of the adjacent major fissure. Pleural retraction, concave lesion notches, spiculation, and polylobular morphology suggest a poor prognosis.





(Left) Axial CECT of a patient with adenocarcinoma shows a right middle lobe lobulated $mass \supseteq$ with intrinsic punctate calcifications. These calcifications may represent engulfed preexistent granulomas or dystrophic tumor calcifications. A small right pleural effusion 😂 is also present. (Right) Axial CECT shows a part-solid nodule 🔁 with a solid component > 5 mm \supseteq , consistent with invasive adenocarcinoma. The size of the solid component is used to determine the T-descriptor for staging purposes.





(Left) Coronal NECT of a patient with multifocal invasive acinar adenocarcinoma shows bilateral ground-glass opacity \blacksquare , part-solid \blacksquare , and solid \blacksquare pulmonary nodules. (Right) Composite image with axial NECT of 2 different patients with metastatic adenocarcinoma shows profuse pulmonary micronodules, consistent with miliary metastases. These imaging manifestations may simulate a miliary pulmonary infection.







(Left) Coronal CECT of a patient with invasive adenocarcinoma shows a central mass encasing and narrowing adjacent central bronchi. Although adenocarcinomas are often peripheral lesions, central lesions also occur. (Right) Composite image with NECT of an untreated adenocarcinoma at initial assessment (left) and 10 years later (right) shows a spiculated right upper lobe solid nodule with significant interval growth, highlighting the indolent nature of some of these neoplasms.





(Left) Coned-down AP chest radiograph of a patient with invasive adenocarcinoma shows a left upper lobe cavitary mass \supseteq As infection and vasculitis may have a similar appearance, short-term follow-up radiographs were recommended. (Right) Composite image with coronal CECT (left) and axial fused FDG PET/CT (right) of the same patient shows a left upper lobe cavitary mass with moderate FDG uptake 🔁 at the periphery of lesion. FDG uptake and presence of true cavitation are poor prognostic indicators.





(Left) AP chest radiograph of a patient with colloid adenocarcinoma shows a large lobulated mass in the left midlung zone. (Right) Axial NECT of the same patient shows a well-defined fluid attenuation left upper lobe mass \supseteq and an adjacent lingular consolidation $\overline{\square}$. Entities, such as congenital pulmonary airway malformation and intrapulmonary bronchogenic cyst, were initially considered instead of malignancy. Low attenuation within colloid adenocarcinoma correlates with intratumoral mucin.

KEY FACTS

TERMINOLOGY

• Squamous cell carcinoma (SCC)

IMAGING

- Radiography
 - Central hilar/perihilar mass
 - Bronchial obstruction with postobstructive atelectasis/pneumonia
 - Mediastinal/hilar lymphadenopathy
 - Peripheral lung nodule or mass
- CT
 - Central nodule/mass ± postobstructive effects
 - Peripheral nodule/mass, assessment of morphologic features, local invasion
 - Assessment of local invasion, lymphadenopathy
- MR
 - Complementary to CT; assessment of brachial plexus, mediastinum, chest wall
- **PET/CT**: Staging and restaging

TOP DIFFERENTIAL DIAGNOSES

- Adenocarcinoma
- Small cell carcinoma
- Lung abscess
- Lung metastasis

PATHOLOGY

- Irregular endobronchial lesion, may be polypoid
- Keratinization &/or intercellular bridging

CLINICAL ISSUES

- Symptoms/signs
 - o Cough, hemoptysis, dyspnea
 - Pancoast syndrome
 - Paraneoplastic hypercalcemia

DIAGNOSTIC CHECKLIST

• Consider SCC in smoker with central lung mass ± postobstructive atelectasis/pneumonia

(Left) Axial CECT of a 68-yearold heavy smoker with squamous cell carcinoma (SCC) shows an irregular left lower lobe mass 🔁 that abuts the pleura \square , concerning for pleural invasion. Note extensive emphysema. (Right) Coronal FDG PET of the same patient shows the FDG-avid left lower lobe malignancy 🔁, mediastinal and supraclavicular $lymphadenopathy \ge$, and a left adrenal lesion 🔁. The findings are consistent with stage IV lung cancer. PET/CT is very useful in the accurate initial staging of lung cancer.





(Left) Axial CECT of a 64-yearold man with SCC shows an irregular left upper lobe soft tissue mass \implies that encases branches of the left upper lobe bronchus. Adjacent groundglass opacity 🔁 is suspicious for perilesional hemorrhage or post-obstructive change. (Right) Fused coronal FDG PET/CT of the same patient shows the primary left upper lobe FDG-avid lesion ा ा and a ≥ solitary osseous metastasis *⊡*. The solitary metastasis and the primary tumor can both be treated with radiation.





Abbreviations

• Squamous cell carcinoma (SCC)

Definitions

• Primary lung malignancy thought to evolve from squamous metaplasia (preinvasive lesion)

IMAGING

General Features

- Best diagnostic clue
 - Endoluminal obstructing lesion with postobstructive atelectasis/pneumonia
- Location
 - o Central: 2/3 in mainstem, lobar, segmental bronchi
- Apical lesion: Pancoast tumor
- Size
 - o Average diameter: ~ 2.5 cm on radiography
- Incidentally detected lesions: ~ 0.8-1.5 cm on CT
- Borders: Spiculated, lobulated, or smooth
- Attenuation: Variable; ± necrosis, cavitation, calcification

Radiographic Findings

- Radiography
 - o Central hilar/perihilar mass with bronchial obstruction
 - Atelectasis: Sublobar, lobar, whole lung
 - □ S-sign of Golden: Atelectasis + central mass, Sshaped atelectatic lung interface
 - Central bronchial stenosis or bronchus cutoff
 - Postobstructive pneumonia: May obscure tumor
 - Regional hyperlucency
 - Reduced ventilation from central obstruction
 Reduced lung density from hypoxic vasoconstriction
 - Mediastinal/hilar lymphadenopathy
 - Wide mediastinum, splayed carina, aortopulmonary window convexity, hilar enlargement
 - o Pulmonary nodule/mass, 1-10 cm
 - Cavitation (15%)

CT Findings

- NECT
 - Disadvantages: Difficult assessment of hilar lymphadenopathy, local invasion, liver metastases
 - Advantages: Improved visualization of calcification, characterization of adrenal nodules
- CECT
 - Central nodule/mass
 - Assessment of bronchial obstruction
 - Increased conspicuity of endobronchial lesion
 - Distinction of tumor from atelectasis/pneumonia
 - Assessment of local invasion
 - Peripheral nodule/mass
 - Assessment of border characteristics
 - Lobulation, spiculation, pleural tags
 - Central necrosis, cavitation, assessment of cavity wall thickness and morphology
 - Cavitation more frequent in larger lesions
 - □ Wall thickness typically > 1.5 cm

- Calcification in ~ 13%
- Assessment of local invasion
 - Mediastinal structures: Heart, pericardium, great vessels, aerodigestive tract
 - Pleura, diaphragm
 - Chest wall: Factors favoring invasion
 - □ > 3-cm tumor-pleura contact
 - Obtuse angle of tumor-pleura interfaceIncreased density of extrapleural fat
- Lymphadenopathy
 - Lymph nodes > 1 cm in short axis: Increased probability of metastases
 - Subcarinal lymph nodes: > 1.2-cm short axis
- Intrathoracic metastases
 - Pulmonary nodules/masses
 - Pleural/pericardial effusion, nodules/masses
- Extrathoracic metastases
 - Adrenal gland
 - Malignancy favored: Mass > 3 cm, poorly-defined margins, irregular rim enhancement, invasion of adjacent structures
 - □ Benign etiology favored if attenuation < 10 HU

MR Findings

- T1WI
 - Chest wall invasion
 - Pleural thickening
 - Tumor signal intensity extending into chest wall
- T2WI
 - Chest wall invasion
 - Pleural thickening with high signal
 - Focal high signal extending into chest wall
- T1WI C+ FS
 - Parietal pleural enhancement
- Generally used for problem-solving in selected cases
 Assessment of local invasion
 - Evaluation of brachial plexus in Pancoast tumors

Nuclear Medicine Findings

- PET/CT
 - Activity > mediastinal background; standard uptake value (SUV) > 2.5 → greater likelihood of malignancy
 - False-positive: Infection, granulomatous disease
 False-negative: Lesions < 1 cm
 - Mediastinum: Activity > background or SUV > 2.5 considered abnormal
 - Specificity 80%; positive result requires pathologic confirmation
 - Futile thoracotomy prevented in 20% of patients by detection of metastases

Imaging Recommendations

- Best imaging tool
 - CT and PET/CT for diagnosis, staging, and surveillance
 - Protocol advice
 - CT for clinical staging: Thorax and adrenal glands
 - Evaluation of primary tumor, lymph nodes, metastases
 - Image-guided biopsy planning
 - CECT for optimal evaluation of hilar lymph nodes and metastases

DIFFERENTIAL DIAGNOSIS

Adenocarcinoma

- Solid, part-solid, or ground-glass nodule or mass
- Spiculated or lobular lesion borders

Small Cell Carcinoma

• Centrally located locally invasive mass, lymphadenopathy

Lung Abscess

- Cavitary mass, lower lobe superior or posterior basilar segments
- Surrounded by consolidation or airspace disease

Lung Metastasis

- Head and neck SCC
- Frequent cavitation
- Up to 46% of solitary nodules in setting of extrapulmonary malignancy are metastases

PATHOLOGY

General Features

- Etiology
 - Postulated progression: Squamous metaplasia → dysplasia → carcinoma in situ → invasive carcinoma
 - Strong association with cigarette smoking
 - Smoking causes 80% of lung cancer death in USA
 - Lung cancer risk directly related to number of cigarettes smoked, length of smoking history, and tar/nicotine content
 - Cessation of smoking reduces lung cancer risk
- Genetics
 - Activating *EGFR* mutation and *ALK* fusions common in adenocarcinoma, typically not present in SCC
 - Mutation of *TP53* and *CDKN2A* alterations frequent in SCC
 - Different genome of never smokers compared with smokers

Staging, Grading, & Classification

- CT and PET/CT for clinical staging
- Thoracentesis: Malignant pleural effusion upstages to M1a
 May provide therapeutic relief in large effusions

Gross Pathologic & Surgical Features

- Irregular endobronchial lesion, may be polypoid
 Near universal bronchial wall invasion
 - Growth along bronchial mucosa, airway obstruction, adjacent lymph node invasion
- Large tumors may exhibit cavitation

Microscopic Features

- Characterized by keratinization &/or intercellular bridging
- High mitotic rates, necrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - 80% of patients are symptomatic
 - Symptoms more common with central lesions and advanced disease

- Cough, hemoptysis, dyspnea, fever
- Other signs/symptoms
 - o Postobstructive pneumonia/atelectasis
 - Chest pain from chest wall invasion
 - Pancoast syndrome
 - Neuropathic pain or atrophy of ipsilateral upper extremity muscles due to brachial plexus involvement
 - Horner syndrome: Sympathetic chain and stellate ganglion involvement
 - Paraneoplastic syndromes: Hypercalcemia due to tumor secretion of parathyroid hormone-like substance

Demographics

- Age
 - Risk of lung cancer increases with age
- Sex
 - o Tobacco-related cancer incidence higher in men
- Ethnicity
 - Higher incidence of lung cancer in African Americans compared with other racial groups
 - May relate to differences in smoking prevalence, metabolism of tobacco smoke products, susceptibility to tobacco-induced lung cancer, &/or socioeconomic status

Natural History & Prognosis

- Lifetime risk of developing lung cancer: 1 in 14 persons (6.95%)
- Decreased survival with increased TNM stage
 - 5-year survival of 3.6% with distant metastases (all lung cancer subtypes)
- Screening with low-dose spiral CT reduced lung cancer mortality by ~ 20%

Treatment

- Stages I-II: Surgical resection with adjuvant chemotherapy in select cases
- Stage IIIA: Surgery, chemotherapy, radiation therapy, or combination
- Stage IIIB: Chemotherapy and radiation therapy
- Stage IV: Chemotherapy with palliative radiation therapy in select cases
 - Resection/radiation of solitary metastasis in selected cases
 - Pembrolizumab approved for first-line treatment in patient with high expression of PD-L1 mutation: Tumor proportion score, 50%
 - Pembrolizumab alone or + carboplatin + taxane
 - PD-L1 1-49%: Platinum-based therapy

DIAGNOSTIC CHECKLIST

Consider

• SCC in smoker with central lung mass ± postobstructive atelectasis/pneumonia

- Feng SH et al: The new 8th TNM staging system of lung cancer and its potential imaging interpretation pitfalls and limitations with CT image demonstrations. Diagn Interv Radiol. 25(4):270-9, 2019
- Yue JY et al: CT-pathologic correlation in lung adenocarcinoma and squamous cell carcinoma. Medicine (Baltimore). 97(50):e13362, 2018

Squamous Cell Carcinoma





(Left) Axial CECT of a 77-yearold man with SCC shows an irregular spiculated peripheral nodule \supseteq with a small central area of cavitation. Cavitation develops due to tumor growth that exceeds blood supply with resultant necrosis. (Right) Axial CECT of a 67-year-old woman shows a small peripheral cavitary SCC 🔁. The patient had a history of tonsillar SCC. The differential diagnosis includes solitary metastasis, primary lung cancer, and infection.





(Left) Axial CECT of a 68-yearman with chronic lymphocytic leukemia shows a small left upper lobe central cavitary nodule \supseteq and right upper lobe tree-in-bud opacities →. The findings were interpreted as consistent with infection. (Right) Axial CECT of the same patient obtained 2 years later shows a spiculated lobulated left upper lobe mass with internal air-bronchograms 🖂 Biopsy showed SCC. Cavitary malignancies may simulate infectious etiologies and lead to late diagnosis.





(Left) PA chest radiograph of a 57-year-old man with SCC who presented with left shoulder pain shows a unilateral illdefined opacity \supseteq in the left apex that represented a Pancoast tumor. (Right) Axial CECT of the same patient shows a left apical heterogeneous mass that obliterates the extrapleural fat \supseteq . Biopsy confirmed SCC. Neuropathic pain or atrophy of ipsilateral upper extremity muscles from brachial plexus involvement are common signs of a Pancoast tumor.

Small Cell Carcinoma

KEY FACTS

TERMINOLOGY

- Small cell lung carcinoma (SCLC)
- Limited-stage small cell lung carcinoma (LS-SCLC)
- Extensive-stage small cell lung carcinoma (ES-SCLC)

IMAGING

- Radiography
 - o Central mass
 - o Bulky mediastinal &/or hilar lymphadenopathy
- CT
 - Central soft tissue mass
 - o Mediastinal &/or hilar lymphadenopathy
 - Invasion of mediastinal structures
 - Distant metastases
- **MR**: Contraindications to IV contrast, assessment of local invasion, brain imaging
- FDG PET/CT: Intense FDG uptake
 - o Initial staging
 - o Evaluation of treatment response and restaging

TOP DIFFERENTIAL DIAGNOSES

- Primary mediastinal large B-cell lymphoma
- Squamous cell carcinoma
- Carcinoid tumor

CLINICAL ISSUES

- Strongly associated with cigarette smoking
- 60-70% have metastatic disease at time of diagnosis
- Staging: Modified VALSG or 8th edition TNM system
 LS-SCLC corresponds to stages I-III
 ES-SCLC corresponds to stage IV
- Treatment
 - LS-SCLC: Chemotherapy and thoracic radiation
 - ES-SCLC: Systemic chemotherapy

DIAGNOSTIC CHECKLIST

• Consider SCLC in patient with a smoking history and a large central mass &/or extensive mediastinal/hilar/extrathoracic lymphadenopathy

(Left) PA chest radiograph of a 73-year-old man with small cell lung carcinoma shows mediastinal \blacksquare and left hilar lymphadenopathy 🖾. (Right) Coronal CECT of the same patient confirms left hilar adenopathy/mass 🛃 and bilateral mediastinal 🔁 lymphadenopathy. Most small cell lung carcinomas initially manifest as mediastinal &/or hilar lymphadenopathy and classically exhibit rapid growth when serial imaging is available due to aggressive biologic behavior.





(Left) Axial CECT of a 77-yearold man with small lung carcinoma shows mediastinal Description → Description mammary 🔁 lymphadenopathy, bilateral pleural effusions with associated pleural nodules \blacksquare , and a pleural mass 🔁, consistent with metastatic disease. (Right) Axial CECT of the same patient shows metastatic disease in the liver ➡, pancreas ➡, and upper abdominal lymph nodes 🛃. If FDG-PET/CT is not available, CECT of the abdomen and pelvis should form part of the initial imaging evaluation.





Abbreviations

- Small cell lung carcinoma (SCLC)
 - Limited-stage small cell lung carcinoma (LS-SCLC)
 Extensive-stage small cell lung carcinoma (ES-SCLC)

Definitions

- Primary pulmonary neuroendocrine malignancy
 - More aggressive than other pulmonary neuroendocrine tumors and non-small cell lung cancers
 - Rapid tumor growth, early metastatic spread, initial responsiveness to therapy
- 13-15% of all lung cancers

Associated Syndromes

- Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
 - Most common paraneoplastic syndrome associated with SCLC
 - ↑ secretion of antidiuretic hormone: Hyponatremia; impaired water excretion
- Cushing syndrome
 - Increased production of adrenocorticotropic hormone: Weakness, hyperglycemia, polyuria, hypokalemic alkalosis
- Eaton-Lambert syndrome
 - Impaired release of acetylcholine: Proximal muscle weakness
- Encephalomyelitis
- Limbic encephalitis
- Acromegaly : \uparrow ectopic growth hormone

IMAGING

General Features

- Best diagnostic clue
 - Central pulmonary nodule or mass
 - Bulky mediastinal &/or hilar lymphadenopathy
 - Encasement/invasion of mediastinal structures
- Location
 - o Central

Radiographic Findings

- Radiography
 - Central pulmonary nodule/mass extending to hilum/mediastinum
 - May produce atelectasis and volume loss
 - S-sign of Golden, Luftsichel sign
 - Bulky mediastinal &/or hilar lymphadenopathy: Mediastinal lymphadenopathy frequently inseparable from hilar lymphadenopathy
 - Pleural effusion

CT Findings

- NECT
 - Central pulmonary nodule or mass (90-95%)
 May produce atelectasis
 - Mediastinal (92%) &/or hilar (84%) lymphadenopathy
 - May be only imaging manifestation of disease
 - Pulmonary lesion may not be evident
 - Peripheral pulmonary nodule or mass uncommon

- o Encasement of mediastinal structures in 68%
- Peripheral nodule without associated lymphadenopathy < 5%
- CECT
 - o Evaluation of vascular involvement
 - Heart and pericardium
 - Pulmonary arteries &/or veins encasement
 - Superior vena cava syndrome
 - Decreased or absent opacification of superior vena cava; invasion by tumor mass
 - Collateral vessels in chest wall, neck, &/or mediastinum
 - Evaluation for lymphadenopathy and metastases
 - Extrathoracic metastases
 - Bone: 19-38%; liver: 17-34%; adrenal glands: 10-17%; brain: 14%

MR Findings

- Thoracic MR not routinely used
 - Contraindications to IV contrast: Renal dysfunction, severe allergy to IV contrast
 - o Indications
 - Assessment of local invasion
 - Heart and pericardium
 - Superior vena cava
 - Other great vessels
- Imaging of brain (preferably with MR) recommended for all patients
 - Metastases in 10-15% of neurologically asymptomatic patients

Nuclear Medicine Findings

- PET/CT
 - Most tumors, affected lymph nodes, and metastases demonstrate intense FDG uptake
 - SCLC very metabolically active
 - Excellent for initial staging
 - PET/CT may lead to change in initial management
 Overall treatment plan &/or radiation treatment plan
 - May be used for evaluation of treatment response &/or restaging

Imaging Recommendations

- Best imaging tool
 - CECT for evaluation of primary tumor and relationship to intrathoracic structures
 - FDG PET/CT for initial staging
 - Brain imaging (MR or CT) recommended for all patients

DIFFERENTIAL DIAGNOSIS

Primary Mediastinal B-Cell Lymphoma

- Diffuse large B-cell lymphoma is most common
 - Non-Hodgkin lymphoma
 - Arises from thymus
- Patients 30-40 years of age
- Systemic symptoms
 Fever, night sweats, weight loss
- Large mediastinal mass
- Associated lymphadenopathy in lower neck &/or chest

Squamous Cell Carcinoma

- Patients 50-60 years of age
- Strongly associated with cigarette smoking
- Central pulmonary nodule or mass
 Cavitation may occur

Carcinoid Tumor

- Patients 40-50 years of age
- Hilar or perihilar nodule/mass
 - May demonstrate intense enhancement
 - Calcification patterns
 - Punctate or diffuse
- Entirely or partially endobronchial
 - May produce varying degrees of atelectasis and volume loss

PATHOLOGY

General Features

- Etiology
 - Strongly associated with cigarette smoking
 > 95% of patients are smokers

Staging, Grading, & Classification

- 8th edition of tumor-node-metastasis (TNM) staging system used to stage SCLC
- Veterans Administration Lung Cancer Study Group (VALSG)
 1st method developed to clinically stage SCLC
 - Modified VALSG
 - Still widely used to stage SCLC
 - Limited stage
 - □ Corresponds to stages TMN I-III
 - □ Disease encompassed by single radiation port
 - □ Ipsilateral &/or contralateral mediastinal &/or supraclavicular lymphadenopathy
 - Ipsilateral pleural effusion
 - Extensive stage
 - Corresponds to stage TMN IV
 - $\hfill\square$ Not confined to single radiation port
 - Metastatic disease
 - NM used to select patients for surgical resection (i.e., T1-2 N0 M0)

Gross Pathologic & Surgical Features

• Majority (90-05%) arise from lobar or mainstem bronchi

Microscopic Features

- High mitotic rate
- Small blue, round or oval cells
 - Pure subtypeCombined subtype
 - Adenocarcinoma, squamous cell carcinoma, large cell carcinoma
- Immunohistochemical evaluation
 - o TTF-1 (thyroid transcriptor factor 1): 80%

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Cough, chest pain, dyspnea, hemoptysis
 - Anorexia, weight loss, and fatigue

- Other signs/symptoms
 - o Superior vena cava syndrome
 - Dyspnea, facial swelling, arm swelling, hoarseness, stridor
 - Paraneoplastic syndromes
 - Symptoms associated with extrapulmonary metastases
 Brain: Ataxia, seizures, altered mental status
 - Bone: Pain

Demographics

- Age
 - o 60-70 years
- Sex
 - Men more frequently affected than women

Natural History & Prognosis

- Aggressive malignancy; increased doubling time
 High rate of metastatic dissemination
- 5-year overall survival 6.3%
 - o LS-SCLC: 10-15%
 - ES-SCLC: 1-2%

Treatment

- Initial high response rates to 1st-line combination chemotherapy, but up to 80% of patients with LS-SCLC and almost all patients with ES-SCLC develop recurrent or progressive disease
- LS-SCLC
 - Can be curable
 - Chemotherapy and early concurrent thoracic radiation
 - Majority of tumors not amenable to surgical resection
 - Consider resection if disease limited to lung nodule or well-defined mass
- ES-SCLC
 - o Primary goal: Prolong survival and improve quality of life
 - Systemic chemotherapy
 - Immunotherapy (atezolizumab or durvalumab) + chemotherapy: Increased overall survival
- Prophylactic cranial radiation
 - Patients with LS- or ES-SCLC who have completed chemotherapy and responded
- Potential molecular targets identified, but target therapy has not demonstrated consistent clinical response

DIAGNOSTIC CHECKLIST

Consider

• SCLC in patients with smoking history and large central mass &/or extensive mediastinal/hilar/extrathoracic lymphadenopathy

Image Interpretation Pearls

• Brain imaging (MR or CT) recommended for all patients

Reporting Tips

• 60-70% have metastatic disease at diagnosis

- Martucci F et al: Impact of 18F-FDG PET/CT in staging patients with small cell lung cancer: a systematic review and meta-analysis. Front Med (Lausanne). 6:336, 2019
- Kalemkerian GP et al: Advances in small cell lung cancer. Hematol Oncol Clin North Am. 31(1):143-56, 2017

Small Cell Carcinoma





(Left) Axial CECT of a 78-yearold man with small cell lung carcinoma shows a left hilar mass &/or lymphadenopathy ➡ No extrathoracic disease was identified. (Right) Axial CECT of the same patient shows a heterogeneously enhancing left hilar mass 🖂 and subcarinal lymphadenopathy 🖂, consistent with limited stage disease. The treatment of choice for limited-stage disease is chemoradiation. Rapid growth tumor, early metastases, and initial response to therapy are typical of small cell carcinoma.





(Left) Coronal whole-body FDG PET shows evidence of extensive-stage small cell lung carcinoma with diffuse and extensive FDG-avid metastases. (Right) Wholebody FDG PET of the same patient obtained 3 months after starting treatment with combined chemotherapy shows significant response to treatment. Despite a high response rate to initial treatment, up to 80% of patients with limited-stage disease and almost all patients with extensive-stage small cell carcinoma develop recurrent or progressive disease.





(Left) Axial CECT of a 65-year old man with limited-stage small cell lung carcinoma shows a small irregular right upper lobe peripheral solid nodule \supseteq , consistent with the primary malignancy and associated right hilar lymphadenopathy 🔁. (Right) Whole-body FDG PET of the same patient shows the FDGavid primary malignancy 🔁 and FDG-avid hilar lymphadenopathy ᠫ. A small percentage of patients with small cell lung carcinoma present with a peripheral pulmonary nodule.

Multifocal Lung Cancer

KEY FACTS

TERMINOLOGY

- Synchronous lung cancers: 2 or more lung cancers detected simultaneously, without metastases
- Metachronous: 2 or more lung cancers detected at different times, without metastases
- 1ary lung cancer with satellite lesion(s)
- 1ary lung cancer with metastases of same histology

IMAGING

- Radiography
 - Multiple nodules, masses, consolidations
- CT
 - o Multiple lung nodules, masses, consolidations
 - Solid &/or subsolid attenuation
 - Dominant lesion may occur
- PET/CT
 - Clinical staging/restaging of malignancy
 - Evaluation of extrathoracic disease

TOP DIFFERENTIAL DIAGNOSES

- Primary lung cancer and benign lung nodules
- Extrapulmonary malignancy with hematogenous metastases

PATHOLOGY

• Synchronous lung cancers differentiated based on histology or molecular analysis

CLINICAL ISSUES

- Survival: Synchronous lung cancers (18-76%)
- Multiple biopsies may be required for diagnosis

DIAGNOSTIC CHECKLIST

- Consider multifocal lung cancer in patients with multiple lung lesions without lymphadenopathy or distant metastases
- Decision to classify two or more lesions as synchronous primary cancers vs. single cancer with satellite nodule(s) should include multidisciplinary discussion

(Left) PA chest radiograph of a patient with metastatic lung cancer shows a dominant right mid lung zone nodule 🔁 and innumerable bilateral smaller pulmonary nodules that represented metastatic disease. (Right) Coronal NECT MIP reformatted image of the same patient shows a dominant spiculated cavitary middle lobe nodule ₽, which represents a primary lung cancer. The innumerable bilateral smaller lung nodules represent hematogenous pulmonary metastases.





(Left) Composite image with axial CECT shows a left upper lobe spiculated lung nodule (top) and a lobulated cavitary lung mass (bottom). In the absence of metastases or lymphadenopathy, these may represent synchronous lung cancers. Histologic and molecular analysis may be required for confirmation. (Right) Axial NECT of a patient with multifocal adenocarcinomas shows multiple nonsolid and partsolid nodules **→**. Biopsy of one of the nodules confirmed invasive adenocarcinoma with acinar pattern.





Definitions

- Multiple primary lung cancers, clinical criteria
 - **Synchronous**: 2 or more separate lung cancers detected simultaneously, without systemic metastases
 - If same histology, should be in different lobes, without N2 or N3 disease
 - **Metachronous**: Detection of 2 or more lung cancers separated by time, without systemic metastases
 - If same histology, ≥ 2-year interval
- Primary lung cancer with satellite lesion(s)
 - Lesions of same histology within same lobe regardless of size, without systemic metastases
- Hematogenous metastases
 - Lung cancer with multiple lung metastases of same histology
 - Lesions of same histology in different lobes with N2 or N3 disease

IMAGING

Radiographic Findings

- Radiography
 - $o \geq 2$ lung nodules, masses, consolidations
 - Dominant lesion may occur
 - o ± lymphadenopathy in metastatic disease
 - ± pleural effusion

CT Findings

- 2 or more lung nodules, masses, consolidations
- Solid &/or subsolid attenuation
- Dominant lesion may occur
- ± lymphadenopathy in cases of metastatic disease
- Pleural effusion, pleural nodules

Nuclear Medicine Findings

- PET
 - Optimal imaging modality for clinical staging
 - Evaluation of extrathoracic disease
 - Does not differentiate between multiple primary neoplasms and metastases

Imaging Recommendations

- Protocol advice
 - Thin-section NECT for evaluation of subsolid nodules

DIFFERENTIAL DIAGNOSIS

Primary Lung Cancer and Benign Lung Nodules

- Majority of lung nodules detected in association with lung cancer are benign
- Atypical adenomatous hyperplasia in patients with adenocarcinoma

Extrapulmonary Malignancy With Hematogenous Metastases

- Clinical history and biopsy critical for diagnosis
- Spherical well-defined nodules with peripheral/basilar predominance

PATHOLOGY

Staging, Grading, & Classification

- Synchronous lung cancers differentiated by histology or molecular analysis
- Same histology: Molecular testing for optimal differentiation of satellite/metastatic lesions from synchronous primaries
- 8th edition of TNM staging system: Primary lung cancer with satellite malignant lesions
 - T3: Satellite lesions in same lobe as primary tumor
 - o T4: Satellite lesions in different ipsilateral lobe as primary tumor
 - o M1a: Satellite lesions in contralateral lung
- Synchronous lesions: Size of largest tumor may be most important factor in surgical decision making

CLINICAL ISSUES

Natural History & Prognosis

- Survival: Synchronous lung cancers (18-76%)
- Differentiation between multiple primary lesions and metastatic disease important for management

Evaluation

- Multiple biopsies may be required to exclude multiple primary lung cancers
- Core needle biopsy recommended
 - Cytologic accuracy for determining lung cancer cell type only 60-80%
 - Improved accuracy with larger specimens
- Careful staging of synchronous lung cancers
 - Brain contrast-enhanced MR
 - Whole-body PET/CT
 - o Mediastinoscopy

Treatment

- Single primary lung cancer with satellite lesion in same lobe • Lobectomy
- Multiple primary lung cancers
 - Resection if no lymph node involvement or distant metastases
- Radiation in poor surgical candidates

DIAGNOSTIC CHECKLIST

Consider

- Multiple primary lung cancers in patients with multiple lung lesions without lymphadenopathy or distant metastases
- Multifocal adenocarcinomas in patients with slow-growing part-solid and nonsolid nodules
- Decision to classify 2 or more lesions as synchronous primary cancers vs. single cancer with satellite nodule(s) should include multidisciplinary discussion

- Carter BW et al: Revisions to the TNM staging of lung cancer: rationale, significance, and clinical application. Radiographics. 38(2):374-91, 2018
- Kozower BD et al: Special treatment issues in non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 143(5 Suppl):e369S-99S, 2013

Lung Cancer Screening

KEY FACTS

BACKGROUND

- Lung cancer
 - Leading cause of cancer-related mortality in USA
 - o 5-year survival rates are only 18.6%
 - Early stage non-small cell lung cancer (NSCLC): Better prognosis, potentially curable
 - Smoking cessation: Best strategy for reducing lung cancer risk

CRITERIA FOR SCREENING

- 50-80 years of age
- \geq 20 pack-year smoking history
- Current smoker or quit within past 15 years

DIFFERENTIAL DIAGNOSIS

- Intrapulmonary lymph node, noncalcified granuloma
 - Extremely common, responsible for large percentage of false-positive lung screens
- Lung cancer

CLINICAL ISSUES

- Potential harms
 - False-positive results
 - False-negative results
 - o Overdiagnosis
 - o Incidental findings
 - Radiation exposure

REPORTING RECOMMENDATIONS

- LungRADS® 1.1
 - American College of Radiology (ACR) tool for standardization of lung cancer screening reporting and management recommendations
 - Reduces confusion in lung cancer screening and reporting
 - Assessment categories (0-4) directly tied to management recommendations
 - Follow-up generally with low-dose chest CT (LDCT), occasionally other (PET-CT, biopsy)

(Left) Axial NECT shows a lobulated 10-mm right upper lobe solid nodule \supseteq with intrinsic macroscopic fat, characteristic of a benign pulmonary hamartoma (LungRADS® category 1). Recommendation: Continue annual screening with LDCT in 12 months. (Right) Axial NECT shows an 18-mm right upper lobe ground-glass nodule 🔁 (LungRADS® category 2). Recommendation: Continue annual screening with LDCT in 12 months. Pure ground-glass nodules < 30 mm or ≥ 30 mm and unchanged or slowly growing fit category 2.



LungRADS® Category 1

LungRADS® Category 2

LungRADS® Category 2



LungRADS® Category 3



Pulmonary Neoplasms

(Left) Axial NECT shows a 6mm perifissural solid nodule Derifissural nodules include solid nodules with smooth margins, ovoid, lentiform or triangular shapes and < 10 mm in size. (LungRADS® category 2). Recommendation: Continue screening with annual LDCT in 12 months. (Right) Axial NECT shows a 7-mm right lower lobe solid nodule 🔁 (LungRADS® category 3, probably benign). Recommendation: Repeat LDCT in 6 months to document stability, assess growth, and determine malignant

potential.

Abbreviations

• Low-dose CT (LDCT)

BACKGROUND

Lung Cancer

- Leading cause of cancer-related mortality in USA
- Majority of patients present with symptoms of locally advanced or metastatic disease
- 2019: 14% (34.1 million) of adults in USA are current smokers (defined as lifetime history of smoking ≥ 100 cigarettes + currently smoke every day or some days)
- Primary risk factors: Age and smoking history
- 5-year survival rate
- o All lung cancers: 18.6%
- Early-stage lung cancer [non-small cell lung cancer (NSCLC)]: 56%; only 16% of lung cancers diagnosed at early stage
- Prevention with smoking cessation: Best strategy for reducing lung cancer risk

National Lung Screening Trial (NLST)

- Prospective randomized controlled trial
- Enrolled 53,454 participants at high risk for lung cancer
- Primary endpoint
 - Lung cancer mortality (relative reduction of 20% in LDCT screened patients)
- Secondary endpoints
 - All-cause mortality (relative reduction of 6.7% in LDCT screened patients)
 - Incidence of lung cancer, lung cancer case survival, lung cancer stage distribution, cost-effectiveness, others
- Number screened to prevent 1 lung cancer death: ~ 320
 - Based on 3 screens; substantial decrease in number if longer screening is performed
- Large number of false-positives
 - Size threshold of 6 mm nodule for LungRADS® decreases false-positives

COMPONENTS OF SCREENING PROGRAM

Low-Dose Chest CT

- Average radiation dose of 1.5 mSv (8 mSv with standard chest CT)
- Multidetector helical technique (≥ 16 detectors) in single breath hold
- Technique
 - Scout view: Single posteroanterior projection
 - Axial unenhanced CT from apices to costophrenic sulci at full inspiration
 - o 120-140 kVp
 - 40-80 mAs, fixed (varies with body habitus)
 - o Collimation: < 2.5 mm
 - Slice thickness: < 2.5 mm ± overlapping slices (≤ 1 mm preferred)
 - Reconstruction algorithm: Soft tissue or lung

Additional Requirements

• Mechanism for referral to smoking cessation program

- ± educational messaging and materials regarding smoking cessation
- Communication of results to qualified health care providers
- Multidisciplinary program (pulmonary medicine, thoracic oncology and surgery) essential for evaluation of positive findings and appropriate management

CRITERIA FOR SCREENING

Asymptomatic, High-Risk Individuals

- United States Preventive Services Task Force (USPSTF): 2021 updated inclusion criteria
- 50-80 years of age
- \geq 20 pack-year smoking history
- Current smokers or former smokers who quit within past 15 years
- Criteria to discontinue or not offer lung cancer screening
 Stopped smoking for > 15 years, > 80 years of age
 - Health condition that limits life expectancy or ability to tolerate curative lung surgery
 - Patient unwilling to undergo curative lung surgery if cancer is discovered

IMAGING FINDINGS

Reporting

- Currently LungRADS® 1.1
- Lung nodules and masses
 - Location of nodule: Lobe, anatomic segment
 - Series and image number of nodule to facilitate comparison
 - Size (mean diameter: Long and short axis to 1 decimal point)
 - True growth: Increase of at least 1.5 mm
 - Nodule density or attenuation
 - Solid, part-solid, ground-glass
 - o Margins
 - Smooth, lobular, spiculated
- Comparison with remote prior CT is often more helpful than comparison to immediate prior for detecting slow growth

DIFFERENTIAL DIAGNOSIS

Intrapulmonary Lymph Node

- Extremely common, responsible for 20% of false-positive lung screens
- Well-circumscribed nodule generally caudal to carina
- Frequent septal or fissural attachment
- Shape: Triangular, rectangular, ovoid, dumbbell, square

Noncalcified Granuloma

- Extremely common, responsible for large percentage of false-positive lung screens
- Spherical shape; smooth contours
- Stable over time

Lung Cancer

• Nodule or mass with ill-defined, lobular, or spiculated margins

Hamartoma

• Solitary nodule or mass, smooth or lobulated borders

Lung Cancer Screening

Lung-RADS

Category	Category Descriptor	Category	Management	Probability of Malignancy
Incomplete	Comparison CT being obtained cannot evaluate part or all of lungs	0	Compare to outside priors or additional imaging	n/a
Negative	No nodules or benign nodule(s)	1	12-month follow-up LDCT	< 1%
Benign appearance or behavior	Nodule(s) with very low likelihood of becoming cancer	2	12-month follow-up LDCT	< 1%
Probably benign	Nodule(s) with low likelihood of becoming cancer	3	6-month follow-up LDCT	1-2%
Suspicious/very suspicious	Finding for which additional testing is advised	4A, 4B, 4X	3-month follow-up LDCT, PET/CT, &/or biopsy depending on characteristics. New large nodule on annual screening, 1 month LDCT may be recommended to exclude infection/inflammation	> 5%
Other	Modifier for potentially significant or significant finding (non-lung)	S	As appropriate to specific finding	10%

Adapted from: American College of Radiology, (LungRADS® Version 1.1 Assessment Categories).

• Intrinsic fat &/or popcorn calcification

Carcinoid

- Calcification in 30% (often eccentric and chunky)
- Close association with bronchus; postobstructive effects (atelectasis, pneumonia, bronchiectasis)
- Slow growing, frequent contrast enhancement

CLINICAL ISSUES

Potential Benefits

- Clinical outcome related to stage at diagnosis
 60% 5-year survival for stage 1 disease
 - < 5% 5-year survival for stage 4 disease
- Screening results in "stage shift" with more cancers detected at potentially curable stages (stages 1 and 2)

Potential Harms

- False-positive results
 - 95% of positive results are not related to lung cancer
 - Majority of "positive results" do not require invasive diagnosis; most resolved with follow-up imaging (additional LDCT or PET/CT)
 - Increased patient anxiety
- False-negative results
- Overdiagnosis
 - Lung cancer that would not normally be detected during patient's lifetime (i.e., patient dying with lung cancer as opposed to dying due to lung cancer)
 - Modeling study predicts 10-12% of all lung cancers are overdiagnosed with LDCT screening
- Incidental findings
 - May lead to more testing and treatment
 - Patient anxiety
- Radiation exposure
 - Theoretical risk of developing radiation-induced malignancy

REPORTING RECOMMENDATIONS

LungRADS® 1.1

- American College of Radiology (ACR) tool for standardization of lung cancer screening reporting and management recommendations
- Assessment categories (0-4) directly tied to management recommendations
 - Category 1: Negative
 - Category 2: Benign appearance or behavior
 - Category 3: Probably benign
 - o Category 4: Suspicious and very suspicious
 - Categories 3 and 4A nodules unchanged on 3 month follow-up LDCT revert to category 2; return to annual LDCT screening
 - Category 4X: Category 3 or 4 nodules with additional suspicious features (spiculation, doubling of ground-glass nodule over a year, lymphadenopathy)
- S modifier: May add on to categories 0-4
 - Clinically significant or potentially significant finding

Updates LungRADS® 1.1

- Category 2: Perifissural nodules < 10 mm
- Category 2: Threshold for pure non-solid nodules from 20-30 mm
- Category 4B management: **New** large nodules may be managed with LDCT at 1 month
- Nodule measurement: Mean nodule diameter
- Modifier C (prior diagnosis of lung cancer who return to screening) no longer used
- Imaging follow-up typically with LDCT; occasionally other examinations or procedures (PET/CT, biopsy)

SELECTED REFERENCES

 American College of Radiology, ((Lung-RADS[™] Version 1.1 Assessment Categories)

Lung Cancer Screening

LungRADS® Category 3



LungRADS® Category 4

LungRADS® Category 4



NECT shows an 18-mm right upper lobe part-solid nodule → with a 3-mm solid component (LungRADS® category 3). Recommendation: Follow-up LDCT in 6 months. If stable at follow-up imaging, the nodule may be coded as category 2 and participant returned to annual LDCT. (Right) Axial NECT shows a right lower lobe part-solid nodule 🔁 with a 10-mm solid component (LungRADS® category 4B). Recommendation: PET/CT and tissue sampling.



LungRADS® Category 4



(Left) Composite image with axial NECT in 2007 (left) and in 2012 (right) shows an enlarging part-solid nodule 🖂 with a solid component that measures > 4 mm, concerning for lung cancer (LungRADS® category 4B). Recommendation: Tissue sampling. (Right) Axial NECT shows a spiculated right upper

lobe part-solid mass 🔁 . (LungRADS® category 4X given the presence of spiculation). Recommendation: Further evaluation with PET/CT and tissue sampling.

LungRADS® Category 4



LungRADS® Category 4



(Left) Axial NECT shows right paratracheal . lymphadenopathy 🔁 associated with a right lower lobe mass (not shown) (LungRADS® category 4X). Recommendation: PET/CT and tissue sampling. (Right) Axial NECT shows a spiculated left upper lobe 3.5-cm mass new on annual follow-up screening CT (LungRADS® category 4B). Recommendation: One month LDCT follow-up recommended for new large nodules that develop on annual screening CT to address potential infectious or inflammatory conditions.

Pulmonary Hamartoma

KEY FACTS

TERMINOLOGY

• Benign pulmonary neoplasm containing multiple mesenchymal tissue elements

IMAGING

- Radiography
 - Solitary pulmonary nodule or mass
 - Calcification in up to 15%
- CT
 - Solitary nodule or mass with smooth or lobular margins
 Classic popcorn calcification in only 10-15%
 - Calcification more common in larger hamartomas
 - Fat attenuation in up to 60%
 - Intrinsic fat and calcium virtually diagnostic
- **FDG PET**: Up to 20% show FDG uptake
- MR
 - o T2-hyperintense cartilaginous components
 - T1WI chemical shift imaging for detection of intravoxel fat

TOP DIFFERENTIAL DIAGNOSES

- Lung cancer
- Carcinoid
- Solitary metastasis
- Lipoid pneumonia

PATHOLOGY

- Most common benign lung neoplasm (75%)
- 8% of all primary lung tumors
- Varying amounts of cartilage, fat, connective tissue, smooth muscle, respiratory epithelial-lined clefts

CLINICAL ISSUES

 Typically detected incidentally on radiography or CT of asymptomatic patients

DIAGNOSTIC CHECKLIST

• Evaluate thin-section CT images of newly detected lung nodules or masses, as identification of calcium and fat is considered diagnostic of hamartoma

(Left) Axial NECT shows a lobulated right lower lobe nodule 🔁 with dense popcorn calcification and intralesional fat (< 40 HU) ➡, findings considered diagnostic of pulmonary hamartoma. Only 10-15% of hamartomas exhibit popcorn calcification. (Right) Coronal NECT of an asymptomatic patient with a right lower lobe hamartoma shows a well-circumscribed, ovoid nodule 🛃 with intrinsic fat and calcification. CT visualization of intralesional fat and calcium increases with increasing nodule size.





(Left) Axial CECT of an asymptomatic 55-year-old man shows a solid, wellcircumscribed left upper lobe nodule 🔁 of soft tissue attenuation. Absence of macroscopic intrinsic fat attenuation or popcorn calcification necessitates further evaluation. (Right) Axial Fused FDG PET/CT of the same patient shows faint lowlevel FDG uptake in the nodule \blacksquare , which is below that of mediastinal blood pool 🖂 consistent with benignity in a nodule of this size. Biopsy confirmed the diagnosis of pulmonary hamartoma.





Synonyms

- Chondromatous hamartoma
- Fibroleiomyomatous hamartoma
- Lipomatous hamartoma
- Mesenchymoma

Definitions

- Derived from "hamartia," Greek work for "error"
- Benign pulmonary neoplasm composed of disordered but mature mesenchymal elements: Hyaline cartilage, fat, smooth muscle, entrapped respiratory epithelium clefts
- Overlapping features with pulmonary chondroma of Carney triad, but typically single rather than multiple; M > F; entrapped respiratory epithelium and fat without fibrous pseudocapsule

IMAGING

General Features

- Best diagnostic clue
 - Solitary pulmonary nodule or mass with **intralesional** calcium and fat
- Location
 - Majority located in lung periphery
 - Endobronchial location < 10% of cases
 - May produce hemoptysis or obstructive symptoms
 No lobar predilection
- Size
 - o Typically 1-4 cm, may be > 10 cm
- Morphology
 - Well circumscribed
 - Smooth, often lobulated margins
- **Radiographic Findings**
- Radiography
 - Solitary pulmonary nodule or mass with smooth or lobulated borders
 - Calcification in up to 15%
 - May exhibit characteristic **popcorn** calcification
 - o Central lesions
 - Obstructive atelectasis, consolidation, bronchiectasis

CT Findings

- NECT
 - **Solitary** pulmonary nodule or mass with smooth or lobulated margins
 - Rarely multiple; if multiple, consider Carney triad
 - 10x more sensitive than radiography for detecting calcification
 - Hounsfield units (HU) > 200 considered calcium
 - Calcification more common with increasing hamartoma size
 - Classic popcorn cartilaginous calcification in only 10-15%
 - Up to 75% in nodules > 5 cm vs. only 10% in nodules < 2 cm
 - $\circ~$ Fat attenuation in up to 60%
 - -40 to -120 HU (measured in ≥ 8 voxels)
 - □ -**33-HU** threshold; ↑ specificity in recent series of 55 patients

- Volume averaging often problematic when measuring regions of interest (ROI) on 5-mm CT sections
- Best visualized with thin-section (0.6- to 1.2-cm) images to avoid volume averaging of thicker sections
- Visualization of macroscopic **intralesional fat and calcium considered diagnostic**
- CECT
 - Heterogeneous enhancement is typical
 - Enhancing internal septa correlate with epithelial-lined clefts
 - Contrast not necessary for diagnosis

MR Findings

- T1WI
 - Intermediate signal intensity
- T2WI
 - Hyperintense to muscle (macroscopic fat and cartilage); hypointense fibrous septa
- T1WIC+
 - Enhancement of smooth muscle and epithelial components: Capsule and epithelial-lined clefts
 - Areas void of enhancement correlate with cartilage and fat
- Chemical shift imaging: T1WI in-phase/opposed-phase
 - Signal loss on opposed-phase images as result of intravoxel lipid
- Characteristic MR features may negate need for unnecessary biopsy or resection

Nuclear Medicine Findings

- PET/CT
 - Up to 20% show FDG uptake; typically below that of mediastinal blood pool
 - Larger masses more likely to be FDG avid
 - Not necessary when typical CT features present

Imaging Recommendations

- Best imaging tool
 - CT is imaging modality of choice, contrast typically not helpful
 - MR may be helpful in lesions with indeterminate CT features
- Protocol advice
 - NECT with thin sections through nodule for optimal visualization of intralesional fat

DIFFERENTIAL DIAGNOSIS

Lung Cancer

- Solitary pulmonary nodule, may exhibit spiculated margins
- Does not exhibit fat and calcium
- 2% of cancers < 3 cm in size exhibit calcification
- Highly FDG avid on PET/CT
- Coexisting emphysema and history of cigarette smoking

Carcinoid

- Hypervascular mass with well-defined lobular margins
- Frequent endobronchial component
- 30% contain calcification
- Low-grade malignancy with metastatic potential
 Surgical resection is treatment of choice

• Intensely avid on 68Ga-DOTA-PET/CT; variable avidity on FDG PET/CT

Solitary Metastasis

- Typically multiple with known malignancy; rarely solitary in select malignancies
 - Colon, breast, renal, and testicular cancers, osteosarcoma, melanoma
- Calcified metastatic nodules may mimic hamartoma (osteosarcoma, mucinous adenocarcinoma)

Lipoid Pneumonia

- Mass-like consolidation containing endogenous or exogenous lipid
 - Classically diagnosed in patient who consumes mineral oil for treatment of constipation
- Calcifications atypical
- Can be FDG avid on PET/CT

Liposarcoma

- Exceedingly rare aggressive neoplasm containing fat and soft tissue
- Typically in chest wall or mediastinum

PATHOLOGY

General Features

- Etiology
 - Unknown; true **benign mesenchymal neoplasm** rather than congenital embryologic rest
- Genetics
 - Chromosomal band recombination (6p21 and 14q24) found in some lesions
- Associated abnormalities

Carney triad

- Nonfamilial disorder characterized by
 - Multiple pulmonary chondromas (radiographically similar but histologically distinct from hamartoma)
 - □ Gastric stromal tumors
 - Functional extraadrenal paraganglioma
- Young female predilection

• Cowden syndrome

- Autosomal dominant disorder
- Characterized by multiple hamartomas of ectodermal, endodermal, and mesodermal origin
- High incidence of malignant tumors
 - □ Breast, thyroid gland, and adnexa

Gross Pathologic & Surgical Features

- Parenchymal: Well-circumscribed, firm mass, with lobules of white, cartilaginous tissue
- Endobronchial: Fleshy polypoid lesion attached to airway by narrow stalk

Microscopic Features

- Encapsulated mass composed of
 Mature but disordered hyaline
 - cartilage ± calcification/ossification
 - Entrapped respiratory epithelial cell-lined clefts
 - Varying amounts of fat and smooth muscle
- Histologically distinct from chondromas seen in Carney triad, which are typically multifocal and lack entrapped epithelium and fat

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Incidental imaging finding in asymptomatic patientsMay be identified on screening CT
- Other signs/symptoms
 - Rarely cough, hemoptysis
 - Recurrent pneumonia

Demographics

- Age
 - Adults > 40 years; peak incidence in 7th decade
 - Rare in pediatric patients
- Sex
- Men 2-3x higher incidence than women
- Epidemiology
 - o Most common benign lung neoplasm (75%)
 - 8% of primary lung tumors
 - o Affects 0.025-0.32% of population

Natural History & Prognosis

- Malignant transformation exceedingly rare and reportable
- Slow growth: Doubling time > 450 days

Diagnosis

- CT imaging may be diagnostic
- MR imaging may be helpful in CT indeterminate lesions
- CT-guided biopsy for diagnosis in absence of diagnostic imaging features

Treatment

- Imaging surveillance
- Surgical resection if symptomatic or rapidly enlarging
 - Curative with only rare case reports describing local recurrence
- Endobronchial hamartoma may be resected bronchoscopically

DIAGNOSTIC CHECKLIST

Consider

• Other etiologies of solitary pulmonary nodules; only 6% are hamartomas

Image Interpretation Pearls

- Thin-section CT images of newly detected lung nodules or masses, as identification of calcium and fat is virtually diagnostic
- MR imaging may be helpful for detection of intralesional cartilage and fat

Reporting Tips

• Hamartomas often grow slowly over time; interval enlargement does not necessitate intervention

- Chatzopoulos K et al: Clinical, radiologic, and pathologic characteristics of pulmonary hamartomas with uncommon presentation. Am J Clin Pathol. 155(6):903-11, 2020
- Hochhegger B et al: Multidetector computed tomography findings in pulmonary hamartomas: a new fat detection threshold. J Thorac Imaging. 31(1):11-4, 2016

Pulmonary Hamartoma





(Left) PA chest radiograph of an asymptomatic 62-year-old man shows a small right perihilar nodule \implies without intrinsic calcification. (Right) Axial NECT of the same patient shows a soft tissueattenuation wellcircumscribed solid nodule with a suggestion of intrinsic hypoattenuating fat 🛃. The nodule had grown slightly over the course of 3 years and represented a pulmonary hamartoma. Such lesions have a reported doubling time of > 450 days.





(Left) Coronal CECT of an 87year-old man shows a large right lung pulmonary hamartoma 🔁 with characteristic fat attenuation, stable for many years. The left upper lobe solid nodule represented primary adenocarcinoma 🔁 (Right) Sagittal CECT of a 72-year-old man with a radiographically detected lung nodule shows the well-circumscribed lobular contours of a hamartoma 🖂 in contradistinction to the spiculated, part-solid morphology of an adenocarcinoma
ightarrow confirmedby surgical resection.





(Left) Graphic demonstrates the characteristic morphologic . features of pulmonary hamartoma, which typically manifests as a well-defined lobulated solid nodule composed of heterogeneous elements, often including fat ➡ and cartilage ➡. (Right) Coronal CECT shows an 83year-old woman with multiple pulmonary nodules and masses that contained areas of low attenuation as well as popcorn 🔁 and laminated 🔁 calcifications that represented multiple pulmonary chondromas, which may mimic hamartomas on imaging.

Bronchial Carcinoid

KEY FACTS

TERMINOLOGY

• Low-grade malignant neuroendocrine neoplasm with metastatic potential

IMAGING

• Radiography

- o Central hilar or perihilar nodule or mass
- Peripheral solitary lung nodule
- Postobstructive atelectasis, pneumonia
- CT
 - Avidly enhancing central nodule or mass
 - o Calcification/ossification in 30%
 - Endobronchial, partially endobronchial, abutting bronchus, peripheral
 - Postobstructive effects: Atelectasis, consolidation, bronchiectasis
- Nuclear medicine
 - o Gallium-68-DOTATATE
 - FDG PET: Frequent false-negative results

TOP DIFFERENTIAL DIAGNOSES

- Adenoid cystic carcinoma
- Hamartoma
- Lung cancer

PATHOLOGY

- Smooth, red, polypoid endobronchial nodule/mass
- Typical and atypical subtypes

CLINICAL ISSUES

- Symptoms/signs: Cough, hemoptysis, wheezing, recurrent pneumonia
- Treatment: Surgical resection

DIAGNOSTIC CHECKLIST

• Consider carcinoid tumor in young/middle-aged patients with well-defined central nodule or mass with endoluminal component &/or chronic airway obstruction/recurrent pneumonia

(Left) Graphic shows the typical morphologic features of bronchial carcinoid, which characteristically manifests as a central lobulated nodule or mass with an endoluminal component. Carcinoid usually has a highly vascularized stroma that results in intense contrast enhancement. (Right) Axial CECT of a 47-year-oldwoman shows a central bronchial carcinoid \supseteq with a large endoluminal component and distal mucus plugging 🖾. Note intense contrast enhancement, a characteristic feature of typical carcinoid tumors.

(Left) Coronal gallium-68-DOTATATE PET of the same patient shows intense metabolic activity in the left lower lobe mass $\overline{\rightarrow}$. Somatostatin receptor imaging has a high detection rate for pulmonary carcinoids. (Right) Axial gallium-68-DOTATATE PET/CT of the same patient shows intense metabolic activity in the tumor *⊡* Somatostatin receptor imaging is also valuable for identification and assessment of metastatic disease and determination of patients' suitability for radiolabeled somatostatin analog therapy.









Synonyms

- Neuroendocrine tumor
 - All neoplasms arising from enterochromaffin cells
 - Not all neuroendocrine tumors are carcinoids, therefore term "neuroendocrine tumor" should be used carefully

Definitions

- Low-grade malignant neuroendocrine neoplasm with metastatic potential
 - Arises from enterochromaffin cells normally scattered throughout bronchial mucosa
 - Gastrointestinal tract carcinoids account for approximately 90% of all carcinoids
 - Lung is 2nd most common location

IMAGING

General Features

- Best diagnostic clue
 - Well-defined nodule or mass near tracheal bifurcation ± associated postobstructive atelectasis, pneumonia, or mucus plugs
- Location
 - Typical carcinoid
 - 85% in mainstem, lobar, or segmental bronchi
 - 15-20% peripheral in location
 - Atypical carcinoid
 - Most develop in lung periphery
 - Hilar/mediastinal lymph node metastases more common
 - Metastases (15% of bronchial carcinoids)
 - Liver, bone (sclerotic), adrenal glands, brain
- Size
 - o Usually 1-5 cm
 - Atypical carcinoids tend to be larger
- Morphology
 - Well-marginated central nodule or mass
 - Lobulated borders
 - Bronchial relationship: Partially or completely endoluminal or close bronchial relationship

Radiographic Findings

- Central hilar or perihilar well-defined nodule or mass
- 4% exhibit calcification/ossification on radiography
- Effects of central airway obstruction
 - o Atelectasis, air-trapping
 - Bronchiectasis, mucoid impaction, finger in glove sign (Vor Y-shaped opacities radiating from hilum)
 - Postobstructive pneumonia, may be recurrent
- Peripheral indeterminate solitary nodule

CT Findings

- Typical bronchial carcinoid
- Nodule or mass with marked contrast enhancement
 Endobronchial
 - □ **"Iceberg" lesion**: Small endoluminal tumor with dominant extraluminal component
 - May be entirely endoluminal
 - □ May abut bronchus

- 30% of central carcinoids exhibit variable calcification/ossification
- Marked, homogeneous contrast enhancement
- 20% are slow-growing, peripheral solitary nodules with well-defined smooth or lobular borders
- Hilar &/or mediastinal lymphadenopathy
 - Metastases
 - Reactive lymph nodes from recurrent pneumonia
- Bronchial obstruction
 - Air-trapping due to ball-valve obstruction
 - Atelectasis
 - Postobstructive pneumonia
 - Bronchiectasis
 - Lung abscess
 - Mucoid impaction
 - □ Fluid-filled (< 20-HU) branching structures
 - □ Peripheral hyperlucency due to air-trapping
- Atypical carcinoid
 - Lung nodule or mass
 - Lobulated or irregular contours
 - Less uniform enhancement
 - More likely to be peripheral
 - Lymph node metastases more common
- Multiple carcinoid tumors and tumorlets: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH)
 - o Multiple bilateral pulmonary nodules
 - Mosaic attenuation
 - Air-trapping on expiratory images (correlates with constrictive bronchiolitis)

MR Findings

• Hyperintense on T2WI

Nuclear Medicine Findings

- PET
 - FDG PET often falsely negative due to relative low metabolism of carcinoid tumors
 - SUV > 5.0 associated with aggressive biologic behavior
 - Better than Gallium-68-DOTATATE for assessment of atypical carcinoids
- Octreotide scan (somatostatin analogue) successfully used to diagnose and locate occult carcinoid tumors
- Gallium-68-DOTATATE
 - More effective than Octreoscan for evaluation of small tumors and identification of lymph node involvement
 - Similar to higher detection rate of typical carcinoid compared to FDG PET

Imaging Recommendations

- Best imaging tool
 - Contrast-enhanced thin-section CT
- Protocol advice
 - IV contrast: Carcinoid tumors are vascular and typically (but not universally) exhibit avid enhancement

DIFFERENTIAL DIAGNOSIS

Adenoid Cystic Carcinoma

- Salivary gland malignancy, often arises in trachea or mainstem bronchi
 - o 10% in lung periphery

• Locally aggressive, requires careful evaluation for extraluminal or mediastinal growth

Hamartoma

- Lung nodule with macroscopic fat on CT
- Calcification common
- Endobronchial location (4%)

Mucoepidermoid Carcinoma

- Rare salivary gland tumor of lobar or segmental bronchi
- Ovoid, polypoid, or lobulated lesion, well-defined margins, calcification in 50%

Lung Cancer

- Margins usually ill-defined, lobular, or spiculated
- Affected patients are older than those with carcinoid
- History of cigarette smoking

Broncholithiasis

• Small endobronchial calcified nodule

Pulmonary Metastases

• Multiple carcinoid tumors/tumorlets mimic metastases

PATHOLOGY

General Features

- Etiology
 - No association with cigarette smoking or inhalation of carcinogens
- Associated abnormalities
 - Small pulmonary tumorlets occasionally associated with carcinoid tumors
 - Tumorlets represent benign neuroendocrine hyperplastic growths

Gross Pathologic & Surgical Features

- Smooth, red, polypoid endobronchial nodule/mass
- Most arise within central bronchi

Microscopic Features

- Neuroendocrine neoplasm in spectrum of more aggressive large cell neuroendocrine and small cell carcinomas
- Typical carcinoid (80-90%)
 - Uniform cells in sheets, trabeculae or gland-like structures, separated by thin fibrovascular stroma
 - Moderate cytoplasm with numerous neurosecretory granules
 - Rare mitotic figures; < 2 mitoses/10 high-power fields
 - Dystrophic calcification, ossification
- Atypical carcinoid (10-20%)
 - Tumor necrosis
 - o Loss of typical architecture with increased cellularity
 - o 2-10 mitoses/10 high-power fields
 - Increased nuclear:cytoplasmic ratio or nuclear pleomorphism

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Cough
 - Hemoptysis in 50% of patients

- Recurrent pneumonia
- o Adult onset "asthma," wheezing
- Other signs/symptoms
 - Cushing syndrome: Ectopic production of ACTH
 - 2% of bronchial carcinoids
 - Carcinoid syndrome
 - Rare with thoracic carcinoid tumors
 - Almost all affected patients have hepatic metastases from gastrointestinal carcinoid

Demographics

- Age
 - o Typical carcinoid: 30-60 years of age
 - Atypical carcinoid: Decade older
 - Most common primary lung neoplasm of childhood
- Sex
 - Bronchial carcinoid: Roughly equal distribution
 - Multiple carcinoid tumors and tumorlets: Predominantly women
- Epidemiology
 - o Bronchial carcinoid: 1-2% of all lung neoplasms

Natural History & Prognosis

- Distinction between typical and atypical carcinoids, most important prognostic factor
- Typical carcinoid: 5% have lymph node metastases at presentation
 - o 5-year survival
 - 90-95% without lymph node involvement
 - 76-88% with lymph node metastases
- Atypical carcinoid: 50-60% have lymph node metastases at presentation
 - o 5-year survival
 - 40-70%, depending on stage at presentation
- Multiple carcinoid tumors and tumorlets
 - Limited data: Generally good prognosis, stable disease even without treatment

Treatment

- Complete surgical excision most effective
- Somatostatin analogs for advanced functional carcinoid
- Everolimus (mTOR kinase inhibitor) for advanced nonfunctional carcinoid
- Systemic chemotherapy for patients with metastases and no other treatment options available

DIAGNOSTIC CHECKLIST

Consider

 Carcinoid tumor in symptomatic young/middle-aged patients with well-defined central nodule or mass with endoluminal component

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- 3. Robelin P et al: Characterization, prognosis, and treatment of patients with metastatic lung carcinoid tumors. J Thorac Oncol. 14(6):993-1002, 2019
- Hann CL et al: Lung and thymic carcinoids. Endocrinol Metab Clin North Am. 47(3):699-709, 2018

Bronchial Carcinoid





(Left) Axial CECT of a 21-yearold man shows an enhancing endoluminal mass \square at the level of the carina. Tissue sampling demonstrated typical carcinoid tumor. (Right) Coronal CECT of the same patient shows a large central mass \implies that involves the right mainstem bronchus. Right lung bronchiectasis 🛃 is secondary to chronic obstruction and postobstructive infection. Typical carcinoid tumor often manifests as a well-defined nodule or mass partially or completely within a bronchial lumen near the carina.





(Left) Axial CECT of a 54-yearold woman who presented with hemoptysis shows a welldefined endoluminal nodule \supseteq in the left upper lobe bronchus. Hemoptysis is a common symptom of these hypervascular tumors. (Right) Coronal CECT of the same patient confirms the presence of an endoluminal nodule \supseteq , consistent with a carcinoid tumor, which was successfully resected. Surgical resection is the preferred treatment option for localized tumors. Systemic therapy is reserved for patients with lymph node &/or distant metastases.





(Left) Axial CECT of a 57-yearold woman with colon cancer shows a well-defined left lower lobe solid nodule 🔁 originally thought to represent a solitary metastasis. (Right) Axial fused FDG PET/CT of the same patient shows minimal FDG uptake in the nodule \implies . Tissue sampling confirmed typical carcinoid. Carcinoids usually exhibit low to moderate FDG uptake on PET/CT. High metabolic activity on FDG PET/CT is associated with aggressive behavior. Sublobar resection was performed and is favored in small peripheral carcinoids.

KEY FACTS

TERMINOLOGY

- Typical carcinoid (TC), atypical carcinoid (AC)
- Small cell lung carcinoma (SCLC)
- Large cell neuroendocrine carcinoma (LCNEC)
- Malignant tumors of neuroendocrine origin

IMAGING

- Radiography
 - Carcinoid: Central nodule ± endoluminal lesion
 - SCLC: Large hilar/mediastinal mass
 - LCNEC: Large peripheral mass
- CT
 - TC and AC: Enhancing nodule ± endobronchial component
 - o SCLC: Invasive hilar or mediastinal mass
 - LCNEC: Discrete or spiculated mass
- PET/CT
 - TC: 68Ga-DOTATATE PET/CT; little/no FDG uptake
 - SCLC and LCNEC: Staging and restaging

TOP DIFFERENTIAL DIAGNOSES

- TC and AC
 - Lung cancer, metastasis, hamartoma
- SCLC
 - Non-small cell lung cancer
 - Lymphoma, thymic carcinoma, metastases
- LCNEC
 - Non-small cell lung cancer

CLINICAL ISSUES

- Symptoms/signs
 - o Cough, wheezing, hemoptysis, pneumonia
 - o SCLC: Superior vena cava syndrome, vocal cord paralysis, paraneoplastic syndrome
- Age
 - o TC and AC: Mean age: 45 years
 - SCLC and LCNEC: Mean age > 60 years
- 10-year survival: TC 85%; AC 35%
- SCLC and LCNEC: Poor prognosis

(Left) Composite image with PA chest radiograph (left) and coronal CECT (right) of a 56year-old woman with facial swelling shows mass effect on the suprasternal trachea \supseteq , mediastinal widening 🔁 due to lymphadenopathy, marked airway stenosis, and obliteration of the right upper lobe bronchus 🔁. (Right) Coronal CECT of the same patient shows heterogeneously enhancing coalescent lymphadenopathy that encases the central airways and great vessels and extends into the right supraclavicular region 🔁.

(Left) High-power

(H&E stain, x 400) shows

the diagnosis of high-grade neuroendocrine carcinoma. (Courtesy P. Pettavel, MD.)

69-year-old man with small

superior vena cava 🔁.









Definitions

- Neuroendocrine (NE) neoplasms
 - Storage, synthesis, and secretion of peptide hormones or bioamines
 - Histologic patterns similar to nonneoplastic NE cells
 - Trabecular or nesting growth pattern
 - Cells with coarsely stippled nuclear chromatin
 - Neurosecretory protein production detectable on immunohistochemical stains
 - Typically chromogranin A and synaptophysin
 - Subdivided into well- and poorly-differentiated NE neoplasms
- Pulmonary NE neoplasms (25% of all NE neoplasms)
 - Malignant pulmonary neoplasms of NE origin
 - Thought to arise from normal Kulchitsky and NE cells of bronchial mucosa
 - WHO classification of Neuroendocrine Tumors (NET)
 - Well-differentiated NE neoplasms
 - □ NET grade 1: Typical carcinoid (TC); low grade
 - NET grade 2: Atypical carcinoid (AC); intermediate grade
 - Poorly-differentiated NE neoplasms
 - NET grade 3: Small cell lung carcinoma (SCLC); high grade
 - NET grade 4: Large cell neuroendocrine carcinoma (LCNEC); high grade
- SCLC
 - Most common and most aggressive NE carcinoma
 - o 13-15% of all lung cancers
 - Thought to arise centrally in mainstem or lobar bronchi

IMAGING

General Features

- Best diagnostic clue
 - TC: Central nodule ± endoluminal component
 - SCLC: Large, central, mediastinal/hilar mass/lymphadenopathy
 - LCNEC: Large, peripheral, upper lobe mass
- Location
 - o TC and AC: Usually central, also peripheral
 - o SCLC: Mediastinal &/or hilar
 - LCNEC: Peripheral, upper lobes, ~ 1/5 central
- Size
 - TC and AC: Size range: 0.5-3.0 cm
 - o SCLC: Large mass/lymphadenopathy at presentation
 - LCNEC: Mass, mean size:; 3.7 cm
- Morphology
 - TC and AC: Spherical/ovoid nodule, well-defined lobulated borders
 - o SCLC: Large mass, locally invasive, necrotic
 - o LCNEC: Large mass, lobulated or spiculated borders

Radiographic Findings

- TC and AC
 - Central hilar/perihilar well-defined nodule or mass
 - ± visible endoluminal component
 - ± postobstructive effects: Atelectasis, consolidation, bronchiectasis

- AC may be larger and peripheral
- SCLC
 - Mediastinal &/or hilar mass, mediastinal widening
 Primary neoplasm and lymphadenopathy
 - Bronchus cut-off
 - o Atelectasis, consolidation
- LCNEC
 - Peripheral, upper lobe, spherical/ovoid mass
 - o May be central with associated atelectasis/consolidation

CT Findings

- CECT
 - TC and AC: Discrete pulmonary nodule
 - Intense enhancement
 - Endobronchial component ± obstruction
 - Distal mucous plugging, atelectasis, air-trapping
 - 30% exhibit calcification or ossification
 - o SCLC
 - Large mediastinal &/or hilar mass
 - Mediastinal lymphadenopathy often involving subcarinal and tracheobronchial lymph nodes
 - Locally invasive: Airway/vascular encasement/obliteration; superior vena cava (SVC) obstruction
 - Lymphadenopathy above and below diaphragm
 - Peripheral nodule or mass ± lymphadenopathy
 - Associated findings
 - □ Atelectasis/pneumonia
 - □ Pleural/pericardial effusion/soft tissue nodules
 - Distant metastases: Bone, liver, adrenal, brain
 - Primary tumor rarely evident; cavitation rare
 - o LCNEC
 - Peripheral spherical or ovoid polylobular mass
 Low-attenuation areas correspond to necrosis
 - Central lesion ± postobstructive changes
 - Differentiation of tumor from surrounding atelectasis/consolidation
 - Associated findings
 - Pleural effusion
 - Hilar/mediastinal lymphadenopathy

MR Findings

- TC and AC: MR rarely used in assessment
- High-grade NE neoplasms
 - Evaluation of mediastinal/chest wall invasion if iodinated contrast contraindicated
 - Brain MR for detection of metastases

Nuclear Medicine Findings

- FDG PET/CT
 - TC and AC: Little or no FDG uptake
 - SCLC and LCNEC: Staging and restaging
 - SUVmax may correlate with prognosis
 - Distinction of neoplasm from adjacent atelectasis/consolidation
- 111In-pentetreotide (Octreoscan) (somatostatin analog)
 Detection of occult NE neoplasm
- 68Ga-DOTATATE PET/CT (TC and AC)
 - Somatostatin receptor 2A binding/not diet dependent
 - Higher sensitivity and specificity than Octreotide scan

Imaging Recommendations

- Best imaging tool
 - CECT is optimal modality for initial assessment
 - SCLC: PET/CT and brain MR for staging
 - LCNEC: PET/CT for staging
- Protocol advice
 - IV contrast
 - Distinction of tumor from atelectasis and consolidation
 - Assessment of hilar lymph nodes

DIFFERENTIAL DIAGNOSIS

Typical and Atypical Carcinoid

- Lung cancer
- Pulmonary metastasis
- Hamartoma

Small Cell Lung Carcinoma

- Lymphoma
- Metastatic lymphadenopathy

Large Cell Neuroendocrine Carcinoma

• Non-small cell lung carcinoma

PATHOLOGY

Staging, Grading, & Classification

- American Joint Committee on Cancer (AJCC) TNM Staging System
- SCLC
 - Veterans' Administration Lung Study Group (VALSG)
 - Limited stage-SCLC (LS-SCLC): One reasonable radiation treatment (RT) field; potentially curable
 - Extensive stage-SCLC (ES-SCLC): Not treatable within one reasonable RT field

Gross Pathologic & Surgical Features

- TC and AC: Discrete nodule, endoluminal component
- SCLC
 - Proximal growth along central bronchial submucosa
 - External compression, endobronchial tumor rare
 - Extensive necrosis and hemorrhage
- LCNEC: Large, necrotic, bulky, > 3-cm mass

Microscopic Features

- TC and AC
 - Homogeneous cellularity
 - o TC: < 2 mitoses/10 high-power fields (HPF); no necrosis
- AC: 2-20 mitoses/10 HPF or necrosis; Ki-67 index: 3-20%
 SCLC
 - Crush artifact commonly present
 - Small cell size and scant cytoplasm
 - Finely granular nuclear chromatin, absent nucleoli
 - o > 20 mitoses/10 HPF; median: ~ 80
 - Immunohistochemistry (IHC): CD56/NCAM (neural cell adhesion molecule) (most sensitive); TTF-1 (90% expression); Ki-67 index: 80-100%
- LCNEC
 - Diagnosis requires surgical biopsy or large tissue samples
 - o Poorly differentiated: > 20 mitoses/HPF; ~ 70

- IHC: Chromogranin A (70%); synaptophysin (70%); TTF-1 (41-75% expression); Ki-67 index (50-100%); CD56
- Diagnosis requires
 - High-grade histology: Mitoses and necrosis
 - NE architecture: Organoid, trabecular, palisading, or rosette patterns
 - Non-small cell lung cancer histology, including large cell size, abundant cytoplasm
 - Positive IHC or LCNEC electron microscopy features

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough, wheezing, hemoptysis, postobstructive pneumonia
 - TC and AC: May be asymptomatic
 - SCLC and LCNEC: Fatigue, weight loss, anorexia; symptoms from metastatic disease
 - o LCNEC: Asymptomatic in 25%
 - SCLC: SVC syndrome, vocal cord paralysis
- Other signs/symptoms
 - TC and AC: Multiple endocrine neoplasia type 1
 - SCLC: Paraneoplastic syndromes
 - Inappropriate secretion of antidiuretic hormone (SIADH), Cushing, hypercalcemia, hyperparathyroidism, Eaton-Lambert, encephalomyelitis, cerebellar degeneration

Demographics

- Age
 - TC and AC: Mean age: 46 years
 - SCLC and LCNEC: Mean age: > 60 years
- Sex
 - TC and AC: M = F
 - SCLC and LCNEC: M > F
- Epidemiology
 - SCLC and LCNEC: Strongly associated with cigarette smoking

Natural History & Prognosis

- 10-year survival: TC; 85%, AC; 35%
- SCLC and LCNEC: Poor prognosis

Treatment

- TC and AC: Surgical resection, chemotherapy (CTx) for metastatic tumors
- SCLC
 - CTx and concurrent radiation; prophylactic cranial irradiation (PCI) in selected patients
 - Surgical resection in patients with limited disease + PCI
- LCNEC: Surgical resection, adjuvant CTx in selected patients

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(Left) PA chest radiograph of a patient with typical carcinoid shows a middle lobe solitary pulmonary nodule 크. Typical and atypical carcinoid are lowand intermediate-grade malignancies, respectively, and are incidentally detected in 25% of cases. (Right) Axial NECT of the same patient shows a discrete middle lobe solid nodule 🔁 with associated mucoid impaction ➡ in the lateral segmental middle lobe bronchi. Bronchial obstruction from carcinoid mav also cause distal atelectasis, consolidation, &/or air-trapping.





(Left) PA chest radiograph of an 87-year-old man shows a large cell neuroendocrine carcinoma that manifests as a large peripheral left lung soft tissue mass with well-defined borders. (Right) Composite image with axial NECT (left) and axial fused FDG PET/CT of the same patient shows that the well-defined peripheral left upper lobe mass ⊇ is intensely FDG-avid. Note FDG uptake in a metastatic left hilar lymph node ₽





(Left) Axial CECT of a 52-yearold woman who presented with left upper quadrant pain secondary to a locally invasive small cell lung carcinoma shows a large soft tissue mass D that invades the left hemidiaphragm and stomach. (Right) Coronal CECT of the same patient shows the large left basilar soft tissue mass 🛃 that invades the diaphragm, stomach, and spleen and multiple left pleural nodules that represented solid metastases. Although most small cell lung carcinomas are central lesions, peripheral tumors also occur.

Kaposi Sarcoma

KEY FACTS

TERMINOLOGY

- Kaposi sarcoma (KS)
- Acquired immune deficiency syndrome with Kaposi sarcoma (AIDS-KS)
- latrogenic Kaposi sarcoma (IKS)
- Low-grade mesenchymal neoplasm of blood and lymphatic vessels, primarily affecting skin

IMAGING

- AIDS-KS
 - o Nodules
 - Flame-shaped, > 1 cm in diameter
 - Peribronchovascular with tendency to coalesce
 - CT halo sign
 - o Peribronchovascular and interlobular septal thickening
 - Fissural nodularity
 - o Lymphadenopathy: Mediastinal, hilar, axillary
 - Pleural effusions (common)

TOP DIFFERENTIAL DIAGNOSES

- Sarcoidosis
- Lymphoma
- Lymphangitic carcinomatosis
- Bacillary angiomatosis

PATHOLOGY

• Human herpesvirus type 8 (HHV-8)

CLINICAL ISSUES

- Symptoms/signs: Dyspnea, cough, CD4 lymphocyte count (< 150-200 cells/mm³)
- Demographics
 - o AIDS-KS: Homosexual/bisexual men with AIDS
- o IKS: Rare
- Treatment
 - AIDS-KS: Highly active antiretroviral therapy ± chemotherapy
 - o IKS: Decrease in immunosuppressive therapy

(Left) Graphic shows morphologic features of pulmonary Kaposi sarcoma with tumor infiltrating along bronchovascular bundles and extending from the hilum to the lung periphery. (Right) Axial CECT shows poorlymarginated flame-shaped nodules (some with groundglass opacity halos) with a peribronchovascular distribution, a classic manifestation of AIDS-Kaposi sarcoma. While infection is more likely, Kaposi sarcoma should be considered based on imaging and in the appropriate demographic.





(Left) AP chest radiograph of a patient with AIDS-Kaposi sarcoma shows diffuse perihilar opacities and thick interlobular septa resembling the appearance of pulmonary edema. Note absence of cardiomegaly. A high index of suspicion is required to suggest the diagnosis of Kaposi sarcoma on chest radiography. (Right) Axial CECT of the same patient shows peribronchovascular consolidations and groundglass opacities, thick interlobular septa *⊡*, and small bilateral pleural effusions.





Pulmonary Neoplasms

Abbreviations

- Kaposi sarcoma (KS)
- Acquired immune deficiency syndrome with Kaposi sarcoma (AIDS-KS): Epidemic KS
- latrogenic Kaposi sarcoma (IKS)
- Highly active antiretroviral therapy (HAART)

Definitions

- Low-grade mesenchymal neoplasm of blood and lymphatic vessels, primarily affecting skin
- Can cause disseminated disease in various organs: Lymphatic system, lungs, airways, abdominal viscera, etc.
- AIDS-KS: KS related to human immunodeficiency virus (HIV)
- IKS: KS related to immunosuppression

IMAGING

General Features

- Best diagnostic clue
 - AIDS-KS: Coexistence of poorly-marginated peribronchovascular nodules, lymphadenopathy, and bilateral pleural effusions

Radiographic Findings

- AIDS-KS
 - Mid to lower lung zone perihilar heterogenous or reticulonodular opacities
 - o Ill-defined pulmonary nodules
 - Cavitation may occur with concomitant opportunistic infection
- IKS
 - Scattered, well-defined pulmonary nodules
 - Reticular or reticulonodular opacities

CT Findings

- AIDS-KS
 - o Nodules
 - Bilateral, symmetric, poorly-marginated, perihilar, flame-shaped
 - Peribronchovascular with tendency to coalesce, usually > 1 cm in diameter
 - Ground-glass opacities surrounding nodules (CT halo sign)
 - Cavitary nodules often associated with opportunistic infection, such as *Pneumocystis jirovecii* pneumonia
 - Interlobular septal thickening
 - Fissural nodularity
 - Lymphadenopathy, may enhance with contrast
 Axillary, mediastinal, hilar
 - Pleural effusions (common)
 - Chylothorax has been described
 - o Pleural implants (rare)
 - Osseous lytic lesions: Sternum, thoracic spine
 - Cutaneous and subcutaneous soft tissue thickening
- IKS
 - Scattered pulmonary nodules
 - Lymphadenopathy, pleural effusion

MR Findings

- Rarely used, but may be useful for assessment of osseous and soft tissue involvement
- T1WI: Hyperintense
- T2WI: Markedly reduced signal
- Strong tumoral enhancement after gadolinium

Nuclear Medicine Findings

- PET/CT
 - o AIDS-KS
 - Foci of AIDS-KS are FDG-avid
 - Useful for detection of occult lesions
 - Anecdotal use in monitoring treatment response
 - o IKS
 - FDG-avid lung nodules and lymphadenopathy
- Gallium-67 and thallium scintigraphy
 - Combined approach helpful for differentiating epidemic KS from infection and lymphoma
 - Gallium-67: Negative in epidemic KS but positive in infection and lymphoma
 - o Thallium: Positive in epidemic KS and lymphoma

DIFFERENTIAL DIAGNOSIS

Pulmonary Edema

- Difficult differentiation from KS
- History of AIDS or transplantation and presence of skin lesions may be helpful

Sarcoidosis

- Thick bronchovascular bundles, lung nodules, and interlobular septal thickening (often nodular); may mimic KS
- Lymphadenopathy more symmetric than that of KS, does not typically enhance

Lymphoma

- Peribronchovascular thickening and lung nodules; may mimic KS
- Lung nodules vary in size but are often larger than KS nodules
- Air bronchograms more common in lymphoma than in KS nodules

Lymphangitic Carcinomatosis

- Peribronchovascular and interlobular septal thickening (often nodular); may mimic AIDS-KS
- Unilateral distribution favors lymphangitic carcinomatosis from primary lung cancer over KS

Infectious Bronchiolitis

- Mycobacterial and bacterial infections
- Nodules < 1 cm
- Centrilobular nodules, frequent tree-in-bud opacities

Bacillary Angiomatosis

- Rare infection due to Bartonella henselae
- Skin lesions, enhancing lymph nodes, and lung nodules; may mimic KS
- Peribronchovascular thickening not as common
- Consider in heterosexual patients with AIDS being evaluated for AIDS-KS

PATHOLOGY

General Features

- Etiology
 - Human herpesvirus type 8 (HHV8 or KS-associated herpesvirus)
 - Also associated with primary effusion lymphoma and multicentric Castleman disease
 - Other co-factors
 - Tumor necrosis factor A
 - Interleukin 6
 - Basic fibroblast growth factor
 - Vascular endothelial growth factor
 - o Mode of transmission not completely understood
 - Adult homosexual male contact (North America)
 - Mother-to-child and child-to-child (Africa and Southern Europe)
 - Reactivation may play role in IKS
- Genetics
 - o Classic KS
 - Patients of European or Mediterranean origin and Ashkenazi Jews
 - o African KS
 - East and Central Africa
 - Most common cancer of men and 2nd most common cancer of women in Uganda
- Associated abnormalities
 - Mucocutaneous KS present in 85% of patients with pulmonary involvement

Staging, Grading, & Classification

- 4 different types
 - o Classic, sporadic, or Mediterranean KS (1st described)
 - Endemic or African KS
 - AIDS-KS (most common)
 - o IKS
- AIDS-KS staging
 - Extent of tumor (T)
 - T0 (good risk): Localized tumor (e.g., KS only in skin &/or lymph nodes, small amount of disease on palate, flat lesions in mouth)
 - T1 (poor risk): Widespread KS
 - 1 or more: Edema, extensive oral KS, lesions in organs other than lymph nodes
 - Pulmonary KS carries poor prognosis
 - o Immune status (I)
 - IO (good risk): CD4 cell count ≥ 200 cells/mm³
 - I1 (poor risk): CD4 cell count < 200 cells/mm³
 - Systemic illness status (S)
 - S0 (good risk): No systemic illness present
 - $\hfill\square$ No history of opportunistic infections or thrush
 - No B symptoms (e.g., unexplained fever, night sweats, weight loss, diarrhea)
 - □ Karnofsky performance status score ≥ 70
 - S1 (poor risk): Systemic illness present with 1 or more of following
 - □ History of opportunistic infections or thrush
 - □ 1 or more B symptoms present
 - □ Karnofsky performance status score < 70

 Other HIV-related illness present, such as neurological disease or lymphoma

Gross Pathologic & Surgical Features

- AIDS-KS
 - Skin lesions may be absent
 - Visceral organs affected
 - Lymph nodes (72%), lung (51%)
 - Gastrointestinal tract (48%), liver (34%), spleen (27%)
 - Thorax affected in 45% of all cases

Microscopic Features

- Spindle-shaped stromal cells
- Abnormal endothelial lining of vascular channels
- Slit-like spaces with extravasated red cells

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dyspnea, cough, hypoxemia
 - o Low CD4 lymphocyte count (< 150-200 cells/mm³)
- Other signs/symptoms

Hemoptysis, weight loss

- Demographics
- Age
 - Classic KS: 50-80 years of age
 - African KS: 4th decade of life
- Sex
 - o Classic KS: M:F = 10-15:1
 - African KS: Male predominance
 - o AIDS-KS: Homosexual or bisexual males with AIDS
- Epidemiology
 - Most common AIDS-related neoplasm; decreased prevalence with HAART

Natural History & Prognosis

- AIDS-KS indicators of shorter survival
 - Visceral involvement (lung, liver, etc.), pleural effusion
 - Prior or coexistent opportunistic infection
 - Systemic symptoms (e.g., unexplained fever > 2 weeks, weight loss > 10%, diarrhea, night sweats)
 - Low CD4 lymphocyte count (< 100-300 cells/mm³)
- Opportunistic infections are cause of death in 80% of patients with AIDS-KS

Treatment

- AIDS-KS: HAART ± chemotherapy
- IKS: Decrease in immunosuppressive therapy

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Flame-shaped nodules on CT are highly suggestive of AIDS/KS in appropriate clinical setting

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Kaposi Sarcoma





(Left) PA chest radiograph of a 37-year-old man with AIDS who presented with cough demonstrates diffuse bilateral small irregular pulmonary nodules. (Right) PA chest radiograph of the same patient obtained 4 months later shows marked interval increase in the size and number of the bilateral pulmonary nodules. The disease progression corresponded with the degree of immunosuppression in this patient.





(Left) Axial CECT of the same patient demonstrates numerous irregular, poorlymarginated pulmonary nodules \supseteq in the right lung with the so-called flameshaped morphology. Bronchoscopy and biopsy showed AIDS-Kaposi sarcoma. (Right) Axial CECT of the same patient shows smooth and nodular interlobular septal thickening \boxtimes and patchy ground-glass opacities \overline{rad} in the right lung. Findings such as peribronchovascular &/or interlobular septal thickening and ground-glass opacities are comparatively less common.





(Left) Axial NECT of a patient with AIDS-Kaposi sarcoma and coexistent Pneumocystis pneumonia shows a cavitary right upper lobe nodule 🖂 Cavitary lesions in affected patients are almost always related to superimposed infection. (Right) Axial CECT of a patient with AIDS-Kaposi sarcoma shows bilateral pleural effusions \square , conspicuous mediastinal 🔁 and enhancing axillary \bowtie lymph nodes, and left anterior chest wall skin thickening 🖾 All these findings are characteristic of AIDS-Kaposi sarcoma.
Follicular Bronchiolitis

KEY FACTS

TERMINOLOGY

- Follicular bronchiolitis (FB)
- Pathological process characterized by lymphoid follicles with germinal centers along bronchial walls

IMAGING

- CT
 - o Centrilobular micronodules and tree-in-bud opacitieso Ground-glass opacities
 - o Mosaic attenuation and expiratory air-trapping

TOP DIFFERENTIAL DIAGNOSES

- Lymphoid interstitial pneumonia
- Respiratory bronchiolitis and respiratory bronchiolitisinterstitial lung disease
- Diffuse aspiration bronchiolitis
- Hypersensitivity pneumonitis
- Viral bronchiolitis

PATHOLOGY

- Primary or idiopathic
- Secondary FB more common, may be associated with
 Connective tissue diseases
 - Immunodeficiency
 - Hypersensitivity reactions
 - o Infections
 - Exposure to nylon; polyethylene flock

CLINICAL ISSUES

- Underlying connective tissue disease: Progressively worsening dyspnea (most common symptom)
- Immunodeficiency: Recurrent pneumonia and dyspnea
- Idiopathic: Cough

DIAGNOSTIC CHECKLIST

• Consider FB in patient with connective tissue disease, without clinical evidence of infection, who exhibits centrilobular micronodules on CT

(Left) Axial HRCT of a 50-yearold man with rheumatoid arthritis and follicular bronchiolitis shows centrilobular micronodules, tree-in-bud opacities \supseteq , and bronchial wall thickening 🔁 (Right) Axial HRCT of the same patient shows left upper lobe centrilobular micronodules 🖂 While the imaging manifestations of follicular bronchiolitis are nonspecific, the presence of centrilobular micronodules in the absence of symptoms of pulmonary infection should raise suspicion for this diagnosis.





(Left) Low-power

photomicrograph (H&E stain) shows follicular bronchiolitis characterized by germinal centers 🔁 surrounding bronchioles 🔁. The germinal centers correlate with the centrilobular micronodules seen on HRCT. Note sparing of the pleura 🔁, typical of a centrilobular process. (Right) Low-power photomicrograph (H&E stain) shows follicular bronchiolitis characterized by lymphoid follicles with germinal centers 🔁 that surround and narrow adjacent bronchioles 🔁.





- Abbreviations
- Follicular bronchiolitis (FB)

Synonyms

• Bronchiolar nodular lymphoid hyperplasia

Definitions

• Pathologic process characterized by lymphoid follicles with germinal centers along bronchial walls

IMAGING

General Features

- Best diagnostic clue
- CT: Centrilobular micronodules
- Size
 - o Micronodules (< 3 mm in diameter)
- Morphology
 - Airway centered process characterized by centrilobular micronodules
 - Diffuse distribution of micronodules in lymphoid interstitial pneumonia (LIP)
- May be associated with other patterns of diffuse lung disease
 - Centrilobular micronodules may not be predominant finding
 - Secondary FB: Predominant findings dictated by underlying disease

Radiographic Findings

- Chest radiographs are typically normal
- Abnormal findings are nonspecific
 - Lung hyperinflation
 - Bronchial wall thickening
 - o Ill-defined, small nodules

CT Findings

- HRCT
 - o Nodules
 - Distribution
 - Centrilobular (most common): Bilateral and diffuse
 - □ Peribronchovascular and subpleural (uncommon)
 - Lower lobe predominant
 - Micronodules are more profuse in areas of groundglass opacity
 - Size
 - □ < 3 mm (i.e., micronodules) (common)
 - 🗆 3-10 mm
 - □ > 10 mm (rare)
 - Attenuation
 - □ Ground-glass or soft tissue
 - Ground-glass opacities
 - Nonsegmental
 - Tree-in-bud opacities
 - Less common findings
 - Bronchial dilatation
 - Bronchial wall thickening
 - Mosaic attenuation
 - Air-trapping on expiratory CT

- Cysts: Overexpanded air spaces caused by hyperinflation beyond partially obstructed bronchioles
- Mediastinal &/or hilar lymphadenopathy

DIFFERENTIAL DIAGNOSIS

Lymphoid Interstitial Pneumonia (LIP)

- Centrilobular nodules
- Ground-glass opacities
- Diffuse interstitial involvement
- LIP vs. FB
 - LIP and FB may coexist
 - Pulmonary cysts more frequent in LIP than in FB
 - Differentiation requires biopsy

Respiratory Bronchiolitis and Respiratory Bronchiolitis-Interstitial Lung Disease

- Centrilobular nodules
- Ground-glass opacities
- Upper lung zone predominant
- Reticular opacities [respiratory bronchiolitis interstitial lung disease (RB-ILD)]
- Peripheral bronchial wall thickening (RB-ILD)
- History of cigarette smoking

Diffuse Aspiration Bronchiolitis

- Tree-in-bud opacities and centrilobular micronodules
- Bronchiectasis
- Risk factors
 - Esophageal disease (hiatus hernia, achalasia, gastroesophageal reflux disease)
 - Neurological impairment affecting deglutition and esophageal motility

Hypersensitivity Pneumonitis (HP)

- Ground-glass opacities
- Ill-defined, centrilobular, ground-glass nodules
- Mosaic attenuation and expiratory air-trapping
 - Three-density (head-cheese) pattern: Coexistent airtrapping, normal lung, ground-glass opacities
- Bronchial and bronchiolar wall thickening
- Cysts
- Reticular opacities with upper lobe zone predominance (fibrotic HP)
- Nonsmokers

Viral Bronchiolitis

- Centrilobular micronodules
- Bronchial wall thickening
- Consolidation
- Clinical manifestations of acute respiratory infection

Diffuse Panbronchiolitis

- Tree-in-bud opacities
- Bronchiectasis and bronchiolectasis
- Basilar and peripheral predominance
- Severe pansinusitis
- Patients from Asia (especially Korea and Japan)

Constrictive Bronchiolitis

• Bronchiectasis

- Mosaic attenuation
- Expiratory air-trapping
- Occasionally centrilobular micronodules

PATHOLOGY

General Features

- Etiology
 - Antigenic stimulation of BALT-producing polyclonal lymphoid hyperplasia
 - Primary or idiopathic FB
 - Variable incidence
 - Secondary FB
 - □ Connective tissue diseases: Rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrome
 - Other immunological disorders: Evans syndrome of autoimmune hemolytic anemia and immune thrombocytopenia, pernicious anemia
 - Immunodeficiency: Acquired immunodeficiency syndrome (AIDS), common variable immunodeficiency
 - □ Hypersensitivity reactions
 - □ Infection: *Pneumocystis jirovecii* pneumonia, *Legionella* pneumonia, active hepatitis
 - Nonspecific airway-centered inflammation: Bronchiectasis
 - □ Exposure to nylon; polyethylene flock
 - Granulomatous lymphoid interstitial lung disease; histologic findings of granulomatous and lymphoproliferative disease (lymphoid interstitial pneumonia, FB, lymphoid hyperplasia) in patient with common variable immunodeficiency
 - COPA syndrome: Monogenic autoimmune disorder due to missense mutations in COPA gene on chromosome 1; characterized by arthritis, FB, cysts, and diffuse alveolar hemorrhage
 - Associated secondary histopathologic component
 - Organizing pneumonia (OP)
 - Nonspecific interstitial pneumonia (NSIP)
 - Usual interstitial pneumonia (UIP)
- Pathology
 - o BALT
 - Subset of mucosa-associated lymphoid tissue (MALT)
 - May be absent in normal lung
 - Development depends on antigenic stimuli
 - Polyclonal proliferations are consistent with benign disease
 - o Monoclonal proliferations are consistent with lymphoma

Microscopic Features

- Hyperplastic lymphoid follicles with reactive peribronchiolar germinal centers
 - Minor interstitial component
- LIP is similar, but exhibits widespread lymphocytic infiltration along alveolar septa and interstitium
- Polyclonal lymphocytes based on immunohistochemistry
- Hyperplastic follicles may be seen in interlobular septa and visceral pleura
- Airway obstruction may lead to pneumonia, OP, or bronchiolar intraluminal neutrophilic exudate

- Reactive lymphoid follicles stain positive for pan-B-cell markers (CD20, CD79a)
- Interstitial component, when present, stains positive for pan-T-cell markers (CD3, CD5)
- Staining for BCL2 absent in reactive germinal centers but present in interstitial T-cells
- Polyclonal pattern present on polymerase chain reaction (PCR) for gene rearrangement (IgH-R)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Underlying connective tissue disease
 - Progressively worsening dyspnea (most common symptom)
 - Diagnosis of connective tissue disease often precedes respiratory manifestations
 - Immunodeficiency (congenital or acquired)
 - Recurrent pneumonia
 - Dyspnea
 - o Idiopathic FB
 - Cough
 - Peripheral eosinophilia
- Other signs/symptoms
 - Pulmonary function tests with variable restrictive, obstructive, and mixed patterns

Demographics

- Age
 - According to clinical presentation (primary or secondary)
 - Connective tissue disease: 5th decade of life
 - Immunodeficiency: Young adults or teenagers
 - Idiopathic FB: Middle-aged or older patients

Natural History & Prognosis

- Overall good prognosis
- Prognosis determined by age and underlying condition

Treatment

- Idiopathic FB
 - Good response to corticosteroids
- Secondary FB
 - Treatment related to management of underlying disease
- Recurrence may occur after discontinuation of corticosteroids

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Consider FB in patient with connective tissue disorder without clinical evidence of infection who exhibits centrilobular micronodules on CT

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Follicular Bronchiolitis





(Left) Axial HRCT of a patient with follicular bronchiolitis shows left upper lobe peribronchovascular opacities 🔁 and parenchymal bands 🔁. (Right) Axial HRCT of a 50year-old man with follicular bronchiolitis shows bronchiectasis 🔁 and bronchiolectasis rightarrow in thebilateral upper lobes. While centrilobular micronodules are a common imaging abnormality in patients with follicular bronchiolitis, bronchial wall thickening and bronchiectasis are nonspecific and uncommon manifestations.





(Left) Axial HRCT of a 45-yearold woman with follicular bronchiolitis shows right upper lobe subpleural nodules $\overline{\rightarrow}$. The presence of nodules > 1 cm is an uncommon CT finding in patients with follicular bronchiolitis. (Right) Axial HRCT of 42-year-old woman with follicular bronchiolitis shows bronchial wall thickening \boxtimes and air-trapping with a lobular distribution. As other bronchiolitides, follicular bronchiolitis is often associated with mosaic attenuation on inspiratory HRCT and air-trapping on expiratory HRCT.





(Left) Axial HRCT of a middleaged man with follicular bronchiolitis and organizing pneumonia pattern shows small solid 🛃 and groundglass opacity nodules 🛃 in the right upper lobe. (Right) Axial HRCT of a young man with follicular bronchiolitis and organizing pneumonia shows a right lower lobe, subpleural, mass-like consolidation 🔁 and a pulmonary nodule \implies that exhibits the CT halo sign. The presence of a mass or consolidation is an uncommon manifestation of follicular bronchiolitis.

KEY FACTS

TERMINOLOGY

- Lymphoid interstitial pneumonia (LIP): Entity that forms part of spectrum of reactive lymphoproliferative disorders
 Associated with systemic disease (frequently autoimmunity)
- Disease classified within rare idiopathic interstitial pneumonias: < 20% of all cases of LIP

IMAGING

- Radiography
 - Basilar predominance reticular or reticulonodular opacities
- CT
 - Ground-glass opacities
 - Poorly-defined centrilobular nodules
 - Thick bronchovascular bundles
 - Interlobular septal thickening
 - Small subpleural nodules
 - o Thin-walled cysts

TOP DIFFERENTIAL DIAGNOSES

- Lymphangioleiomyomatosis
- Birt-Hogg-Dubé syndrome
- Hypersensitivity pneumonitis
- Amyloidosis
- Follicular bronchiolitis
- Light chain deposition disease
- Pulmonary Langerhans cell histiocytosis

PATHOLOGY

- Inflammatory pulmonary response of bronchus-associated lymphoid tissue (BALT)
- Genetic predisposition to develop LIP

DIAGNOSTIC CHECKLIST

• Consider LIP in patients with basilar predominant thinwalled cysts, ground-glass opacities, and centrilobular micronodules in the appropriate clinical setting

(Left) Axial HRCT of a 53-yearold man with lymphoid interstitial pneumonia and Sjögren syndrome shows multiple thin-walled cysts \supseteq , qround-qlass $opacities <math>\Xi$, and bronchovascular thickening Lymphoid interstitial pneumonia is associated with autoimmunity, and especially with Sjögren syndrome. (Right) Coronal HRCT of the same patient shows multiple thinwalled cysts \square , bilateral ground-glass opacities 🖂, bronchovascular bundle thickening 🔁, and peribronchovascular consolidation 🔁.





(Left) PA chest radiograph of a 63-year-old-man with idiopathic lymphoid interstitial pneumonia shows basilar predominant bilateral reticular opacities. (Right) Coronal HRCT of the same patient shows multiple thinwalled cysts 🖂, traction $bronchiectasis \square, and$ subpleural reticulation 🔁 from concomitant diffuse fibrosing interstitial lung disease, a not uncommon association, especially in patients with autoimmunity.





Abbreviations

• Lymphoid interstitial pneumonia (LIP)

Synonyms

• Lymphoid interstitial pneumonia

Definitions

- Reactive inflammatory response of bronchus-associated lymphoid tissue (BALT)
- Clinicopathological entity in spectrum of reactive lymphoproliferative disorders
 - Associated with systemic disease (frequently autoimmune) or infection
- Classified within rare idiopathic interstitial pneumonias • < 20% of all cases of LIP

IMAGING

General Features

- Best diagnostic clue
 - o Thin-walled cysts
 - Centrilobular micronodules
 - Ground-glass opacities
- Location
 - Basilar predominance

Radiographic Findings

- Radiography
 - Reticular or reticulonodular opacities
 - Basilar predominance
 - o Ill-defined nodules
 - Ground glass opacities/consolidation
 - Disease progression

CT Findings

- HRCT
 - Ground-glass opacities
 - Poorly-defined centrilobular nodules
 - Thick bronchovascular bundles
 - o Interlobular septal thickening
 - o Small subpleural nodules
 - o Thin-walled cysts (68-82%)
 - Ball-valve mechanism from lymphocytic Infiltration of bronchiolar wall
 - Lower lung predominance
 - Few in number
 - 1-30 mm in diameter
 - Involve < 10% of lung
 - Mediastinal lymphadenopathy
 - Less common findings
 - Large nodules (> 10 mm) &/or consolidations
 Should suggest possibility of coexisting lymphoma
 - Calcified nodules
 - Interstitial abnormalities
 Reticulation
 - Honeycombing
 - Bronchiectasis &/or bronchiolectasis
 - Emphysema

Imaging Recommendations

Best imaging tool
 HRCT

DIFFERENTIAL DIAGNOSIS

Lymphangioleiomyomatosis

- Rare neoplastic disease characterized by smooth muscle cell proliferation in lungs and lymphatic spaces
- Sporadic (S-LAM) or associated with tuberous sclerosis complex (TSC)
- Premenopausal women
- Diffuse thin-walled lung cysts
- Chylous pleural effusions
- Renal angiomyolipomas
- Mediastinal and retroperitoneal lymphangioleiomyomas

Birt-Hogg-Dubé Syndrome

- Rare inherited disorder caused by mutations in folliculin (*FLCN*) gene
- Lung cysts
 - Basilar predominance
 - Disproportionate number of paramediastinal elliptical cysts
- Skin lesions
 - Facial papules (fibrofolliculomas or trichodiscomas)
- Renal tumors
 - Range from benign oncocytomas to malignancies

Hypersensitivity Pneumonitis

- Rare, random cysts
- Focal areas of air-trapping

Amyloidosis

- Heterogeneous group of diseases with extracellular deposition of abnormal insoluble proteins
- Systemic or localized
- Thin-walled lung cysts
 - o Rare
 - Peripheral predominance
 - Association with Sjögren syndrome or mucosaassociated lymphoid tissue (MALT) lymphoma
- Calcified nodules

Light Chain Deposition Disease

- Deposition of monoclonal light chains in kidneys and other organs (lung)
- Pulmonary cysts
- Pulmonary vessel within cyst wall &/or traversing cyst
- Pulmonary nodules

Follicular Bronchiolitis

- Pathologic process characterized by lymphoid follicles with germinal centers along bronchial walls
- Idiopathic or secondary
- Thin-walled lung cysts
 - o Rare
 - Overexpanded air spaces caused by hyperinflation distal to obstructed bronchioles
- Centrilobular micronodules
- Bronchial wall thickening

Pulmonary Langerhans Cell Histiocytosis

- Cystic disease in spectrum of smoking-related disorders
- Initially nodular with peribronchovascular distribution and progression to cavitation
 - Nodules exhibit characteristic bizarre shapes
- Upper lobe predominance; relative sparing of lung bases

PATHOLOGY

General Features

- Etiology
 - Inflammatory pulmonary response of BALT
 - Exact disease mechanism unknown
 - Abnormal expression of human leukocyte antigen-D related (HLA-DR) with exaggerated production of transforming growth factor-beta
- Genetics
 - Genetic predisposition to develop LIP
 - Autosomal dominance with incomplete penetrance
- Associated abnormalities
 - o Dysgammaglobulinemia
 - Polyclonal hypergammaglobulinemia
 - Autoimmune disorders
 - Sjögren syndrome
 - □ 1% of patients with Sjögren syndrome develop LIP
 - □ 25% of LIP associated with Sjögren syndrome
 - Systemic lupus erythematosus
 - Rheumatoid arthritis
 - Primary biliary cirrhosis
 - Polymyositis
 - Infection
 - Human immunodeficiency virus
 - Acquired immunodeficiency syndrome (AIDS)defining illness in individuals younger than 13 years
 - Epstein-Barr virus
 - Legionella pneumophila
 - Other conditions
 - Allogeneic bone marrow transplant
 - Pulmonary alveolar microlithiasis
 - Pulmonary alveolar proteinosis
 - Castleman disease (multicentric)
 - Common variable immunoglobulin deficiency

Microscopic Features

- Diffuse interstitial cellular infiltrates, which expand and widen interlobular and alveolar septa
 - Polymorphous infiltrates: Admixture of small lymphocytes, immunoblasts, plasma cells, and histiocytes
 - T-cells that express CD3
- Reactive lymphoid follicles
 - Along peribronchiolar regions with lymphocyte infiltration of bronchiolar epithelium
 - B-lymphocytes that express CD20
- Multinucleated giant cells &/or poorly-formed nonnecrotizing granulomas
- Inconspicuous and loosely arrangedInterstitial fibrosis and honeycombing
 - Later in disease course

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Insidious (symptoms from 2 months to 12 years before diagnosis)
 - Dyspnea on exertion
 - Nonproductive cough
- Other signs/symptoms
 - o Chest pain
 - o Systemic symptoms (fever, weight loss, night sweats)
 - Symptoms related to associated condition
 - Occasionally incidental finding in asymptomatic subject
- Pulmonary function tests
 - Restrictive ventilatory defect
 - Decreased diffusion capacity

Demographics

- Age
 - Varies according to underlying disease
 - 30-60 years (idiopathic or associated to systemic condition)
 - HIV-associated most common in children
- Sex
 - o M:F = 1:2.75
 - Men more likely to develop idiopathic LIP
 - Women more likely to develop LIP related to autoimmune disorder

Natural History & Prognosis

- Variable prognosis
 - o Benign
 - Asymptomatic
 - Complications
 - Associated infections
 - Pulmonary fibrosis
 - Transformation into lymphoma
 - □ Patients with Sjögren syndrome
 - Rare and controversial

Treatment

- Based on management of underlying conditions
 - o Steroids
 - Stabilization or improvement (50-60% of patients)
 - Other immunosuppressive agents (cyclophosphamide, rituximab, hydroxychloroquine)
 - Variable response

DIAGNOSTIC CHECKLIST

Consider

• LIP in patients with basilar predominant thin-walled cysts, ground-glass opacities, and centrilobular micronodules in the appropriate clinical setting

- Ruano CA et al: Multimodality imaging in connective tissue disease-related interstitial lung disease. Clin Radiol. 76(2):88-98, 2021
- Panchabhai TS et al: Lymphocytic interstitial pneumonia. Clin Chest Med. 37(3):463-74, 2016





(Left) Axial HRCT of a 48-yearold woman with lymphoid interstitial pneumonia and rheumatoid arthritis shows diffuse bilateral thin-walled cysts \supseteq of variable size. (Right) Coronal HRCT of the same patient shows numerous thin-walled pulmonary cysts ➡ of variable size, most of which are associated with vascular structures. Lymphoid interstitial pneumonia is common in the context of autoimmunity, and Sjögren syndrome and rheumatoid arthritis are the two most common associated diseases.





(Left) Coronal HRCT of a 70year-old man with lymphoid interstitial pneumonia and Sjögren syndrome shows multiple thin-walled cysts \supseteq , ground-glass centrilobular micronodules 🖾, and bronchovascular thickening (Right) Coronal HRCT minIP reformatted image of the same patient helps highlight the cystic nature of lymphoid interstitial pneumonia. The differential diagnosis includes other cystic lung diseases, such as lymphangioleiomyomatosis, light chain deposition disease, and Birt-Hogg-Dubé syndrome.





(Left) PA chest radiograph (coned-down to the left lower lobe) of a patient with Sjögren syndrome and lymphoid interstitial pneumonia shows left basilar linear opacities \supseteq . (Right) Axial HRCT of the same patient shows diffuse lower lobe ground-glass opacity with mild superimposed smooth interlobular septal thickening *⊡*. While cystic change is the characteristic finding of lymphoid interstitial pneumonia, cysts may be scant or even absent in a minority of affected patients.

Nodular Lymphoid Hyperplasia

KEY FACTS

TERMINOLOGY

- Nodular lymphoid hyperplasia (NLH)
- Reactive nodular lymphoid proliferation that manifests with pulmonary nodule(s)/mass(es)

IMAGING

- Radiography
 - Pulmonary nodule(s): Discrete or ill-defined, solitary (65%), multiple (35%)
 - May exhibit air bronchograms
- CT
 - Pulmonary nodule with solid or ground-glass attenuation
 - Nodule may exhibit air bronchograms
 - o Lymphadenopathy (rare)
 - Pleural effusion (rare)
- PET/CT
 - Nodule(s) may exhibit FDG uptake (SUV = 2.5)

TOP DIFFERENTIAL DIAGNOSES

- Low-grade B-cell lymphoma
- Lymphoid interstitial pneumonia
- Follicular bronchiolitis

PATHOLOGY

- Well-circumscribed gray to white-tan nodule(s)
- Abundant reactive germinal centers with sheets of interfollicular plasma cells
- Interfollicular fibrosis of variable degree often present

CLINICAL ISSUES

- Symptoms/signs
- Asymptomatic (most)
- o Cough, dyspnea, pleuritic chest pain
- Good prognosis
 - Surgical resection curative
 - May regress without treatment

(Left) Coned-down PA chest radiograph of an asymptomatic patient with nodular lymphoid hyperplasia (NLH) shows an ill-defined soft tissue nodule \blacksquare in the middle lobe. (Right) Composite image with axial NECT (left) and fused FDG PET/CT (right) of the same patient shows a slightly spiculated peribronchovascular middle lobe solid nodule 🔁 that exhibits moderate FDG avidity ➡ on fused PET/CT. A solitary pulmonary nodule is the most common imaging manifestation of this lymphoproliferative process.

(Left) Composite image with axial NECT (left) and coronal fused FDG PET/CT (right) of a patient with NLH shows a subpleural left lower lobe nodule \supseteq that exhibits moderate FDG uptake 🔁. (Right) Composite image with axial NECT of 2 different patients with NLH shows small solid and subsolid nodules 🔁 (left) and multiple larger discrete nodules D with *intrinsic air bronchograms* (right). Multiple nodules with or without air bronchograms are common imaging manifestations of NLH.









- Abbreviations
- Nodular lymphoid hyperplasia (NLH)

Definitions

• Reactive nodular lymphoid proliferation that manifests with pulmonary nodule(s)/mass(es)

IMAGING

General Features

- Location
 - Subpleural or peribronchial location
- Size
 - o 2- to 4-cm nodules
- Morphology
- Discrete or ill-defined nodule(s)/mass(es)

Radiographic Findings

- Pulmonary nodule(s)
 - o Solitary pulmonary nodule (65%)
 - o Multiple nodules (35%)
 - Air bronchograms within lung nodules

CT Findings

- Pulmonary nodule
 - Solid or ground-glass attenuationIntrinsic air bronchograms
- Lymphadenopathy (rare)
- Pleural effusion (rare)

Nuclear Medicine Findings

• PET/CT

• Nodule(s) may exhibit FDG uptake (SUV = 2.5)

DIFFERENTIAL DIAGNOSIS

Low-Grade B-Cell Lymphoma

- Similar imaging findings
- Histologic, immunohistochemical, and molecular characterization allows differentiation

Lymphoid Interstitial Pneumonia (LIP)

- Imaging: Cysts and ground-glass opacities on CT
- Pathology: Diffuse reticulonodular or small nodular infiltrates

Follicular Bronchiolitis

• Imaging: Centrilobular micronodules on CT

PATHOLOGY

General Features

- Etiology
 - o Unknown
 - Most cases not associated with autoimmune disease, immunodeficiency, or prior viral infection; these entities associated with follicular bronchiolitis and LIP
- Formerly known as pseudolymphoma
 - Some cases may have represented low-grade B-cell lymphoma of bronchus-associated lymphoid tissue (BALT)

 NLH considered a reactive condition with specific histologic, immunophenotypic, and genotypic criteria
 Immunohistochemical and molecular studies may be necessary for definitive diagnosis

Gross Pathologic & Surgical Features

- Well-circumscribed gray to white-tan nodule(s)
- Multiple nodules (~ 30%)
- Subpleural or peribronchial distribution
- Mediastinal &/or hilar lymphadenopathy (~ 30%)

Microscopic Features

- Abundant reactive germinal centers with sheets of interfollicular plasma cells
 - Reactive germinal centers may occur along alveolar septa
- Lymphoepithelial lesions
- Interfollicular fibrosis of variable degree often present
- Occasional giant cells (rare)
- Plaque-like pleural involvement

Immunohistochemical and Molecular Studies

- Reactive lymphoid follicles stain positive for B-cell markers (CD20, CD79-a)
- Intrafollicular lymphocytes stain positive for T-cell markers (CD3, CD43, CD5)
- Plasma cells are polyclonal on PCR analysis and stain positive for κ and λ -light chains
- No coexpression of CD20 and CD43 by lymphocytes, unlike cases of low-grade B-cell lymphoma

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic (most) with incidental lung nodule found on imaging
 - o Cough
 - o Dyspnea
 - Pleuritic chest pain

Demographics

- Age
 - o Average: 60 years (range: 19-80 years)
- Sex
 F:M = 4:3

Natural History & Prognosis

• Good prognosis

Treatment

- Surgical resection curative
- May regress without treatment

- Fang L et al: Pulmonary nodular lymphoid hyperplasia: a rare benign disease with malignant mask. Ann Transl Med. 7(3):43, 2019
- Yell M et al: Pulmonary nodular lymphoid hyperplasia. Arch Pathol Lab Med. 143(9):1149-53, 2019
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KEY FACTS

TERMINOLOGY

• Post-transplant lymphoproliferative disease (PTLD)

IMAGING

- Intrathoracic PTLD
 - Most common in lung transplants
 - Also in combined heart/lung and heart transplants
- Radiography
 - o Nodules or masses (50%) most common manifestation
 - Hilar and mediastinal lymphadenopathy also common
 - o Consolidation
 - Associated pleural effusion
- CT
 - Identification of lung disease and lymphadenopathy not visible on radiography
 - Mediastinal lymphadenopathy (10-50% of patients with intrathoracic PTLD)

TOP DIFFERENTIAL DIAGNOSES

- Fungal pneumonia
- Cryptogenic organizing pneumonia
- Lung cancer
- Metastases

PATHOLOGY

 Related to Ebstein-Barr virus (EBV) infection: Immunosuppression allows proliferation of EBV-infected cells, which may become monoclonal and malignant

CLINICAL ISSUES

• Treatment: Reduction of immunosuppression (especially decreased cyclosporine dose)

DIAGNOSTIC CHECKLIST

• Consider infection, PTLD and lung cancer in transplant recipients with new lung masses &/or consolidations

(Left) PA chest radiograph of a patient with post-transplant lymphoproliferative disease after liver transplantation shows bilateral lung nodules \square and a large right lower lobe mass 🔁. (Right) Axial NECT of the same patient shows multiple bilateral pulmonary nodules \square and a large right lower lobe mass *⊠*. Note associated small right pleural effusion. Single or multiple pulmonary nodules &/or masses represent the most common intrathoracic manifestation of posttransplant lymphoproliferative disease.





(Left) Axial NECT shows bilateral consolidations 🖂, nodular opacities \square , and small pleural effusions. Consolidation is an uncommon manifestation of intrathoracic post-transplant *lymphoproliferative disease* that occurs in approximately 10% of reported cases. (Right) Axial NECT of a patient with post-transplant lymphoproliferative disease shows a solitary left lower lobe mass \supseteq and a small pleural effusion \supseteq . Solitary pulmonary nodule or mass is one of the most common thoracic manifestations.





Abbreviations

• Post-transplant lymphoproliferative disease (PTLD)

Synonyms

• Post-transplant lymphoproliferative disorder

Definitions

- Post-transplant disorder of **B-cells, T-cells, or natural killer** cells usually related to Ebstein-Barr virus (EBV) infection
- Tumor resembling Hodgkin lymphoma also included in definition if it occurs post transplant

IMAGING

General Features

- Best diagnostic clue
 - Single or multiple lung nodules or masses
 - ± mediastinal and hilar lymphadenopathy; ± consolidation
- Location
 - Site of involvement (e.g., lung, liver, bowel, kidney) varies depending on transplanted organ
 - Thoracic involvement most common with transplants of lung > combined heart/lung > heart > liver > kidney

Radiographic Findings

- Nodule(s) or mass(es) most common intrathoracic manifestation
 - Solitary pulmonary nodule or mass (50%)
 - Smooth or irregular borders
 - Average size: 2-3 cm (range: 3 mm to 5 cm)
 - Rarely cavitary
 - Variable growth rate, usually slow progression
 - Multiple pulmonary nodules or masses
 - Similar features as solitary lesions
 - Random distribution without lobar predilection
- Consolidation
 - Multifocal consolidation (7-10% of lung transplant recipients with PTLD)
 - Usually subsegmental
 - Bronchovascular location with air bronchograms
 - Nodules and consolidations may coexist
 - Typically PTLD is primarily nodular or primarily consolidative
- Thoracic lymph node involvement
 - Hilar and mediastinal lymphadenopathy (10-50%)
 - Typically paratracheal, anterior mediastinal, aortopulmonary window lymph nodes
 - Size range: 1.0-7.5 cm; average size of 2.0 cm in series of 35 patients with intrathoracic PTLD
 - Rarely large mass (10%) that encases mediastinal vessels
 - Lymph node involvement of bronchus-associated lymphoid tissue (BALT); airway narrowing
- Lung nodules/consolidation + lymphadenopathy highly suggestive of PTLD in appropriate setting
- Pleural involvement
 - Pleural effusions may accompany other forms of thoracic involvement

CT Findings

• CECT

- Nodules and lymphadenopathy not apparent on radiography
- Nodules or masses (most common intrathoracic manifestation)
 - ± low-density centers and CT halo sign
 - Usual location along peribronchovascular or subpleural regions
- Mediastinal lymphadenopathy (10-50% of patients with intrathoracic PTLD)
 - Usually associated with pulmonary nodules or consolidation
- Ground-glass opacities, centrilobular nodules, thinwalled cysts: Suggest lymphoid interstitial pneumonia (LIP)
- o Thymic involvement rare; relatively specific for PTLD
- Pericardial thickening or effusion (10%)
- Esophageal wall thickening
- Chest wall mass

Nuclear Medicine Findings

- PET
 - Especially useful for evaluation of occult extranodal involvement
 - o More aggressive PTLD; often higher overall SUV

Imaging Recommendations

- Best imaging tool
 - CT characterizes both lung abnormalities and thoracic lymphadenopathy
- Protocol advice
 - CECT of neck, chest, abdomen, and pelvis: Widespread disease of multiple lymph node and extranodal sites
 - PET/CT for evaluation of occult disease

DIFFERENTIAL DIAGNOSIS

Fungal Pneumonia

- Clinical symptoms of infection
- Commonly associated with pleural effusion
- Nodules less well-defined, more commonly cavitary than in PTLD
- CT halo sign in early angioinvasive aspergillus infection

Organizing Pneumonia

- Often peripheral, peribronchial, and basilar distribution in solid organ transplant recipients; upper lung distribution in stem cell transplant recipients
- Focal rounded consolidations
- Air bronchograms common
- Good response to steroids

Lung Cancer

- Heterogeneously enhancing soft tissue mass on CECT
- May be indistinguishable from PTLD
- Biopsy often required to establish diagnosis

Metastases

- Multiple bilateral lung nodules and masses
- Mediastinal and hilar lymphadenopathy

• Transplant recipients: ↑ risk of malignancy possibly secondary to long-term immunosuppressive therapy

Diffuse Alveolar Hemorrhage

- Widespread parenchymal opacity; usually not nodular
- May be associated with hemoptysis and anemia

PATHOLOGY

General Features

- Etiology
 - Usually related to EBV infection
 - Immunosuppression with cyclosporine allows unrestricted proliferation of EBV-infected cells
 - May become monoclonal and malignant
 - EBV virus is herpesvirus
 - Nearly 100% of adult population seropositive
 - Clinical syndrome of infectious mononucleosis in adolescents and adults
 - EBV seropositivity is most important risk factor for development of PTLD
 - Risk of developing PTLD in EBV-positive donor and EBV-negative recipient is 25-50%
- PTLD thought to be stepwise progression from benign lymphoid polyclonal hyperplasia to frank lymphoma
 - Early diagnosis important before disease evolves into aggressive form

• Extranodal PTLD (2/3 of patients)

- Head and neck: Waldeyer ring (nasopharynx, oropharynx, tonsils)
- o Esophageal/bowel wall thickening
- o Splenomegaly
- Liver: Focal low-attenuation masses (1-4 cm in diameter) or diffuse hepatic infiltration
- o Central nervous system: Focal intraaxial masses
- Nodal PTLD (1/3 of patients)
 - Lymphadenopathy in any lymph node group: Retroperitoneal, mesenteric, axillary

Staging, Grading, & Classification

- Classification
 - Early (reactive hyperplasia)
 - Polymorphic (polyclonal)
 - Monomorphic (monoclonal B-cell or T-cell)
 - o Lymphoma
 - Classic Hodgkin lymphoma
 - B-cell non-Hodgkin lymphoma
 - T-cell non-Hodgkin lymphoma

Microscopic Features

- Categories
 - o Plasmacytic hyperplasia
 - Most common in oropharynx or lymph nodesUsually polyclonal
 - Polymorphic B-cell hyperplasia and lymphoma
 - Lymph nodes or extranodal sites
 - Usually monoclonal
 - o Immunoblastic lymphoma or multiple myeloma
 - Widespread disease
 - Monoclonal

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Localized symptoms/signs depending on organ involved by disease
 - o Infectious mononucleosis-like syndrome (20%)
 - o Tonsillitis, sinusitis, otitis media
 - Lymphadenopathy
- Other signs/symptoms
 - Asymptomatic: Incidental finding on follow-up imaging

Demographics

- Age
 - Can occur at any age: Highest incidence in children
- Epidemiology
 - Incidence varies based on type of transplant
 - Multi-visceral transplants (13-33%)
 - Bowel transplant (7-11%)
 - Heart-lung transplant (9.4%)
 - Lung transplant (2-8%)
 - Heart, pancreas, or liver transplants (1-5%)
 - Blood stem cell transplantation (donor B-cells) or kidney transplants (< 1%)
 - Incidence correlates with degree of immunosuppression (i.e., higher immunosuppression equals greater risk of PTLD)

Natural History & Prognosis

- Most common within 1st year post transplant (60%)
- Recent data suggests longer interval to development of PTLD (36-40 months)
- Uncommon 5 years after transplantation (< 10%)
- Lethal if untreated; 20% mortality
- Poor prognostic factors
 - Early onset, infectious mononucleosis presentation, disease extent, CNS involvement, monoclonal tumor, Tcell origin (90% are of B-cell origin)

Treatment

- Reduction of immunosuppression (especially decreased cyclosporine dose)
 - May develop graft rejection with treatment of PTLD
 - May have to be retransplanted
- Rituximab if reduction in immunosuppression fails
 Monoclonal antibody against B-cell receptor
- Chemotherapy ± radiation therapy or surgery for aggressive disease

DIAGNOSTIC CHECKLIST

Consider

• Infection, PTLD, and lung cancer in transplant recipient with new lung mass &/or consolidation or intrathoracic lymphadenopathy

- Ferla V et al: Biological difference between Epstein-Barr Virus positive and negative post-transplant lymphoproliferative disorders and their clinical impact. Front Oncol. 10:506, 2020
- Hirama T et al: Epstein-Barr virus-associated smooth muscle tumors after lung transplantation. Transpl Infect Dis. 21(3):e13068, 2019





(Left) PA chest radiograph of a patient with post-transplant lymphoproliferative disease shows thickening of the right paratracheal stripe \square , consistent with mediastinal lymphadenopathy. (Right) Axial CECT of the same patient shows multiple enlarged right paratracheal → and left axillary → lymph nodes. Mediastinal and hilar lymphadenopathy is reported in 10-50% of patients with intrathoracic post-transplant lymphoproliferative disease.





(Left) PA chest radiograph of a patient who developed posttransplant lymphoproliferative disease after heart transplantation shows multifocal bilateral nodules \square with ill-defined borders. (Right) Coronal NECT of the same patient shows multiple pulmonary nodules \supseteq with illdefined and spiculated borders, some with groundglass opacity halos 🔁. The differential diagnosis should include multifocal infection, metastatic disease, and posttransplant lymphoproliferative disease.





(Left) Coronal FDG PET of the same patient shows intense FDG uptake within the bilateral pulmonary nodules. Post-transplant lymphoproliferative disease was confirmed on biopsy. FDG PET helps identify occult sites of extranodal involvement. (Right) Composite image with lateral chest radiograph (left) and sagittal CECT (right) shows subcarinal lymphadenopathy 🔁 manifesting as the donut sign on the lateral chest radiograph.

Pulmonary Lymphoma

KEY FACTS

TERMINOLOGY

- Non-Hodgkin lymphoma (NHL)
- Mucosa-associated lymphoid tissue (MALT) lymphoma
- IMAGING
- Radiography
 - Single or multiple nodules and masses
 - Consolidation(s)
- CT
 - o Single or multiple nodules and masses
 - o Consolidation, ground-glass opacity
 - Peribronchovascular and subpleural distribution
 - ± air bronchogram
 - ± cavitation
 - Lymphadenopathy, pleural effusion
- PET
 - Staging and monitoring response to treatment
 - o Low-grade lymphoma not always FDG avid

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary nodules
 - Septic emboli, fungal infection, metastases
- Peribronchovascular, subpleural opacities
 - Sarcoidosis, organizing pneumonia
- Consolidation
- Pneumonia, organizing pneumonia, lung cancer
- CLINICAL ISSUES
- Treatment
- Pulmonary resection of localized disease
- Chemotherapy
- Presentation and prognosis widely variable

DIAGNOSTIC CHECKLIST

 Consider primary pulmonary lymphoma in immunocompromised patients and in patients with autoimmune disorders and chronic multifocal nodules, masses, or consolidations not responsive to antimicrobials

(Left) Axial CECT of a 62-yearold woman with primary pulmonary mucosa-associated lymphoid tissue (MALT) lymphoma shows peribronchovascular groundglass opacities 🔁 and micronodules 🖂 (Right) Coronal CECT of the same patient shows bilateral peribronchovascular groundglass opacities \supseteq and nodules ▶ MALT lymphoma is the most common primary pulmonary lymphoma and carries a 5-year survival greater than 85%. Up to 30% of cases are associated with autoimmune disorders.





(Left) Axial NECT of an asymptomatic 51-year-old man with primary MALT lymphoma shows a left lower lobe nodule 🔁. The patient was initially treated with antibiotics. (Right) Fused axial FDG PET/CT of the same patient obtained when the left lower lobe nodule failed to resolve on treatment shows low-level metabolic activity in the nodule \blacksquare , similar to that of mediastinum. Nearly 50% of patients with primary MALT lymphoma are asymptomatic and are diagnosed incidentally on imaging.





Abbreviations

- Primary pulmonary lymphoma (PPL)
 - Non-Hodgkin lymphoma (NHL)
 - Mucosa-associated lymphoid tissue (MALT) lymphoma
 - Diffuse large B-cell lymphoma (DLBCL)
 - Lymphomatoid granulomatosis (LG)
 - Hodgkin lymphoma (HL)
- Secondary pulmonary lymphoma (SPL)

Synonyms

- Low-grade primary pulmonary B-cell lymphoma
- MALT lymphoma

Definitions

- PPL
 - Pulmonary clonal lymphoid proliferation in patient with no detectable extrapulmonary lymphoma for at least 3 months after initial diagnosis
 - Represents 0.5% of primary lung malignancies
 - Almost all cases of PPL are NHL
 - ~ 70 cases of primary pulmonary HL reported
 - Represents only 3-4% of cases of primary **extranodal** NHL
 - Most common subtypes: MALT lymphoma, high-grade DLBCL, LG
 - MALT lymphoma: Low-grade extranodal B-cell lymphoma, represents majority of cases of PPL
 - Uncommon subtypes: Pulmonary intravascular lymphoma, primary pulmonary plasmacytoma

• SPL

- Common as manifestation of systemic involvement by HL and NHL
- Lung involvement rate higher in HL (85%) than in NHL (24%), but NHL is far more common and represents up to 90% of all SPL
- o Mechanisms of lung involvement
 - Invasion from hilar or mediastinal lymph nodes
 - Hematogeneous or lymphatic dissemination

IMAGING

General Features

- Location
 - Similar pulmonary findings in PPL and SPL
 - Reflects distribution of pulmonary lymphatics: Along bronchovascular bundles, interlobular septa, and subpleural regions

Radiographic Findings

- Radiography
 - Single or multiple lung nodules and masses
 - o Consolidation
 - o Associated mediastinal/hilar lymphadenopathy
 - Pleural effusion

CT Findings

- Solitary or multiple pulmonary nodules/masses
 Well-defined or ill-defined margins
 - ± cavitation

• ± air bronchograms

Airspace opacity

$\circ~$ Consolidation with air bronchogram

- Intrinsic dilated bronchi considered good diagnostic sign
- Ground-glass opacities ± interlobular septal thickening
- Ill-defined opacities along bronchovascular bundles and interlobular septa
- Atelectasis or postobstructive pneumonia due to airway obstruction/compression by adjacent lymphadenopathy
- Endobronchial tumor (rare): Lobar atelectasis
- Lymphadenopathy or mediastinal mass
- Pleural effusion
- Other features of PPLs

• MALT lymphoma

- Multiple bilateral nodules
- Bubbly lucencies, ground-glass opacities
- Dilated bronchi
- Reticular opacities

High-grade B-cell lymphoma

- Subpleural, peribronchial opacities
- Hilar/mediastinal lymphadenopathy in 30% of cases
- ∘ LG
 - Multiple lower lobe predominant nodules or masses
 - □ Central low attenuation or cavitation
 - Peripheral enhancement
 - □ Halo sign, reversed halo sign

• Pulmonary intravascular lymphoma

- Normal-appearing CT
- Mild ground-glass or reticular opacities

Imaging Recommendations

- Best imaging tool
 - PET/CT provides comprehensive assessment of disease extent during staging
 - Response to treatment: Anatomic and metabolic information

Nuclear Medicine Findings

- PET
 - Increased FDG uptake at sites of involvement
 - Detection of lymphoma in normal-sized lymph nodes
 - Detection of extranodal disease
 - Monitor treatment response
 - Better than CT in differentiating viable tumor from post-treatment necrosis and fibrosis
 - Variable FDG uptake; some low-grade lymphomas are not FDG avid

DIFFERENTIAL DIAGNOSIS

Pulmonary Nodules

- Fungal infection
- Septic emboli
- Metastatic disease
- Granulomatosis and polyangiitis
 May mimic LG

Peribronchovascular, Subpleural Opacities

- Sarcoidosis
- Organizing pneumonia

- Reversed halo sign typical; also seen in lymphoma and alveolar sarcoidosis
- Nonspecific interstitial pneumonia
 - Traction bronchiectasis helpful if present

Consolidation

- Pneumonia
 - Persistence of consolidation after appropriate antimicrobial treatment should prompt further diagnostic work-up
- Organizing pneumonia
- Pulmonary hemorrhage
- Lung cancer

PATHOLOGY

General Features

- Etiology
 - Bronchial MALT lymphoma: Chronic antigenic stimulation in autoimmune disorders
 - Autoimmune disorders present in up to 30% of cases
 Sjögren syndrome
 - □ Systemic lupus erythematosus
 - □ Multiple sclerosis
 - High-grade B-cell primary pulmonary NHL
 - Solid organ transplantation with immunosuppression
 - Human immunodeficiency virus (HIV) infection
 - Sjögren syndrome
 - Epstein-Barr virus (EBV) infection
 - o LG
 - EBV infection

Staging, Grading, & Classification

- Low-grade B-cell NHL: 58-87% of PPL
 Bronchial MALT lymphoma accounts for up to 90%
 Follicular lymphoma, mantle lymphocytic lymphoma
- High-grade B-cell NHL: 11-19% of PPL
 Diffuse large B-cell NHL most common
- LG
 - Rare, angiocentric, EBV-positive B-cell lymphoproliferative disease with reactive T-cells
- Primary pulmonary plasmocytoma: Extremely rare
- Pulmonary intravascular lymphoma: Extremely rare

Microscopic Features

- Absence of Reed-Sternberg cells
- Clonal proliferation of either T- or B-cell origin
- Immunohistochemistry helpful for diagnostic confirmation and classification
- Low-grade B-cell NHL
 - Proliferation of small lymphoid cells analogous to marginal zone cells of Peyer patches or spleen follicles
- High-grade B-cell NHL
 - o Blast-like lymphoid cells with strong mitotic activity
- LG
 - Angioinvasive lymphoid infiltration composed of lymphocytes, plasma cells, and histiocytes
 - Grading based on number of neoplastic large B-cells and degree of cytological atypia
 - o Grade 3 lesion treated as large B-cell lymphoma

CLINICAL ISSUES

Demographics

• PPL is more common in patients with autoimmune disorders and immunocompromised subjects

Mucosa-Associated Lymphoid Tissue Lymphoma

- Nearly 1/2 asymptomatic, incidental imaging abnormality
- Cough, mild dyspnea
- Age at diagnosis: 50-60 years
- Diagnosis: Transbronchial biopsy + bronchoalveolar lavage, transthoracic needle biopsy, surgery
- Treatment
 - Surgical resection of localized disease
 - Chemotherapy: 1 or multiple agents
- 5-year survival > 80%; mean survival > 10 years

High-Grade B-Cell Non-Hodgkin Lymphoma

- Dyspnea, fever, weight loss
- Age at onset ~ 60 years
- Diagnosis: Transbronchial or transthoracic biopsy
- Treatment
 - Surgical resection
 - Combination chemotherapy
- Mean survival ~ 8-10 years, lower in transplant recipients and patients with HIV

Lymphomatoid Granulomatosis

- Fever, weight loss, cough, dyspnea
- Age ~ 30-50 years
- May also involve skin, nervous system
- Diagnosis: Requires surgical biopsy
- Treatment: Chemotherapy
- Prognosis widely variable; poor for high-grade lesions

Primary Pulmonary Plasmacytoma

- Usually asymptomatic, age at onset ~ 40 years
- Diagnosis and treatment: Surgical resection
- 5-year survival: 40%
 - o 15-30% develop multiple myeloma

Pulmonary Intravascular Lymphoma

- Fever, hypoxemia
- Diagnosis: Transbronchial or surgical biopsy
- Treatment: Combination chemotherapy

DIAGNOSTIC CHECKLIST

Consider

 PPL in immunocompromised patients &/or patients with autoimmune disorders who present with chronic multifocal nodules, masses, or consolidations not responsive to antimicrobials

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- Deng W et al: Pulmonary MALT Lymphoma has variable features on CT. Sci Rep. 9(1):8657, 2019
- 3. Yao D et al: Clinical and misdiagnosed analysis of primary pulmonary lymphoma: a retrospective study. BMC Cancer. 18(1):281, 2018
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Pulmonary Lymphoma





(Left) Axial CECT of a 92-yearold man with gastric MALT lymphoma shows a left lower lobe nodule 🔁 with an air bronchogram. Air bronchograms and bronchial dilation are commonly found in pulmonary lymphoma that manifests as nodules or consolidations. (Right) Coronal FDG PET of the same patient shows metabolic activity in the left lower lobe nodule \overline{E} and in the stomach \supseteq . Biopsy confirmed pulmonary MALT lymphoma. Most cases of pulmonary MALT lymphoma originate in another organ.





(Left) Axial CECT of a 67-yearold man with non-Hodgkin lymphoma shows a welldefined left upper lobe mass with a peripheral air bronchogram. (Right) Coronal CECT of same patient shows multifocal bilateral nodules and masses \supseteq consistent with multifocal lung involvement. Secondary lung involvement by Hodgkin lymphoma is more common than involvement by non-Hodgkin lymphoma, but non-Hodgkin lymphoma is a much more common disease that represents 80-90% of all cases of secondary pulmonary lymphoma.





(Left) Axial CECT of a 39-yearold woman with a history of non-Hodgkin lymphoma shows a lobulated left upper lobe mass 🖂 (Right) Coronal FDG PET of the same patient shows metabolic activity within the left upper lobe mass →. In addition, there are FDG-avid $\overline{\underline{A}}$ lymph nodes and FDG uptake in the spleen 🔁. In contrast to primary pulmonary lymphoma, secondary pulmonary lymphoma is frequent and should be suspected in any patient with known lymphoma and lung lesions or lymphadenopathy.

Hematogenous Metastases

KEY FACTS

TERMINOLOGY

- Spread of cancer to lung via hematogenous routes
- Lungs third most common site of metastases
- Common malignancies: Breast, gastrointestinal, pancreaticobiliary, urogenital, head/neck, skin, sarcomas

IMAGING

- Radiography
 - o Multiple, bilateral, well-defined lung nodules/masses
 - o Variable in size; more numerous in lower lobes
- CT
 - Bilateral basilar predominant lung nodules/masses
 - Nodules typically angiocentric or periseptal/juxtapleural
 - Hemorrhagic metastases: Ground-glass opacity halo
 - Tumor emboli: Dilated vessels with nodular contours
 - Lymphangitic carcinomatosis: Peribronchovascular and nodular interlobular septal thickening
 - Thin-slab maximum intensity projection reconstructions (MIPs) improve lung nodule detection

TOP DIFFERENTIAL DIAGNOSES

- Granulomas
- Infection
- Granulomatosis with polyangiitis
- Lung cancer

PATHOLOGY

- Well-defined white/tan parenchymal lesions, variable size, may coalesce
- Histology typically reflects histologic origin

CLINICAL ISSUES

- Dyspnea, pleuritic pain, cough, hemoptysis; may be asymptomatic
- Stage IV disease with poor prognosis

DIAGNOSTIC CHECKLIST

• Consider metastases in cancer patient with multiple lung nodules/masses, lymphadenopathy, nodular septal thickening, &/or pleural effusion

(Left) PA chest radiograph of a patient with metastatic sarcoma shows multiple welldefined lung nodules and masses of varied sizes that are more extensively distributed in the lower lobes, reflecting the pulmonary perfusion gradient. (Right) Composite image with axial MIP reformatted image (top) and CECT (bottom) shows hemorrhagic metastases with perilesional ground-glass opacity in choriocarcinoma (top) and treated bladder cancer (bottom). Hypervascular metastases may induce diffuse alveolar hemorrhage.





(Left) Axial CECT of a patient with metastatic osteosarcoma shows irregular, predominantly calcified peribronchovascular masses \blacksquare and right hilar lymph nodes *⊠*, compatible with lung metastases that contain osteoid matrix. (Right) Axial CECT of a patient with metastatic bladder cancer shows mixed solid 🄁 and cavitary \implies metastatic lung nodules. Histologies prone to cavitation include squamous cell carcinoma, sarcomas, colon cancer, and many tumor types following treatment.





Definitions

- Bloodborne spread of cancer cells to lung (primary filtration organ)
- Tumorlets may form within pulmonary arteries, interstitium, lymphatics, airways, pleura, lymph nodes

IMAGING

General Features

- Best diagnostic clue
 - o Multiple, bilateral, well-defined pulmonary nodules
- Location
 - Most numerous in lung bases and lung periphery
 - Random distribution within secondary pulmonary lobule – Angiocentric, peribronchovascular, septal, juxtapleural
 - Intravascular tumor emboli focally expand pulmonary vessels
 - Lymphangitic carcinomatosis obstructs and dilates interlobular septa
 - o Pleural metastases form on visceral and parietal pleura

Radiographic Findings

- Multifocal bilateral lung nodules, masses, or consolidations
 Solitary metastasis atypical
- Predominant involvement of lower lobes
- Size varies due to temporal variation, monoclonal growth
- Borders sharp or ill-defined
- May exhibit cavitation
- Endobronchial metastases: Postobstructive atelectasis/consolidation
- Mediastinal/hilar lymphadenopathy ± pleural effusion

CT Findings

- Multifocal, bilateral, well-defined pulmonary nodules/masses
- Most metastases in outer 1/3 of lung; 80% within 2 cm of pleura
- Thin-slab maximum intensity projection reconstructions (MIPs) improve pulmonary nodule detection
- Vascular pattern
 - o Multiple, bilateral, variably sized spherical lung nodules
 - Lower lobe predominant due to blood flow gradient and larger lung volume
 - "Miliary" metastases (1-3 mm): Medullary thyroid, pancreas, prostate, ovarian cancers and melanoma
 - "Cannonball" metastases (> 2-3 cm): Colorectal and renal cell carcinomas, sarcomas, melanoma
 - Hemorrhagic metastases (ground-glass opacity margins): Angiosarcoma, choriocarcinoma, renal and thyroid carcinomas
 - o Calcifications in sarcomas and adenocarcinomas
 - Osteoid matrix found in all subtypes of sarcomas
 - Dystrophic calcification in adenocarcinomas, especially mucinous subtype
 - Cavitation: Squamous cell cancers (head and neck, cervical), sarcomas, colon cancer
 - Solitary metastases unusual: Renal cell, breast, colon, and urothelial carcinomas, sarcomas, melanoma
 - Spontaneous pneumothorax may occur, especially in juxtapleural cavitary sarcomatous metastases

Endobronchial pattern

- o Hematogenous dissemination to airway wall
 - Endobronchial "aerogenous" seeding rare; associated with mucinous adenocarcinoma
- o Lung, lobar, or segmental atelectasis
- Postobstructive pneumonia or mucoid impaction
- Breast, colon, cervical, uterine, and renal cell cancers, sarcomas, melanoma
- May represent contiguous airway invasion by affected lymph node or lung lesion

Tumor embolus pattern

- Bloodborne tumor cells lodge/grow within pulmonary artery lumen
- Segments of central or peripheral vascular dilation with beaded/nodular contour
- May manifest as tree-in-bud opacities (mimic bronchiolitis)
- ↑ risk of right heart strain, pulmonary infarction
- Gastric, hepatocellular, renal and breast cancers
- Intravascular nodular/tubular soft tissue attenuation helps differentiate from bland thrombus
- Consolidation pattern
 - Mimics pneumonia; peripheral consolidation with airbronchograms
 - o Gastrointestinal adenocarcinomas and lymphoma

Pleural pattern

- Hematogenous ± lymphatic spread
- Pleural effusion; may be large ± loculation
- o Pleural soft tissue nodules/masses less common on CT
- Lung, breast, ovarian, and gastric cancers, lymphoma, melanoma

Lymphangitic pattern

- o Usually hematogenous with secondary lymphatic spread
- o Peribronchovascular and interlobular septal thickening
 - Micronodular contours
 - May be asymmetric, lobar, unilateral, or diffuse
- Ground-glass opacities, ± pleural effusion,
- lymphadenopathy o Breast, gastric, pancreas, and prostate cancers
- Lymph node involvement: Mediastinal/hilar
 - lymphadenopathy
 - Hematogenous ± lymphangitic spread

Sarcoid-like granulomatosis with lymphadenopathy

- CT findings simulate sarcoidosis (lymphadenopathy ± parenchymal findings)
- Often confused with disease progression; lymph node biopsy shows granulomatous inflammation

Nuclear Medicine Findings

- PET/CT
 - Detects foci of high tumor glucose metabolism
 - Sensitivity and specificity ~ 90% for nodules > 10 mm
 - Pitfalls: Subcentimeter nodules, superimposed lung infection/inflammation, non-FDG-avid tumors, misregistration artifact

Imaging Recommendations

- Best imaging tool
 - CT provides optimal structural delineation of spectrum of hematogenous metastases

• PET/CT provides depiction of tumor-concordant glucose metabolism, complements anatomic findings

DIFFERENTIAL DIAGNOSIS

Multiple Pulmonary Nodules

- Granulomas
 - o Usually exhibit benign patterns of calcification
 - Associated with splenic/hepatic calcifications
 - Amorphous lesions ± eccentric calcification suggest metastases over benign etiology
- Infection
 - Miliary pattern: Tuberculosis, fungal and viral pneumonias
 - Septic emboli: Angiocentric, often cavitate
 - Angioinvasive fungal infection: May cavitate
 - Tree-in-bud opacities: Infectious bronchiolitis
- Granulomatosis with polyangiitis
 - Cavitary nodules/consolidations (up to 50%)
 - Chronic sinusitis, intrathoracic airway stenosis

Endobronchial Mass

- Lung cancer
 - More common than endobronchial metastasisSmoking history

Interstitial Lung Disease

- Sarcoidosis
 - Perilymphatic and peribronchovascular micronodules
 - Paratracheal and symmetric bilateral hilar lymphadenopathy
 - Upper lung zone predominant involvement
- Silicosis/coal worker's pneumoconiosis
 - o Well-circumscribed lung nodules (2-5 mm)
 - o Predominantly upper lobes and posterior lung
 - Occupational exposure history

Chronic Consolidation

- Primary lung adenocarcinoma
- Ground-glass/part-solid opacities in multiple lobes; may coalesce to consolidation
- Organizing pneumonia
 Peribronchovascular opacities, subpleural sparing, perilobular distribution, reticulation, septal lines
- Pulmonary alveolar proteinosis
 - Geographic ground-glass opacities with intrinsic interlobular and intralobular lines (crazy-paving pattern)

Pulmonary Embolus

- Acute onset of symptoms
- No beaded vascular contour or soft tissue attenuation

PATHOLOGY

General Features

- Etiology
 - Transport, establishment, and growth of hematogenous metastases; multifactorial cascade
 - Related to complex properties and interactions of cancer cells and host tissue ("pre-metastatic niche")
- Associated abnormalities
 - o Hepatic, lymphatic, skeletal metastases

o Treatment-related thoracic complications

Staging, Grading, & Classification

• Generally regarded as stage IV in TNM (tumor, node, metastasis) systems

Gross Pathologic & Surgical Features

• Well-defined white/tan parenchymal lesions, variable size, may coalesce

Microscopic Features

- Histology typically reflects histologic origin
- Well-demarcated lesions, often expansile/destructive of alveolar architecture
- Endobronchial: Tumor cells in lesion and adjacent airway submucosal lymphatics
- Tumor emboli: Clustered tumor cells mixed with organized thrombus within small arteries/arterioles
- Pleural: Parietal/visceral surfaces studded with tumorlets, fibrinous exudate, reactive mesothelium
- Lymphangitic: Neoplastic cells fill/dilate lymphatic channels

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Vary with pattern of spread: Dyspnea, pleuritic pain, cough, hemoptysis
 - May be asymptomatic

Demographics

- Age
 - Any age; more common in adults
- Epidemiology
 - Lungs are third most common site of metastases
 30-55% of cancer patient autopsies
 - Metastases to lymph nodes and liver are more common
 - Most common malignancies metastatic to lung (World Health Organization): Breast, gastrointestinal, pancreaticobiliary, urogenital, head/neck, skin, sarcomas

Natural History & Prognosis

• Generally poor, but depends on primary tumor type

Treatment

- Depends on histology of primary neoplasm; generally palliative radiation or chemotherapy
- Metastasectomy considered when lung is only involved site
 + limited lesion number/size
 - o 5-year survival varies widely
- Percutaneous ablation promising palliative therapy

DIAGNOSTIC CHECKLIST

Consider

• Metastatic disease in cancer patient with multiple lung nodules/masses, lymphadenopathy, nodular septal thickening, lobar collapse, or pleural effusion

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Hematogenous Metastases





(Left) Graphic shows typical morphologic features of hematogenous pulmonary metastases characterized by multifocal pulmonary nodules of various sizes predominantly affecting the peripheral lower lung zones. (Right) Composite image with axial CECT in lung (top) and soft tissue (bottom) window shows intravascular tumor emboli that manifest as bilateral lower lobe dilated and beaded vessels 🛃. Note corresponding nodular and tubular intravascular filling defects 🔁 of soft tissue attenuation.





(Left) Coronal CECT of a patient with metastatic uterine sarcoma and acute dyspnea shows an obstructing left upper lobe endobronchial metastasis *∋*, associated left upper lobe atelectasis Ξ , and multiple bilateral metastatic lung nodules/masses. (Right) Coronal CECT of a patient with pancreatic cancer and lymphangitic carcinomatosis shows diffuse bilateral interlobular septal thickening \blacksquare , some of which is nodular, and multifocal patchy groundglass opacities. The latter may represent alveolar edema or hemorrhage.





(Left) Axial CECT of a patient with renal cell carcinoma metastatic to the lungs and pleura shows a right lower lobe peripheral lung mass 🕰, a right pleural effusion, and multiple pleural soft tissue nodules 🛃. (Right) Axial CECT (bone window) of a 22-yearold man with Ewing sarcoma shows calcified $pulmonary \square$, pleural 🖾, and mediastinal lymph node 🔁 metastases. Metastases that calcify include those from sarcoma (all subtypes), mucinous adenocarcinomas, and occasionally treated metastases.

KEY FACTS

TERMINOLOGY

- Lymphangitic carcinomatosis (LC)
- Infiltration of lymphatic channels secondary to tumor emboli or direct spread from affected lymph nodes
- Majority of LC cases secondary to adenocarcinoma
 LC may be unilateral (50%), bilateral, focal, diffuse,
- LC may be unilateral (50%), bilateral, rocal, dirruse, symmetric, or asymmetric
 Unilateral LC is most frequent in lung capsor
 - Unilateral LC is most frequent in lung cancer

IMAGING

- Radiography
 - Normal chest radiograph (~ 50%)
 - Involvement of peripheral interstitium (subpleural and interlobular septal thickening)
 - Involvement of axial interstitium (peribronchovascular thickening)
- HRCT
 - Nodular or smooth thickening of interlobular, peribronchovascular, and centrilobular interstitium

- o Preserved secondary pulmonary lobule architecture
- Ancillary findings
 - Metastatic pulmonary nodules, ground-glass opacities (pulmonary edema or superimposed infection), lymphadenopathy, pleural effusion

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary edema
- Sarcoidosis
- Idiopathic pulmonary fibrosis
- Silicosis
- Alveolar proteinosis

CLINICAL ISSUES

- Dyspnea and dry cough (most common symptoms)
- LC is marker of disseminated disease and poor prognosis

DIAGNOSTIC CHECKLIST

• Consider LC in patients with nodular interlobular septal thickening, pulmonary nodules, and lymphadenopathy

(Left) Graphic illustrates the classic perilymphatic distribution of lymphangitic carcinomatosis involving lymphatic channels in both the peripheral 🔁 and axial 🔁 interstitium. Pleural effusion rightarrow is present in 50% of cases.(Right) Low-power photomicrograph (H&E stain) of a specimen from a patient with lymphangitic carcinomatosis shows small *tumor foci involving lymphatic* channels in the centrilobular \square , interlobular septal \square , and subpleural 🔁 interstitium that correlate with typical HRCT findings.





(Left) PA chest radiograph of a 65-year-old woman with breast cancer shows diffuse interstitial opacities in the right lung and peripheral interlobular septal thickening (Kerley B lines) 🔁. (Right) Coronal CECT of the same patient shows thickening of the right lung peripheral interstitium with interlobular septal thickening and polygonal arcades 🖂 consistent with lymphangitic carcinomatosis. Note scattered ground-glass opacities 🔁 that may represent pulmonary edema or superimposed infection.





Abbreviations

• Lymphangitic carcinomatosis (LC)

Synonyms

• Lymphangitic spread

Definitions

- Infiltration of lymphatic channels by tumor emboli (common) or direct retrograde spread from affected hilar lymph nodes
- LC results primarily from adenocarcinomas (80%)
 - o Lung
 - o Breast
 - Other: Stomach, colon, pancreas, prostate
- Involvement of lymphatic channels in interlobular and subpleural interstitium (i.e., peripheral interstitium) &/or central lymphatic channels in bronchovascular and centrilobular interstitium (i.e., axial interstitium)

IMAGING

General Features

- Best diagnostic clue
 - Nodular or smooth interlobular septal and subpleural thickening
- Location
 - Unilateral (50%), bilateral, focal, diffuse, symmetric or asymmetric
 - Unilateral involvement is most common in lung cancer
- Size
 - Variable degrees of interstitial thickening
- Morphology
 - Smooth or nodular

Radiographic Findings

- Radiography
 - Normal chest radiograph (~ 50%)
 - Involvement of peripheral interstitium
 - Kerley B lines (septal lines)
 - Fissural thickening
 - Involvement of axial interstitium
 - Diffuse interstitial &/or nodular opacities
 - Peribronchial cuffing
 - o Distribution
 - Unilateral: Focal, diffuse
 - Bilateral: Symmetric or asymmetric
 - Ancillary findings
 - Pleural effusion (50%)
 - Mediastinal &/or hilar lymphadenopathy (20-50%)

CT Findings

- HRCT
 - Nodular or smooth thickening of interlobular, peribronchovascular, &/or centrilobular interstitium
 - Polygonal arcades [septal thickening outlining secondary pulmonary lobules (SPL)]
 - Fissural thickening
 - Thick bronchovascular bundles
 - Centrilobular branching and Y-shaped opacities (center of SPL)

- Preserved SPL architecture
- Ancillary findings
 - Metastatic pulmonary nodules
 - Ground-glass opacities secondary to associated pulmonary edema or superimposed infection
 - Mediastinal &/or hilar lymphadenopathy
 - Pleural effusion (50%)
 - Visualization of primary lung or breast cancer
 - Extrathoracic metastatic disease

Nuclear Medicine Findings

- PET/CT
 - ↑ FDG uptake adjacent to tumor (above background); sensitivity 94% and specificity 84%
 - ↑ FDG uptake in areas involved by LC
 - Patterns
 - Segmental
 - 🗆 Lobar
 - Diffuse
- V/Q scan
 - Often normal
 - Perfusion defects have been described as secondary to LC or tumor microemboli

Imaging Recommendations

- Best imaging tool
 - HRCT

DIFFERENTIAL DIAGNOSIS

Pulmonary Edema

- Acute onset
- Cardiomegaly
- Smooth basilar predominant interlobular sepal thickening (Kerley B lines)
- Peribronchial (peribronchovascular) cuffing
- Airspace opacities with gravitational and central distribution
- Bilateral pleural effusions

Sarcoidosis

- Multisystem granulomatous disease with eye and skin lesions (erythema nodosum, plaques, scars)
- Lung involvement
 - o Bilateral involvement is typical
 - Small perilymphatic micronodules
 Centrilobular micronodules
 - Fissural nodules (highly specific)
 - Large nodules, masses, or areas of consolidation
 - Upper-mid lung zones
 - Architectural distortion (late stage)
 - Lymphadenopathy
 - Bilateral hilar (90%) and right paratracheal (60%)
 - Left paratracheal and aortopulmonary window (common)
 - Partially calcified lymph nodes (3-20%)
 May exhibit eggshell calcification

Idiopathic Pulmonary Fibrosis

- Slow progression
- Reticular opacities
- Honeycombing and architectural distortion

- Subpleural, apicobasal gradient
- Traction bronchiectasis/bronchiolectasis
- Nodular septal thickening and pleural effusion (uncommon)

Silicosis

- Occupational lung disease
- Perilymphatic nodules
 - Diffuse distribution with upper lobe and posterior predominance
- Multiple nodules/masses
 - Conglomerate masses: Progressive massive fibrosis
- Abnormal lymph nodes
 - Enlarged or normal-sized ± eggshell calcification

Alveolar Proteinosis

- Idiopathic in 90% of cases
- May be associated with silica exposure, infection, and malignancy
- Crazy-paving pattern
 - Patchy distribution
 - Ground-glass opacities
 - Smooth septal thickening
- Consolidation

PATHOLOGY

General Features

- Etiology
 - Frequent form of tumor spread found in 33-50% of patients with solid malignancy at autopsy
 - Common primary malignancies
 - Lung
 - Breast
 - Stomach
 - Pancreas
 - Prostate
 - Majority of cases result from hematogeneous dissemination to small pulmonary arterioles with subsequent interstitial and lymphatic invasion
 Lymphadenopathy often absent
 - Less frequently from extrathoracic tumors metastatic to mediastinal and hilar lymph nodes with retrograde spread along lymphatic channels into lungs
 - Lymphadenopathy usually present
 - Primary lung cancer may directly invade pulmonary lymphatics
 - o Typical histology: Adenocarcinoma
- Associated abnormalities
 - Non-small cell lung cancer associated with specific mutations i.e., anaplastic lymphoma kinase (*ALK*)

Staging, Grading, & Classification

- Variable thickening of interlobular and peribronchovascular interstitium
 - Septal thickening secondary to
 - Desmoplastic reaction
 - Edema
 - Tumor cells within interstitium and lymphatic spaces

Gross Pathologic & Surgical Features

• Delineation of central and peripheral interstitium by tumor infiltration

- Polygonal arcades: SPL outlined by thick interlobular septa
- Tumoral thickening of bronchovascular and centrilobular interstitium
- Lung biopsy (transbronchial or open) is preferred diagnostic tool

Diagnosis

- Characteristic imaging findings in patient with malignancy
- In absence of known primary malignancy or if there is need for confirmation
 - Biopsy (transbronchial or open)
 - Additional diagnostic procedures
 - Sputum cytology
 - Pleural fluid cytology

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea and dry cough (59% and 33%, respectively)
 - o Weight loss
 - o Fatigue
 - o Hemoptysis
 - Symptoms often occur before imaging abnormalities

Demographics

- Mean age of 49.2 years; incidence ↑ with age
- Same as age of initial manifestation of primary tumor

Natural History & Prognosis

- LC is marker of disseminated disease and worse prognosis
 Affected patients have poor survivals
- Survival at 6 months ~ 15%
- LC may be first manifestation of occult malignancy

Treatment

- Systemic chemotherapy to treat primary malignancy
 - If lung cancer with ALK(+), targeted therapy with specific tyrosine kinase inhibitors may improve outcomes
- General support measures

DIAGNOSTIC CHECKLIST

Consider

• LC in patients with known malignancy, interstitial opacities, smooth or nodular septal thickening, pulmonary nodules, and lymphadenopathy

Image Interpretation Pearls

- Nodular interlobular septal thickening should always be concerning for LC
 - Must be differentiated from sarcoidosis

Reporting Tips

• Clinical history of intra- or extrathoracic adenocarcinoma

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- Jreige M et al: Pulmonary lymphangitic carcinomatosis: diagnostic performance of high-resolution CT and 18F-FDG PET/CT in correlation with clinical pathologic outcome. J Nucl Med. 61(1):26-32, 2020
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Lymphangitic Carcinomatosis





(Left) CECT of a 53-year-old woman with biopsy-proven poorly differentiated primary non-small cell lung carcinoma with ALK(+) mutation shows a left upper lobe mass 🔁 and adjacent thick interlobular septa. (Right) Axial CECT of a the same patient shows diffuse interlobular septal thickening \supseteq that outlines secondary pulmonary lobules and produces so-called polygonal arcades. Patients with ALK mutation may have higher propensity to develop lymphangitic carcinomatosis as compared to patients with other mutations.





(Left) Axial NECT of a 75-yearold man with primary lung adenocarcinoma shows a right upper lobe lobulated mass $\overline{\Xi}$ with pleural retraction. (Right) Axial NECT of the same patient shows thickening of , the peribronchovascular (axial) interstitium → and thick interlobular septa (peripheral interstitium) 🖂, consistent with lymphanaitic carcinomatosis with bilateral and asymmetric distribution. In patients with extrapulmonary malignancy, lymphangitic carcinomatosis tends to be diffuse and bilateral.





(Left) Axial NECT of a 72-yearold woman with primary lung cancer shows a lobulated right upper lobe mass 🔁 that encases central airways with adjacent thick interlobular septa \supseteq , consistent with lymphangitic carcinomatosis. (Right) Axial fused FDG PET/CT of the same patient shows the FDG-avid right upper lobe mass ₽ and FDG uptake \blacksquare (higher than that of background) adjacent to the tumor. Increased peritumoral FDG uptake is reported to have high sensitivity and specificity for lymphangitic carcinomatosis.

Tumor Emboli

KEY FACTS

TERMINOLOGY

- Pulmonary vascular occlusion by tumor cells
- Pulmonary tumor thrombotic microangiopathy (PTTM)

IMAGING

• Radiography

- Focal/diffuse linear/nodular opacities; miliary nodules
- Subpleural lower lobe opacities; lung infarcts
- Cardiomegaly, pulmonary hypertension

• CT

- Nodular filling defects in dilated pulmonary arteries; may enhance with contrast
- Nodule/mass in inferior vena cava/right heart chambers
- Right heart enlargement, pulmonary hypertension
- Tree-in-bud opacities: Tumor-filled centrilobular arteries
- **MR**: Demonstration of endoluminal filling defect, assessment of heart chambers and pulmonary arteries
- Nuclear medicine: Multiple small peripheral subsegmental perfusion defects on V/Q scan

TOP DIFFERENTIAL DIAGNOSES

- Bland venous pulmonary thromboembolism
- Pulmonary artery sarcoma
- Vasculitis (Behçet syndrome)
- Metastases with extravascular involvement

PATHOLOGY

- Most common in mucin-producing malignancies
- Involvement ranges from large central to small peripheral arteries

CLINICAL ISSUES

- Progressive dyspnea, cough, hemoptysis
- Treatment: Anticoagulation, chemotherapy

DIAGNOSTIC CHECKLIST

• Consider tumor emboli in patients with dyspnea, distended beaded pulmonary arteries, and malignancies involving vena cava &/or right heart chambers

(Left) Graphic shows the morphologic features of tumor emboli, which may affect pulmonary arteries of various sizes and may manifest with filling defects in central arteries, centrilobular nodules \square , tree-in-bud opacities, and beaded pulmonary arteries 🔁. (Right) Axial NECT MIP reformatted image of a patient with pancreatic adenocarcinoma and tumor embolism shows profuse clustered subpleural pulmonary micronodules. Diagnosis required open lung biopsy to differentiate this entity from infection.





(Left) Axial CECT of a patient with pelvic chondrosarcoma and pulmonary tumor embolism shows a large filling defect within the distal right pulmonary artery 🔁. (Right) Axial CECT of the same patient shows right upper lobe tubular opacities 🔁 and discrete clustered nodules \square , that correspond to dilated pulmonary arteries filled and expanded by tumor (note adjacent normal sized bronchus 乏), which propagates directly from the central tumor embolus.





Definitions

- Embolic occlusion of pulmonary arteries by tumor cells
 - Macroscopic fragments may occlude large caliber pulmonary arteries
 - Microscopic tumor cell emboli may induce local coagulation and fibrocellular intimal proliferation: Pulmonary tumor thrombotic microangiopathy (PTTM)

IMAGING

General Features

- Best diagnostic clue
 - Dilatation and beading of peripheral pulmonary arteries in patient with malignancy
- Location
- Peripheral more common than central
- Size
 - Variable size; may increase with time
- Morphology
 - Dilated beaded pulmonary arteries
 - o Tree-in-bud opacities (dilated centrilobular arteries)

Radiographic Findings

- Chest radiograph often normal
- Focal/diffuse linear/nodular opacities; miliary nodules
- Subpleural lower lobe opacities; lung infarcts
- Cardiomegaly
- Pulmonary hypertension: Enlarged pulmonary trunk/central pulmonary arteries, peripheral vascular pruning
- May mimic lymphangitic carcinomatosis

CT Findings

- NECT
 - Dilated &/or beaded pulmonary arteries; 1 over time
 Subsegmental > segmental > lobar/central
- CECT
 - Nodular filling defects in dilated pulmonary arteries; may enhance with contrast
 - Nodule/mass in inferior vena cava/right heart chambers
 - Vascular extension of abdominal malignancy (e.g., liver and kidney cancers)
 - Right heart enlargement, pulmonary hypertension
- HRCT
 - Focal/multifocal, unilateral/bilateral
 - $\circ~$ Dilated and beaded peripheral pulmonary arteries
 - **Tree-in-bud opacities**: Centrilobular arteries filled with tumor cells
 - Centrilobular nodules: Arteriolar involvement
 - Miliary nodules: Diffuse hematogenous intravascular dissemination
 - Nodule surrounded by halo of ground-glass opacity; illdefined margins from perilesional hemorrhage
- CTA
 - **Filling defects** in central, lobar, and segmental pulmonary arteries
 - Peripheral wedge-shaped opacities; infarcts
 - Right atrial/ventricular filling defect/mass

- Mosaic perfusion: Small vessel occlusion, ↓ vessel caliber in hyperlucent lung
 - No air-trapping

MR Findings

- T1WIC+
 - Demonstration of endoluminal filling defect
 - o Assessment of heart chambers and pulmonary arteries
 - o Delayed enhancement in endovascular tumor
 - May allow differentiation of tumor emboli from bland thrombus

Angiographic Findings

- Pruning and tortuosity of 3rd- to 5th-order arteries
- Delayed filling of segmental pulmonary arteries
- Subsegmental pulmonary artery filling defects
- Large filling defects
- Variant
 - Lung cancer with systemic arterial tumor emboli
 - Filling defect or occlusion of medium-sized or small arteries

Nuclear Medicine Findings

- Bone scan
 - Sarcoma emboli may exhibit Tc-99m MDP uptake
- PET/CT
 - Greater FDG uptake than bland emboli; linear FDG uptake
- V/Q scan
 - Multiple small peripheral subsegmental perfusion defects
 - Visualization of interlobar fissures
 - Useful for evaluation of patients with normal CT and suspected microvascular disease

Imaging Recommendations

- Best imaging tool
 - CECT: Modality of choice for evaluation of endovascular metastases and tumor emboli
 - CTA: Modality of choice for assessment of pulmonary vessels
 - MR: Subtracted images for identification of tumor enhancement
 - HRCT &/or ventilation perfusion scintigraphy may suggest diagnosis
- Protocol advice
 - Ventilation perfusion scintigraphy
 - Reduce dose of macroaggregated albumin to 100,000-200,000 particles in patients with pulmonary hypertension: Macroaggregated albumin may further occlude small vessels, exacerbate heart failure, and lead to cardiac arrest

DIFFERENTIAL DIAGNOSIS

Bland Venous Thromboembolism

- ↑ frequency in patients with cancer (5%)
- Difficult distinction from tumor emboli
- Typical treatment response without progression

Pulmonary Artery Sarcoma

 Central, expansile, solid intraarterial filling defect ± contrast enhancement

Vasculitis (Behçet Syndrome)

• Pulmonary artery aneurysms with in situ thromboses

Infection

- Tree-in-bud opacities from small airways bronchiolitis
- Mosaic attenuation with air-trapping on expiration
- No pulmonary artery hypertension
- Neoplastic Vascular Invasion
- Dominant lung mass contiguous with vascular filling defect

Lesions With CT Halo Sign

- Invasive aspergillosis
 - Neutropenic febrile patient
 - Fulminant, rapid progression
- Candidiasis
 - Immunocompromised, acutely ill, septic patient
 - Usually on broad spectrum antibiotics with central line(s) in place
- Granulomatosis with polyangiitis (GPA)
 - Renal failure, upper airway disease
 - Multiple cavitary nodules &/or consolidations
- Tuberculosis
 - Upper lobe location, cavitation
- Adenocarcinoma
 - Airway involvement, not intravascular
 - No extrapulmonary source of emboli

Treatment-Related Pulmonary Disease

- Hypersensitivity pneumonitis
 - May be secondary to chemotherapeutic drugs, especially methotrexate
 - Centrilobular fuzzy nodules
 - Response to steroids
- Organizing pneumonia
 - Multifocal consolidations, perilobular/peribronchovascular distribution, reversed halo sign
 - Peripheral wedge-shaped opacities that may resemble infarcts
 - Rarely small centrilobular nodules
 - Response to steroid treatment

PATHOLOGY

General Features

- Etiology
 - Occlusion of pulmonary vessels by tumor cells
 - Most common in mucin-producing tumors
 - Breast, lung, colon, stomach, pancreas, prostate
 - Sarcomas (osteosarcoma, chondrosarcoma, angiosarcoma, soft tissue sarcomas)
 - Choriocarcinoma
 - Thyroid carcinoma
 - Tumors that tend to invade systemic veins
 - Hepatocellular carcinoma may invade hepatic veins
 - Renal cell carcinoma may invade renal vein and inferior vena cava
 - Angiosarcoma may invade systemic veins &/or right heart

Gross Pathologic & Surgical Features

Involvement ranges from large central to small peripheral arteries

Microscopic Features

- Multiple levels of microscopic pulmonary vessels
 Elastic arteries to alveolar septal capillaries
- PTTM
 - Extensive fibrocellular intimal hyperplasia of small pulmonary arteries
 - o Initiated by tumor microemboli
- Progressive and irreversible obstruction of vascular bed
- Peritumoral halo: Hemorrhage from fragile vessel rupture

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Progressive dyspnea, cough
 - Chest and abdominal pain
 - o Hypoxia, hemoptysis
 - Acute right heart failure
 - Progressive cor pulmonale over weeks or months
 - o Cardiovascular collapse
- Other signs/symptoms
 - Risk of tumor embolization increased by treatment of primary tumor (e.g., chemotherapy, radiation, surgical excision) due to therapy-induced fragmentation

Demographics

- Age
 - Children to older adult subjects
- Sex
- 0 M=F
- Epidemiology
 - 2-26% of autopsies

Diagnosis

- Cytology of blood aspirated from wedged pulmonary artery catheter
- Biopsy
- Autopsy

Treatment

• Anticoagulation, chemotherapy

Natural History & Prognosis

- Prognosis: Grave
- Dependent on response to therapy
- PTTM rarely identified antemortem

DIAGNOSTIC CHECKLIST

Consider

 Tumor emboli in patients with malignancies that involve the vena cava or right heart chambers who present with dyspnea and exhibit distended beaded pulmonary vessels

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Tumor Emboli





(Left) Axial CECT of a patient with papillary thyroid carcinoma shows a dilated beaded left upper lobe tubular $structure \implies$ that represents a tumor embolus within a pulmonary artery. (Right) Axial CECT of the same patient shows a low-attenuation pulmonary artery filling defect ➡ that represented a tumor embolus. Tumor emboli are indistinguishable from bland pulmonary thromboemboli, and the diagnosis is rarely made antemortem. Visualization of endoluminal tumor in the vena cava or right heart should raise suspicion.





(Left) Axial CECT of a patient with hepatocellular carcinoma . shows a filling defect 🛃 in a right lower lobe pulmonary artery branch and a small right pleural effusion 🛃. (Right) Axial CECT of the same patient shows the pulmonary artery branch distended by the tumor embolus 🔁. A perilymphatic pattern of metastatic disease suggestive of lymphangitic carcinomatosis is also present, and manifests with multiple tiny centrilobular, fissural, and septal micronodules \supseteq .





(Left) Axial CECT of a patient with renal cell carcinoma shows a left lower lobe tubular structure 🔁 that corresponds to a tumor-filled pulmonary artery. Note the right lower lobe hematogenous pulmonary metastases \implies (Right) Axial HRCT of a patient with right atrial rhabdomyosarcoma shows multiple tiny tumor emboli that manifest with tree-in-bud opacities 🖾 Ground-glass opacity halos 🛃 surround the small lung nodules and represent hemorrhage due to fragile neovascular tissue.

SECTION 6 Interstitial, Diffuse, and Inhalational Lung Disease

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Background

The general term "diffuse lung disease" subjectively encompasses interstitial lung disease, which could be fibrosing, non-fibrosing, &/or inhalational lung disease. Overall, these diseases cause diffuse pulmonary involvement but may exhibit a predominant anatomic distribution of imaging abnormalities. Most of these diseases involve not only the pulmonary interstitium but also other anatomic structures of the thorax, including the bronchi, the bronchioles, the epithelial and vascular cells of the pulmonary alveoli, and the pleura. These diseases typically affect both lungs and exhibit acute, subacute, or chronic manifestations. Moreover, many of these entities demonstrate an overlap of their clinical, imaging, physiologic, and pathologic findings.

Idiopathic Interstitial Pneumonias

Interstitial pneumonias may be idiopathic diseases or may occur secondary to other entities such as connective tissue disease, reactions to drugs, etc. The last American Thoracic Society(ATS)/European Respiratory Society (ERS) 2013 iteration recognized several idiopathic interstitial pneumonias, including: Idiopathic pulmonary fibrosis, Idiopathic nonspecific interstitial pneumonia, respiratory bronchiolitis-interstitial lung disease, desquamative interstitial pneumonia cryptogenic organizing pneumonia, acute interstitial pneumonia, idiopathic lymphoid interstitial pneumonia, and the newly included idiopathic pleuroparenchymal fibroelastosis. The idiopathic interstitial pneumonias are an an ever controversial and evolving topic which will continue to change as better understanding is reached.

In 2018, an official ATS/ERS/Japanese Respiratory Society (JRS)/Asociación Latinoamericana de Tórax (ALAT) clinical practice guideline was proposed for the diagnosis of idiopathic pulmonary fibrosis with the principal goal to standardize the diagnosis of usual interstitial pneumonia (UIP), a diagnosis that carries a poor prognosis and for which typical imaging findings are diagnostic and preclude further diagnostic intervention other than multidisciplinary discussion.

Other Diseases

Occupational and environmental exposures are common causes of diffuse lung disease. Additional causes include granulomatous disorders (e.g., sarcoidosis), inhalational diseases, eosinophilic lung diseases, and various metabolic and miscellaneous disorders.

Imaging Modalities

Although imaging abnormalities are frequently nonspecific, chest radiography remains a robust tool for the detection of diffuse lung disease. Once identified, further characterization is achieved with HRCT. Imaging findings of early disease may be incidentally detected on chest radiography, and may trigger further assessment with HRCT and pulmonary function studies. Typical radiographic findings of diffuse fibrosing interstitial lung disease may be detected on radiography and include subpleural, lower lobe predominant, reticular opacities &/or honeycombing. Nevertheless, HRCT remains the cornerstone of the diagnosis of diffuse fibrosing and nonfibrosing interstitial lung diseases.

With the development and broad availability of multidetector helical CT, which provides high quality thin-section images of the lung, the definition of HRCT has evolved accordingly. However, HRCT is still defined as the acquisition of thinsection (1.25 mm or less) imaging using a bone algorithm and supine and prone inspiratory and supine expiratory image acquisitions.

Anatomic Distribution of Imaging Patterns

Abnormalities detected on HRCT should be analyzed for their relationship to the secondary pulmonary lobule (SPL). Such findings may involve the interlobular septa or the intralobular structures or may be centrilobular in distribution. A perilymphatic distribution of abnormalities manifests with findings along the axial peribronchovascular interstitium &/or the peripheral, subpleural interstitium (including the interlobar fissures), with or without involvement of the interlobular septa of the SPL.

HRCT may reveal specific imaging patterns of various diseases (e.g., nodules, reticulation, ground-glass opacity, consolidation, traction bronchiectasis) and allows delineation of their anatomic distribution. Determination of the pattern of disease and its distribution enables radiologists to provide a concise list of differential diagnostic possibilities. For example, reticular opacities in a subpleural and bibasilar distribution suggest the UIP pattern; ancillary findings may include traction bronchiectasis and reduced lung volume. Correlation with clinical findings may lead to an imaging differential diagnosis of idiopathic pulmonary fibrosis, connective tissue disease, or occupational lung disease. In another instance, detection of small nodules in a perilymphatic distribution with predominant involvement of the mid and upper lung zones is very suggestive of sarcoidosis, with or without the presence of hilar and mediastinal lymphadenopathy. Smooth thickening along the same perilymphatic pathways is characteristic of pulmonary edema (typically bilateral and symmetric), although the same finding may be a manifestation of lymphangitic carcinomatosis, a process that may be focal or multifocal, unilateral, or bilateral. Associated clinical findings and temporal considerations are useful factors in narrowing the list of differential diagnostic possibilities.

Physiologic Considerations

Diseases related to inhalation of various agents often manifest with upper &/or mid lung zone predominant findings. Because of ventilation and perfusion gradients in the human lung and enhanced clearance in the lower lung zones (more effective coughing), there is less effective clearance of inhaled agents from the upper lung zones. Sarcoidosis (postulated inhaled unknown etiologic agent), silicosis (inhaled silicates), and pulmonary Langerhans cell histiocytosis (inhaled cigarette smoke) may produce very similar imaging findings (reticulonodular opacities that predominantly involve the mid and upper lung zones). An exception is the retention of asbestos fibers in the lower lung zones, as asbestos fibers penetrate deeply into the lung tissues and are often resistant to normal clearing mechanisms.

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Approach to Interstitial, Diffuse, and Inhalational Lung Disease

Idiopathic Pulmonary Fibrosis



Idiopathic Pulmonary Fibrosis



(Left) PA chest radiograph of a patient with idiopathic pulmonary fibrosis shows reduced lung volume and peripheral and predominantly bibasilar reticular opacities, representing usual interstitial pneumonia. (Right) Composite image with axial HRCT of a patient with moderately advanced idiopathic pulmonary fibrosis and low lung volume shows coarse peripheral reticular opacities, architectural distortion, and honeycombing 乏. Note irregular interfaces along the mediastinal pleural surfaces \nearrow .

Nonspecific Interstitial Pneumonia



Sarcoidosis

(Left) Axial CECT of a patient with nonspecific interstitial pneumonia demonstrates patchy ground-glass opacities with underlying reticulation and focal areas of traction bronchiolectasis
. (Right) HRCT of a patient with sarcoidosis shows small nodules in a perilymphatic distribution, disposed along bronchovascular structures in the subpleural lung, and along interlobular septa ₽. Small nodules were also demonstrated along interlobar fissures (not shown).

Lymphangitic Carcinomatosis



Lymphoid Interstitial Pneumonia



(Left) Axial HRCT of a patient with lymphangitic carcinomatosis shows smooth thickening of interlobular septa and the peribronchovascular \blacksquare and subpleural interstitium along the major fissure 🛃 Although the distribution of disease is also perilymphatic, lymphangitic carcinomatosis should not be confused with sarcoidosis or silicosis. (Right) Axial CECT of a patient with lymphoid interstitial pneumonia shows thin-walled cysts with surrounding groundglass opacity 🔁.

KEY FACTS

TERMINOLOGY

• Acute respiratory distress syndrome (ARDS)

IMAGING

- Imaging and pathologic findings discussed in terms of hours, days, weeks, months
- Radiography/CT
 - Hours: May be normal in first 12-24 hours
 - Days: Bilateral airspace opacities and consolidation within 24 hours
 - Weeks: Decreased consolidation, persistent reticular opacities
 - Months: Subpleural reticular opacities and honeycombing
- Pulmonary injury: Consolidation and ground-glass opacity equally common; asymmetric
- Extrapulmonary injury: Ground-glass opacity more common than consolidation; symmetric

TOP DIFFERENTIAL DIAGNOSES

- Acute interstitial pneumonia
- Cardiogenic pulmonary edema
- Noncardiogenic pulmonary edema
- Pulmonary hemorrhage

PATHOLOGY

• Diffuse alveolar damage (DAD)

CLINICAL ISSUES

- ARDS may be complicated by pneumonia
- Survivors may develop fibrosis and honeycombing
- Treatment: Mechanical ventilation with high peak endexpiratory pressure

DIAGNOSTIC CHECKLIST

• Consider ARDS in intubated patients who develop bilateral airspace opacities and consolidation

(Left) AP chest radiograph of a patient with acute respiratory distress syndrome following esophageal surgery shows diffuse bilateral heterogeneous pulmonary opacities and small bilateral pleural effusions 🖂 (Right) Axial NECT of the same patient shows diffuse crazypaving opacities bilaterally and small bilateral pleural effusions. This particular phenotype of acute respiratory distress syndrome has lower lung compliance and higher mortality.





(Left) Axial NECT of a patient with sepsis of extrapulmonary origin shows patchy heterogeneous ground-glass opacities with areas of spared lung parenchyma. This *imaging phenotype of acute* respiratory distress syndrome has lower mortality. (Right) Axial CECT of a patient with a remote history of acute respiratory distress syndrome shows subpleural anterior honeycombing. Fibrosis can be seen in survivors with a predilection for the nondependent lung areas.





Abbreviations

• Acute respiratory distress syndrome (ARDS)

Synonyms

• Adult respiratory distress syndrome

Definitions

• Syndrome of acute respiratory failure caused by noncardiogenic pulmonary edema.

• Berlin criteria

- Onset within 1 week of clinical insult or new/worsening respiratory symptoms
- Chest radiography: Bilateral opacities (not explained by pleural effusion, lobar/lung collapse, or nodules)
- PF ratio < 300 mm Hg with minimum of 5-cm H20 positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP)
 - PaO₂:FiO₂ = PF ratio: Ratio of arterial oxygen tension to fraction of inspired oxygen
- Respiratory failure not fully explained by cardiac failure/fluid overload

IMAGING

Radiographic Findings

- Radiography
 - 3 phenotypes
 - Diffuse bilateral opacities evenly distributed
 - □ Lower lung compliance, higher mortality
 - Significant alveolar recruitment without significant overdistension with PEEP
 - Lobar with lower lobe predominance
 - Patchy bilateral unevenly distributed
 - Survivors with resolution of opacities or reticular opacities

CT Findings

- HRCT
 - Hours: May be normal 12-24 hours after injury
 - o Days
 - General
 - Bilateral airspace opacities and consolidations within 24 hours
 - Dependent atelectasis
 - Interlobular septal thickening and pleural effusions less common than in cardiogenic pulmonary edema
 - Pulmonary injury
 - Consolidations and ground-glass opacities equally common
 - Asymmetric lung involvement
 - Extrapulmonary injury
 - Ground-glass opacities more common than consolidations
 - Symmetric lung involvement
 - Weeks: Consolidation decreases
 - Patchy airspace or reticular opacities persist
 - Ground-glass opacities
 - Months: Subpleural reticular opacities and honeycombing
 - May exhibit anterior predominance

 Atelectasis/consolidation may "protect" posterior lungs from effects of mechanical ventilation

DIFFERENTIAL DIAGNOSIS

Cardiogenic Pulmonary Edema

- Central > peripheral opacities (bat-wing distribution)
- Kerley B lines, peribronchial cuffing, pleural effusions
- Cardiomegaly

Pulmonary Hemorrhage

- Diffuse bilateral airspace opacities
- Normal heart size

Pneumocystis jirovecii Pneumonia

• Diffuse bilateral opacities; may be indistinguishable from ARDS on imaging

PATHOLOGY

General Features

- Etiology
 - Pulmonary injury: Pneumonia, aspiration, inhalational injury, trauma
 - o Extrapulmonary injury: Sepsis and nonthoracic trauma

Microscopic Features

- Characterized by diffuse alveolar damage (DAD)
 - Early exudative stage (hours after precipitating event): Endothelial cell edema, capillary congestion, and minimal interstitial hemorrhage/edema
 - Late exudative stage (1 day to 1 week): Necrosis of type I pneumocytes, pulmonary edema, hemorrhage
 - Proliferative or reparative stage (1 week to 1 month):
 Proliferation of type II pneumocytes, fibroblast proliferation, collagen deposition
 - Fibrotic stage (months): Interstitial fibrosis

CLINICAL ISSUES

Presentation

Most common signs/symptoms
 Shortness of breath, tachypnea, hypoxia

Natural History & Prognosis

- ARDS may be complicated by pneumonia
 Dense consolidation in nondependent location
- Survivors may develop fibrosis and honeycombing

Treatment

• Mechanical ventilation with high peak end-expiratory pressure

DIAGNOSTIC CHECKLIST

Consider

• ARDS in intubated patients who develop bilateral airspace opacities and consolidations

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TERMINOLOGY

 Acute interstitial pneumonia (AIP): Idiopathic interstitial pneumonia characterized by rapidly progressive respiratory failure of unknown etiology with histologic features of diffuse alveolar damage (DAD)

IMAGING

• Radiography

- o Diffuse bilateral symmetric heterogenous opacities
- Evidence of mechanical ventilation

• CT/HRCT

- Early phase (exudative): Bilateral ground-glass opacities &/or consolidations with anterior-posterior gradient
- Late phase (organizing): Coarse reticulations, groundglass and reticular opacities; traction bronchiectasis associated with poor outcome
- Complications: Pneumonia, abscess, pneumothorax, pneumomediastinum, pulmonary interstitial emphysema

TOP DIFFERENTIAL DIAGNOSES

- Acute respiratory distress syndrome
- Multilobar pneumonia
- Acute exacerbation of interstitial lung disease
- Diffuse alveolar hemorrhage
- Hydrostatic pulmonary edema

PATHOLOGY

- AIP is not a pathological diagnosis
- DAD is histologic manifestation of AIP; but DAD is seen in other conditions

CLINICAL ISSUES

- Flu-like prodrome 7 -14 days prior to presentation: Headache, myalgia, sore throat, malaise, dry cough, fever
- Progressive shortness of breath, fever, cough
- Treatment: No effective treatment known; corticosteroids with variable response (usually poor)
- Poor prognosis; mortality rate $\geq 50\%$

(Left) AP chest radiograph of a 62-year-old man with acute interstitial pneumonia (early phase) who presented with progressive dyspnea shows diffuse bilateral heterogeneous and reticular opacities. (Right) Axial CECT of the same patient shows crazypaving and bronchiectasis 🖂 Acute interstitial pneumonia is not a pathologic diagnosis but requires documentation of histologic findings of diffuse alveolar damage, absence of an identifiable etiology, presence of acute symptoms, and pulmonary opacities on radiography.





(Left) Coronal CECT of the same patient shows bilateral symmetric ground-glass and reticular opacities with upper lobe predominance. While opacities tend to affect all lung lobes, the upper lobes are more commonly involved. Symmetric involvement is also classic. (Right) Low-power photomicrograph (H&E stain) of a specimen of diffuse alveolar damage shows hyaline membranes 🖂 manifesting as layers of pink, amorphous, and homogeneous material lining the alveolar lumina. (From DP: Thoracic.)





Acute Interstitial Pneumonia

TERMINOLOGY

Abbreviations

- Acute interstitial pneumonia (AIP)
- Diffuse alveolar damage (DAD)
- Acute respiratory distress syndrome (ARDS)

Synonyms

• Hamman-Rich syndrome

Definitions

- Idiopathic interstitial pneumonia characterized by rapidly progressive respiratory failure of unknown etiology with histologic DAD
- AIP definition
 - Acute respiratory symptoms with severe hypoxia and acute respiratory failure (in most cases)
 - o Bilateral pulmonary opacities on radiography
 - No identifiable etiology (e.g., infection, connective tissue disease, trauma, heart failure, drug toxicity, etc.)
 - Histologic documentation of DAD
- ARDS and AIP are not equivalent: AIP is idiopathic ARDS; not all ARDS patients have AIP
 - ARDS definition
 - Acute onset, within 7 days of defined event (e.g., sepsis, pneumonia, etc.)
 - Partial pressure of arterial O₂: Fraction of inspired O₂ (PaO₂:Fi₂O) ≤ 200 mm Hg
 - Bilateral pulmonary opacities on radiography or CT
 - Abnormalities not fully explained by heart failure or fluid overload based on clinical parameters

IMAGING

General Features

- Best diagnostic clue
 - Radiography: Diffuse heterogeneous opacities involving all lung lobes
 - CT: Extensive symmetric ground-glass opacities associated with traction bronchiectasis

Radiographic Findings

- Nonspecific diffuse bilateral and symmetric heterogenous opacities
- No zonal predilection, all lobes involved
- Evidence of mechanical ventilation
- Pleural effusions/septal lines less common than in cardiogenic edema
- Honeycombing rare (late phases)

CT Findings

- CT more sensitive than radiography
- General
 - Ground-glass opacities and consolidations
 - > 50% of lung; patchy (2/3), diffuse (1/3)
 - Frequent focal lobular sparing (geographic pattern)
 - Distribution
 - Lower lung zone (40%)
 - □ Upper lung zone (15%)
 - Symmetric (common)
 - May be seen in all histologic phases of AIP; acute inflammation or fibrosis

- More extensive ground-glass opacities without traction bronchiectasis associated with better outcome
- o Consolidation
 - Involves < 25% of lung; subpleural distribution in 20%
 - Also seen in all histologic phases of AIP
 - More extensive ground-glass opacities (without traction bronchiectasis) may have better outcome
- AIP may progress to subpleural abnormalities that resemble fibrotic idiopathic interstitial pneumonias
 - Subpleural reticulation &/or honeycombing with apicobasal gradient and traction bronchiectasis
- Less common findings: Interlobular septal thickening, crazy-paving, nodular opacities, thick bronchovascular bundles, lymphadenopathy (5%)
- Early phase (exudative)
 - Bilateral ground-glass opacities &/or consolidations
 - Anterior-posterior gradient
 - Bronchial dilatation within ground-glass opacity areas; may represent traction bronchiectasis or may be reversible
 - Pleural effusions (common)
- Late phase (organizing)
 - Coarse reticular opacities
 - Ground-glass and reticular opacities
 - Diffuse (most common)
 - Nondependent lucencies (honeycombing/bullae) postulated to represent fibrosis in areas less protected from barotrauma than consolidated lung
 - Subpleural lower lobe honeycombing suggests acute exacerbation of occult or underlying interstitial lung disease rather than AIP
 - Traction bronchiectasis
 - Central airways involvement > peripheral
 Segmental and subsegmental airways
 - Traction bronchiectasis usually out of proportion to severity of reticular opacities or honeycombing
 - Associated with poorer outcome
 - May persist in survivors
 - Architectural distortion
- Complications: Pneumonia, abscess, pneumothorax, pneumomediastinum, pulmonary interstitial emphysema
- Sequelae of AIP
 - Hypoattenuation foci, lung cysts, reticulation, nondependent architectural distortion

Imaging Recommendations

- Best imaging tool
 - CT for characterization of diffuse pulmonary disease

DIFFERENTIAL DIAGNOSIS

Acute Respiratory Distress Syndrome

- Known etiology (direct or indirect insult)
- Consolidation > ground-glass opacities
- Honeycombing less common
- More likely asymmetric, more extensive areas of normal lung than in AIP
- Interlobular septal thickening more common

Multilobar Pneumonia

• Infection should be excluded for diagnosis of AIP

Acute Exacerbation of Interstitial Lung Disease

- Rare complication of interstitial lung disease
 - Criteria: Dyspnea exacerbation within 1 month, new diffuse pulmonary opacities, worsening hypoxemia (minimum 10 mm Hg), no infection or heart failure
- Diffuse but patchy ground-glass opacities on background of changes of idiopathic pulmonary fibrosis
- Honeycombing more profuse than superimposed groundglass opacity
- Poor prognosis

Diffuse Alveolar Hemorrhage

- Diffuse ground-glass opacities, often evolve to reticulation
- Features of pulmonary fibrosis generally occur with repeated episodes
- Anemia and hemoptysis common (80%)

Hydrostatic Pulmonary Edema

- Bilateral airspace opacities, interlobular septal thickening
- Cardiomegaly
- Pleural effusions
- History of heart disease

Desquamative Interstitial Pneumonia

- Symptoms not as severe; mechanical ventilation not required
- Heavy smoking history
- Diffuse ground-glass opacities, no architectural distortion

Invasive Mucinous Adenocarcinoma

- Diffuse bilateral ground-glass opacities
- No fibrosis (architectural distortion, traction bronchiectasis)
- Insidious onset, progressive course; mechanical ventilation not required

PATHOLOGY

General Features

- Etiology
 - o Idiopathic
- Temporal uniformity suggests injury related to single event
- AIP is not pathologic diagnosis
- DAD is histologic manifestation of AIP; but is seen in other conditions
 - Infections (22%): *Mycoplasma pneumoniae*, viruses, *Legionella*, *Pneumocystis*
 - Bone marrow transplantation (17%)
 - Acute exacerbation of idiopathic pulmonary fibrosis (16%)
 - Connective tissue disease (16%): Systemic lupus erythematosus, rheumatoid arthritis
 - Drug-induced (10%): Bleomycin, busulfan, carmustine (BCNU), gemcitabine, crack cocaine, methotrexate, nitrofurantoin
 - Toxins (< 5%): Nitrogen dioxide, oxygen toxicity, paraquat, chlorine gas
 - Aspiration

Microscopic Features

- Acute exudative phase (1st week)
 - o Edema
 - Hemorrhagic fluid in air spaces

- o Type 1 pneumocyte necrosis
- Hyaline membranes [not seen in usual interstitial pneumonia (UIP) or cryptogenic organizing pneumonia]
- Proliferative phase (after 2nd week)
 - Type 2 pneumocyte proliferation
 - Fibroblasts exceed collagen
- Fibrotic phase
- Fibrosis within alveoli and interstitium (may be severe)
- Fibroblasts more extensive than collagen (unlike UIP)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Flu-like prodrome 7-14 days prior to presentation: Headache, myalgia, sore throat, malaise, dry cough, fever
 - Progressive shortness of breath, fever, cough
 - o Hypoxemia (mean PaO₂ 45 mm Hg)
 - Often considered in patients with diagnosis of pneumonia who fail to respond to antibiotics
 - Acute onset (over period of 1-3 weeks)
 - 50% of patients present in 1st week of onset
 - 25% have indolent course and present within 30 days of onset
 - Rapid progression to respiratory failure, often require mechanical ventilation
 - 90% meet clinical criteria of ARDS
- Other signs/symptoms
 - Clubbing suggests preexisting interstitial lung disease

Demographics

- Age
 - o Mean age: 50-55 years
- Sex

0 M=F

Natural History & Prognosis

- Poor prognosis (mortality rate usually ≥ 50%; most deaths within 2 months of onset)
- Survivors may have complete recovery of lung functionPersistent stable restrictive physiology also common
- Recurrence may occur but is rare

Treatment

- No effective treatment
- Variable response (usually poor) to steroids
- Supportive care is mainstay of therapy
 - Mean duration of mechanical ventilation: 30 days

DIAGNOSTIC CHECKLIST

Consider

• AIP in patient with rapid onset of respiratory symptoms and respiratory failure without identifiable cause or predisposing illness with symmetric extensive ground-glass opacities on imaging

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- Ichikado K: High-resolution computed tomography findings of acute respiratory distress syndrome, acute interstitial pneumonia, and acute exacerbation of idiopathic pulmonary fibrosis. Semin Ultrasound CT MR. 35(1):39-46, 2014





(Left) Axial CECT of a 50-yearold man with acute interstitial pneumonia (early phase) shows diffuse, bilateral ground-glass opacities on a background of interlobular septal thickening, the socalled crazy-paving pattern. (Right) Axial CECT of the same patient shows extensive , bilateral ground-glass opacities on a background of interlobular septal thickening (crazy-paving pattern) 🔁 Note that the imaging appearance is similar to that of pulmonary edema, infection, and diffuse alveolar hemorrhage.





(Left) Axial CECT of a 57-yearold man with acute interstitial pneumonia (early phase) shows multifocal bilateral ground-glass opacities \square and consolidations 🔁. Note anterior-posterior gradient of involvement with more consolidations in the dependent aspects of the lungs. (Right) Axial CECT of the same patient shows extensive bilateral mid lung and basilar consolidations with intrinsic air bronchograms 🖂. Consolidations are most severe in the dependent lungs (anterior-posterior gradient).





(Left) Axial CECT of the same patient obtained 3 months later (late phase) shows evolution of lung opacities to areas of reticulation \supseteq . Areas of fibrosis tend to primarily involve the nondependent regions of the lung, which are postulated to suffer more barotrauma than the posterior previously consolidated areas. (Right) Axial CECT of the same patient (late phase) shows evolution of pulmonary consolidations into areas of reticulation and irregular opacities 🔁.

TERMINOLOGY

- Idiopathic pulmonary fibrosis (IPF)
- Idiopathic usual interstitial pneumonia (UIP)
- Fibrosing idiopathic interstitial pneumonia with histologic pattern of UIP on surgical biopsy
- ~ 40% of all idiopathic interstitial pneumonias

IMAGING

Radiography

- Basilar reticular opacities
- o Low lung volume
- Pulmonary hypertension
- HRCT/CT
 - Basilar predominant reticulation
 - Traction bronchiectasis or bronchiolectasis
 - o Honeycombing
 - Ground-glass opacities (less extensive than reticulation)
 - Persistent/growing nodule/mass suggests lung cancer

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic nonspecific interstitial pneumonia
- Asbestosis
- Fibrotic hypersensitivity pneumonitis
- Rheumatoid arthritis
- Progressive systemic sclerosis
- Drug-induced lung disease

PATHOLOGY

• Usual interstitial pneumonia

CLINICAL ISSUES

- Symptoms: Dyspnea, nonproductive cough
- Age: 55-70 years; M:F ~ 2:1
- Inexorable progression with poor prognosis

DIAGNOSTIC CHECKLIST

Idiopathic subpleural and basilar reticulation with honeycombing supports HRCT diagnosis of IPF

(Left) PA chest radiograph of a patient with idiopathic pulmonary fibrosis shows diffuse, bilateral peripheral subpleural reticular opacities and basilar predominant distribution of the abnormalities. (Right) Axial CECT of the same patient shows extensive basilar predominant honeycombing with traction bronchiectasis 🔁 and bronchiolectasis that would be reported as usual interstitial pneumonia (UIP) pattern. Honeycombing is the most specific CT feature of idiopathic pulmonary fibrosis.

(Left) Low-power

the prototypic temporal

with areas of relatively

adjacent to extensively remodeled lung 🔁. (Right)

⊠, consistent with a UIP pattern. The CT pattern is specific, and histologic









Abbreviations

• Idiopathic pulmonary fibrosis (IPF)

Synonyms

- Idiopathic usual interstitial pneumonia (UIP)
- Cryptogenic fibrosing alveolitis

Definitions

- Fibrosing idiopathic interstitial pneumonia associated with histologic UIP pattern on surgical biopsy
- ~ 40% of all idiopathic interstitial pneumonias

IMAGING

General Features

- Best diagnostic clue
 - Reticulation and honeycombing with subpleural distribution and apicobasal gradient; traction bronchiectasis and architectural distortion
 - Absence of atypical features: Micronodules, sparing of lung bases, extensive air-trapping, consolidation, &/or ground-glass opacity
- Location
- Subpleural; mid and lower lung zones
- Morphology
 - Reticulation, traction bronchiectasis/bronchiolectasis, honeycombing

Radiographic Findings

- Radiography
 - Reticular or reticulonodular opacities
 - Subpleural/peripheral; mid and lower lung zones
 Mild subpleural opacities may affect upper zones
 - o Lower lung zone volume loss
 - Spurious preservation of lung volume with coexistent emphysema
 - Pulmonary hypertension
 - Enlarged pulmonary trunk and right heart chambers

CT Findings

- HRCT
 - More sensitive and specific than radiography
 - Reticular opacities
 - Subpleural predominance; apicobasal gradient (i.e., lower lobe predominance)
 - Less prominent in upper lungs
 - Traction bronchiectasis/bronchiolectasis
 - Predominance in subpleural and basilar lungs
 - Usually associated with reticular opacities
 - Honeycombing
 - Most specific manifestation of IPF
 - Subpleural cysts, usually in clusters or rows
 - Cysts may vary in size depending on phase of respiratory cycle
 - Average diameter: 3-10 mm; may be as large as 25 mm
 - Overall extent and severity of honeycombing may change over time
 - Ground-glass opacity
 - Fine fibrosis below spatial resolution of HRCT

- Often associated with reticular opacities, traction bronchiectasis/bronchiolectasis
- Less extensive than reticular opacities
 - Extensive ground-glass opacity suggests hypersensitivity pneumonitis or nonspecific interstitial pneumonia (NSIP)
 - May reflect acute exacerbation of IPF in patients with acute respiratory illness
- o Volume loss (advanced cases)
- o Coexistent emphysema (30%)
 - Combined pulmonary fibrosis and emphysema: Distinct clinical phenotype
 - Usually related to cigarette smoking
 - □ Associated with very poor prognosis
- Lung nodule/mass
 - If persistent or growing should raise suspicion for primary lung cancer
- o Mediastinal lymph node enlargement (70%)
 - Usually occult on radiography
 - No correlation with extent of disease
- Acute exacerbation of IPF: New ground-glass opacities &/or consolidations ± bronchial dilatation on background of preexisting reticulation &/or honeycombing and traction bronchiectasis

Imaging Recommendations

- Best imaging tool
 - HRCT for disease detection and characterization

DIFFERENTIAL DIAGNOSIS

Idiopathic Nonspecific Interstitial Pneumonia

- May be indistinguishable from UIP
- Honeycombing absent or not predominant feature

Asbestosis

- May be indistinguishable from UIP in cases with extensive honeycombing
- Subpleural curvilinear opacities: Common early findings
- Discontinuous partially calcified pleural plaques often present

Fibrotic Hypersensitivity Pneumonitis

- Common cause of honeycombing
 - Indistinguishable from IPF if subpleural and lower lobe predominant
 - Peribronchovascular honeycombing somewhat specific (may also be seen in sarcoidosis)
- Expiratory air-trapping (common)
- Poorly-defined centrilobular nodules common in hypersensitivity pneumonitis; reflect cellular bronchiolitis

Rheumatoid Arthritis

- UIP pattern more frequent than NSIP pattern
 - Indistinguishable from idiopathic UIP and NSIP
 May progress more slowly than IPF
- Ancillary findings: Joint erosions, serum markers (e.g., rheumatoid factor), pleural effusion, rheumatoid nodules

Progressive Systemic Sclerosis

NSIP pattern much more common than UIP pattern
 Predominant ground-glass opacities

- Interstitial, Diffuse, and Inhalational Lung Disease
- Honeycombing uncommon except in advanced, longstanding disease
- Patulous esophagus common
- Cutaneous findings usually present: Sclerodactyly, calcinosis cutis, drawn facies

Drug-Induced Lung Disease

- May be indistinguishable from IPF in cases with extensive honeycombing
- Typical drugs: Nitrofurantoin or chemotherapy drugs

PATHOLOGY

General Features

- Etiology
 - o Unknown etiology
 - Suspected but unproven association with cigarette smoking
- Genetics
 - Familial cases of IPF reported (probable autosomal dominant inheritance)
 - Associated with protein surfactant C deficiency
 - Affected family members may exhibit different patterns of interstitial pneumonia
 - No genetic markers yet identified
 - No human leukocyte antigen (HLA) associations
 - Putative link with a-1 antitrypsin inhibition alleles on chromosome 14

Staging, Grading, & Classification

- Clinical and HRCT features sufficient to establish diagnosis of IPF in 50-70% of patients with > 90% specificity
 HPCT criteria (ATS 2018)
 - HRCT criteria (ATS 2018)
 - UIP: Subpleural and basilar predominant; distribution often heterogeneous; honeycombing ± peripheral traction bronchiectasis or bronchiolectasis
 - Probable UIP: Subpleural and basilar predominant; distribution often heterogeneous; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis; may have mild ground-glass opacity
 - Indeterminate for UIP: Subpleural and basilar predominant; subtle reticulation; may have mild ground-glass opacity or distortion ("early UIP pattern"); CT features &/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")
 - Alternative Diagnosis
 - Findings suggestive of another diagnosis, including: Marked mosaic attenuation, predominant ground-glass opacity, profuse micronodules, centrilobular nodules, nodules, consolidation
 - □ Predominant distribution: Peribronchovascular, perilymphatic, upper or mid-lung
 - Other: Pleural plaques (consider asbestosis), dilated esophagus (consider connective tissue disease), distal clavicular erosions (consider rheumatoid arthritis), extensive lymph node enlargement (consider other etiologies), pleural effusions, pleural thickening (consider connective tissue disease/drugs)

Gross Pathologic & Surgical Features

• Peripheral subpleural honeycombing

Microscopic Features

- Fibrosis: Subpleural predominant, characteristic fibroblastic foci, dense acellular collagen
- Mild to moderate interstitial inflammation: Histiocytes, plasma cells, lymphocytes, type II pneumocyte hyperplasia
- Honeycombing: Cysts lined by bronchiolar epithelium
- Spatial and temporal heterogeneity: Prototypic of UIP
 Coexistence of normal lung and fibrosis; variable architectural remodeling and end-stage honeycombing

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Insidious onset of dyspnea on exertion
 - Nonproductive cough
- Other signs/symptoms
 - Digital clubbing
 - Fine inspiratory ("Velcro") crackles
 - Signs of right heart failure
 - Pulmonary function tests: Restrictive physiology with decreased diffusing capacity for carbon monoxide (DLCO)

Demographics

- Age
 - o 55-70 years of age
- Sex
 - o M:F ~ 2:1
- Epidemiology
 - o Incidence: 7-10 cases/100,000 per year
 - Prevalence: 3-6/100,000

Natural History & Prognosis

- Inexorable progression, poor prognosis
- Median survival following diagnosis: 3.5 years
- Rapid decline and death after period of relatively slower progression (rare)
 - Acute exacerbation of IPF
 - o Diffuse alveolar damage on histologic examination
- Lung cancer (10%)
 - Most patients current or former smokers
 - Many patients not surgical candidates because of underlying IPF

Treatment

- No treatment with proven survival improvement
- Mild to moderate IPF: Pirfenidone or Nintedanib
- Azathioprine, prednisone, acetylcysteine: No longer recommended
- Lung transplantation

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- Raghu G et al: Diagnosis of idiopathic pulmonary fibrosis. an official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med. 198(5):e44-68, 2018





(Left) Axial HRCT of a patient with UIP shows subpleural honeycombing associated with large pulmonary cysts ⊇. While unusual, honeycomb cysts may be as large as 2.5 cm. (Right) Axial CECT of the same patient demonstrates enlarged paratracheal and aortopulmonary window lymph nodes ⊇. Nonneoplastic mediastinal lymphadenopathy is seen in

lymphadenopathy is seen in 70% of affected patients, is often reactive, and does not correlate with the severity of interstitial lung disease.





(Left) Coronal CECT of a patient with idiopathic pulmonary fibrosis shows extensive bilateral groundglass opacity with a crazypaving pattern and traction bronchiectasis 🔁. Acute exacerbation of idiopathic pulmonary fibrosis should be considered in acutely ill patients with extensive ground-glass opacity. (Right) Low-power photomicrograph (H&E stain) of a specimen from the same patient shows interstitial inflammation, acute and organizing hyaline membranes \square , and patchy acute inflammation \square .





(Left) PA chest radiograph of a patient with idiopathic pulmonary fibrosis shows peripheral and basilar reticulation and a subtle left perihilar nodule 🔁, which can easily be overlooked given the extent of underlying interstitial lung disease. (Right) Axial NECT of the same patient shows a spiculated left upper lobe nodule \supseteq abutting the oblique fissure. As incidence of lung cancer is increased in patients with idiopathic interstitial fibrosis, any discrete nodule should be regarded as highly suspicious for malignancy.

TERMINOLOGY

- Nonspecific interstitial pneumonia (NSIP)
- Type of idiopathic interstitial pneumonia
- IMAGING
- Radiography
 - Lower lung zone predominant, bilateral, reticular, heterogeneous opacities
- CT/HRCT
 - Bilateral ground-glass and reticular opacities with traction bronchiectasis/bronchiolectasis
 - Absent or sparse honeycombing
 - Subpleural sparing ± peribronchovascular fibrosis
 - Apicobasal gradient (lower lobe predominant)

TOP DIFFERENTIAL DIAGNOSES

- Usual interstitial pneumonia (UIP)
- Drug-induced interstitial lung disease

- Connective tissue disease-associated interstitial lung disease (CTD-ILD)
- Fibrotic hypersensitivity pneumonitis
- Cryptogenic organizing pneumonia (COP)

PATHOLOGY

- Idiopathic
- Growing body of evidence suggests idiopathic NSIP is occult manifestation of autoimmune disorder
- Variable amounts of interstitial inflammation and fibrosis with uniform distribution

CLINICAL ISSUES

- Dyspnea and nonproductive cough
- Patients are 1 decade younger (5th decade) than those with UIP
- Treatment: Immunosuppressive &/or immunomodulatory drugs, antifibrotic agents
- Prognosis more favorable than that of UIP

(Left) AP chest radiograph of a 61-year-old woman with idiopathic nonspecific interstitial pneumonia shows bilateral heterogeneous reticular opacities with basilar predominance 🖂 (Right) Axial HRCT of the same patient shows bilateral ground-glass opacities and $reticulations \supseteq along$ bronchovascular bundles and in the subpleural lungs with associated traction bronchiectasis 🔁. The combination of imaging findings and the absence of honeycombing suggest the correct diagnosis.











Abbreviations

• Nonspecific interstitial pneumonia (NSIP)

Definitions

- Type of idiopathic interstitial pneumonia (IIP)
- NSIP may be idiopathic or may be associated with connective tissue/autoimmune disease, drug toxicity, hypersensitivity pneumonitis, and other etiologies

IMAGING

General Features

- Best diagnostic clue
 - Bilateral ground-glass &/or reticular opacities ± traction bronchiectasis/bronchiolectasis
 - Subpleural sparing ± peribronchovascular fibrosis
- Location
 - Apicobasal gradient (lower lobe predominant)

Radiographic Findings

• Lower lung zone predominant, bilateral, reticular, or hazy/heterogeneous opacities

CT Findings

- Coexistent bilateral ground-glass &/or reticular opacities ± traction bronchiectasis/bronchiolectasis
- Subpleural sparing ± peribronchovascular fibrosis
- Absent or sparse honeycombing

Imaging Recommendations

Best imaging tool
 HRCT (or thin-section CT)

DIFFERENTIAL DIAGNOSIS

Usual Interstitial Pneumonia (UIP)

- Basilar honeycombing strongly favors UIP
- Subpleural sparing and extensive ground-glass opacity are uncommon
- May be indistinguishable from NSIP

Drug-Induced Interstitial Lung Disease

- NSIP pattern, indistinguishable from idiopathic NSIP
- Large list of potential causative drugs
 Methotrexate, nitrofurantoin, amiodarone, bleomycin
 - Molecular targeting agents and immune checkpoint inhibitors

Connective Tissue Disease-Interstitial Lung Disease (CTD-ILD)

- Often manifests as NSIP pattern on CT and histology
- Not idiopathic, has definable cause: Systemic sclerosis, polymyositis/dermatomyositis, mixed CTD

Fibrotic Hypersensitivity Pneumonitis (HP)

- Lobular areas of decreased attenuation and vascularity; expiratory air-trapping
- Mid and upper lung zone predominant fibrosis
- Considerable number of cases of fibrotic HP may be indistinguishable from NSIP and UIP on imaging
- Honeycombing may be present

Cryptogenic Organizing Pneumonia

- Patchy consolidation or nodules
- Perilobular pattern
- Reversed CT halo sign

PATHOLOGY

General Features

- Etiology
- o Idiopathic
- Growing body of evidence suggests idiopathic NSIP is occult manifestation of autoimmune disorder

Staging, Grading, & Classification

• Cellular and fibrotic NSIP; mixed cases classified as fibrotic

Microscopic Features

- Variable amounts of interstitial inflammation and fibrosis with uniform distribution
- Temporal and spatial homogeneity, in contrast to UIP
- Honeycombing: Less prominent than in UIP

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Dyspnea, nonproductive cough
- Other signs/symptoms
 Restrictive physiology on pulmonary function tests

Demographics

- Age
 - Patients are 1 decade younger (5th decade) than those with UIP

Natural History & Prognosis

- Variable: May improve with treatment, remain stable, or progress to end-stage fibrosis
- Prognosis more favorable than that of UIP

Treatment

• Immunosuppressive &/or immunomodulatory drugs, antifibrotic agents

DIAGNOSTIC CHECKLIST

Consider

- Underlying autoimmune process, hypersensitivity pneumonitis, or drug-induced interstitial lung disease in patients with NSIP pattern on HRCT
- Multidisciplinary diagnosis (integration of clinical, HRCT, and histologic features) is reference standard

Image Interpretation Pearls

• Reticulation and ground-glass opacities with lower lung zone predominance, particularly with subpleural sparing or peribronchovascular involvement should suggest NSIP

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- Teoh AKY et al: Nonspecific interstitial pneumonia. Semin Respir Crit Care Med. 41(2):184-201, 2020

(Left) Axial HRCT of a 69-yearold man with idiopathic nonspecific interstitial pneumonia shows lower lobe predominant subpleural ground-glass opacities. Note absence of honeycombing. (Right) Axial prone HRCT of the same patient shows persistent subpleural groundglass opacities. Prone imaging is critical in the assessment of interstitial lung disease, as it allows differentiation of true ground-glass opacity from dependent atelectasis, which is a normal finding that classically resolves on prone imaging.





(Left) Sagittal HRCT of the same patient shows lower lobe predominant subpleural ground-glass opacities \supseteq and sparing of the upper lobes. Such lower lobe predominance (sometimes referred to as apicobasal gradient) is a classic finding of both nonspecific interstitial pneumonia and usual interstitial pneumonia. (Right) Low-power photomicrograph (H&E stain) of a specimen from the same patient shows pulmonary interstitial fibrosis \square with temporal and spatial homogeneity (i.e., fibrosis in similar stages).





(Left) Axial HRCT of a patient with idiopathic nonspecific interstitial pneumonia shows peribronchovascular reticular opacities, traction bronchiectasis, and subpleural sparing \square . The latter is a classic finding of nonspecific interstitial pneumonia. (Right) Composite image with initial axial HRCT (left) and follow-up axial HRCT obtained 4 months after initiation of glucocorticoids (right) of a 37year-old woman with idiopathic nonspecific interstitial pneumonia shows improvement of subpleural ground-glass opacities.









(Left) PA chest radiograph of a 58-year-old woman with nonspecific interstitial pneumonia and organizing pneumonia shows bilateral opacities and reticulation with . lower lung zone predominance. (Right) Axial HRCT of the same patient shows bilateral lower lobe predominant patchy areas of ground-glass opacity, reticulation, \square and consolidation 🖾. Foci of organizing pneumonia are common pathologic patterns of lung injury often found in patients with nonspecific interstitial pneumonia.





(Left) Low-power photomicrograph (H&E stain) of a specimen from the same patient shows interstitial fibrosis 🔁 with temporal homogeneity characterized by disease at similar stages of fibrosis and foci of pulmonary ossification 🖂 (Right) Lowpower photomicrograph (H&E stain) of the same specimen shows organizing pneumonia (intraalveolar loose myxoid polyps) 🔁 amid nodular lymphoid aggregates 🔁. Honeycombing is less common in nonspecific interstitial pneumonia compared to usual interstitial pneumonia.





(Left) Axial HRCT of a patient with nonspecific interstitial pneumonia associated with unclassified connective tissue disease shows subpleural reticulation and traction bronchiectasis 🖂. (Right) Axial HRCT image from a patient with known scleroderma shows patchy ground-glass opacities 🔁, traction bronchiectasis \square , and a dilated esophagus 🔁. Nonspecific interstitial pneumonia is the most common pulmonary manifestation of many connective tissue diseases.

Organizing Pneumonia

KEY FACTS

TERMINOLOGY

- Organizing pneumonia (OP)
- OP: Relatively common manifestation of acute lung injury

IMAGING

- Classic pattern (68-81%)
 - Bilateral peribronchovascular &/or subpleural consolidations
 - Mid and lower lung zone predominance
 - Consolidations may regress spontaneously
- HRCT
 - Consolidation &/or ground-glass opacities
 - Pulmonary nodule or mass (single or multiple)
 - Reversed halo sign
 - Reticular opacities
 - Parenchymal bands
 - Bronchial dilatation
 - Diffuse micronodular pattern

TOP DIFFERENTIAL DIAGNOSES

- Chronic eosinophilic pneumonia
- Lymphoma
- Primary lung adenocarcinoma
- Granulomatosis with polyangiitis

PATHOLOGY

• Granulation tissue (i.e., Masson bodies) consisting of fibroblasts and myofibroblasts amid loose connective tissue matrix within lumina of distal pulmonary airspaces

CLINICAL ISSUES

- Fever, cough, malaise, progressive dyspnea
- Anorexia and weight loss
- Corticosteroids are mainstay of therapy

DIAGNOSTIC CHECKLIST

• Consider OP in patients with migratory pulmonary opacities on radiography that exhibit a peribronchovascular or perilobular distribution or the reversed halo sign on CT

(Left) Axial CECT of a 35-yearold woman with systemic lupus erythematosus and organizing pneumonia shows bilateral nodules with central ground-glass opacity and a peripheral rim of consolidation ☐ (reversed halo sign). This may also be referred to as perilobular pattern, which is highly specific for organizing pneumonia. (Right) Axial CECT of the same patient shows bilateral basilar predominant peribronchovascular and subpleural consolidations 🔁 with relative sparing of an adjacent secondary pulmonary lobule 🔁









(Left) Low-power photomicrograph (H&E stain) of a specimen of cryptogenic organizing pneumonia shows intraalveolar plugs of loose connective tissue 🔁 associated with an interstitial lymphocytic and plasmatic cell infiltration 🔁 (Right) Highpower photomicrograph (Trichrome stain) of the same specimen shows fibroblastic polyps 🔁, also called Masson bodies, that obstruct lumina of alveoli, alveolar ducts, and bronchioles (hence the former term "bronchiolitis obliterans" organizing pneumonia).

Organizing Pneumonia

TERMINOLOGY

Abbreviations

- Organizing pneumonia (OP)
- Cicatricial organizing pneumonia (CiOP)
- Cryptogenic organizing pneumonia (COP)

Synonyms

• Bronchiolitis obliterans organizing pneumonia (BOOP): Term no longer in use

Definitions

- OP: Pathological pattern defined by intraalveolar buds of granulation tissue consisting of fibroblasts and myofibroblasts intermixed with loose connective tissue matrix, especially consisting of collagen
- OP is relatively common manifestation of acute lung injury
- CiOP: Intraluminal collagen deposition on background of otherwise classic OP with formation of peculiar fibrous nodules or fibrotic linear bands
- COP: Clinical pathological entity without known cause, histologically characterized by OP

IMAGING

General Features

- Classic pattern (68-81%)
 - Bilateral peribronchovascular &/or subpleural consolidations
 - Mid and lower lung zone predominance
 - o Spontaneous regression of some areas of consolidation
- May progress to pulmonary fibrosis [similar to nonspecific interstitial pneumonia (NSIP)]
 - While controversial, it is postulated that some cases of NSIP may be sequela of OP
- Occasional subpleural sparing
- Similar clinical and radiologic findings in patients with COP and secondary OP

Radiographic Findings

- Patchy subpleural &/or peribronchovascular consolidations
- Migratory opacities (i.e., waxing and waning)
- Less common abnormalities
 - Solitary pulmonary nodule or mass
 - Multiple pulmonary nodules
 - Parenchymal bands
 - Basilar reticular opacities

CT Findings

- HRCT
 - o Consolidation
 - Patchy, subpleural &/or peribronchovascular
 - Middle lobe, lingular, and lower lobe predominance
 - Migratory (i.e., waxing and waning)
 - o Ground-glass opacities (90%)
 - Bilateral
 - Patchy distribution
 - Solitary pulmonary nodule or mass
 - Peripheral
 - > 3-cm polygonal shape, irregular margin
 - < 3-cm ovoid or rounded shape with regular or smooth borders

- Air bronchograms or small bubble-like lucencies
- Multiple pulmonary nodules
 - < 4 mm or micronodules (peribronchial or centrilobular distribution)
 - 4-10 mm or acinar opacities (peribronchovascular or peripheral distribution)
 - 10 mm or large
 - □ Irregular margins (88%
 - □ Air bronchograms (45%)
 - Pleural tags (23%)
 - Focal interlobular septal thickening (near nodules)
- Perilobular pattern
 - Subpleural curvilinear opacities surrounding spared secondary pulmonary lobules
 - Specific finding
- Reversed halo sign (19%)
 - Ground-glass opacity surrounded by crescent or ring of parenchymal consolidation
 - Ground-glass opacity corresponds to alveolar wall inflammation
 - Ring of parenchymal consolidation corresponds pathologically to OP in distal airspaces
- Reticular opacities
 - Associated with other findings of fibrosis (honeycombing, traction bronchiectasis), ground-glass opacities, &/or consolidation
- Parenchymal bands
 - Smooth or irregular lines of variable length and thickness
- Bronchial dilatation
 - Within consolidation or ground-glass opacity
- Diffuse micronodular pattern
 - Uncommon
 - Peribronchial or centrilobular
- o Enlarged mediastinal lymph nodes
- o Pleural effusion (uncommon)
- Cavitation (uncommon)

Nuclear Medicine Findings

- PET/CT
 - o OP typically demonstrates FDG avidity

DIFFERENTIAL DIAGNOSIS

Chronic Eosinophilic Pneumonia

- Subpleural ground-glass opacities &/or consolidations
- Upper lobe predominance
- Band-like opacities parallel to chest wall
- History of asthma (75%)
- High peripheral blood eosinophilia (usually > 1,500/µL)

Lymphoma

- Consolidation (not migratory except in lymphomatoid granulomatosis)
- Multiple pulmonary nodules
- Lymphadenopathy
- Pleural effusion

Bacterial Pneumonia

- Consolidation (not migratory)
- Acute clinical manifestations (fever, shortness of breath)

- Interstitial, Diffuse, and Inhalational Lung Disease
- Other findings described in COP are uncommon

Lung Cancer

- Mass-like consolidation (not migratory)
- Lymphadenopathy
- Smoker (uncommon in COP)

Granulomatosis With Polyangiitis (GPA)

- Migratory ground-glass opacities, nodules, or consolidations
- Peripheral blood eosinophilia
- Renal disease

Acute Fibrinous Organizing Pneumonia

- Histopathological pattern characterized by intraalveolar fibrin deposits, hyperplasia of type II pneumocytes, associated OP, and absence of hyaline membranes
- Acute and subacute forms
 - o Acute
 - Fulminant course, typically leads to respiratory failure and death
 - Imaging manifestations similar to those of diffuse alveolar damage (noncardiogenic pulmonary edema)
 - Subacute: Imaging manifestations similar to those of OP pattern

PATHOLOGY

General Features

- Etiology
 - OP may be idiopathic or associated with
 - Autoimmune diseases (e.g., systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, GPA, small vessel vasculitis)
 - Drugs
 - □ Amiodarone, chemotherapy
 - Recreational: Cocaine
 - Infections
 - 🗆 Bacteria (e.g., Mycoplasma, Haemophilus)
 - Mycobacteria (tuberculosis and nontuberculous mycobacteria)
 - Viruses [e.g., human immunodeficiency virus (HIV), influenza, SARS-CoV-2]
 - Fungi (e.g., Pneumocystis jirovecii)
 - □ Parasites (e.g., *Plasmodium vivax*)
 - Pulmonary disease
 - Hypersensitivity pneumonitis, chronic eosinophilic pneumonia, airway obstruction, alveolar hemorrhage, abscess, infarction, neoplasm, aspiration
 - Radiation
- Presence of OP has variable clinical implications
 - May manifest with clinical symptoms and signs
 - Little significance if found surrounding granulomatous processes or malignancy; may be minor component of hypersensitivity pneumonitis, eosinophilic pneumonia

Gross Pathologic & Surgical Features

- Bronchoalveolar lavage
 - Nonspecific findings; may help exclude hemorrhage, malignancy, and infection

Microscopic Features

- Multifocal process characterized by organizing fibrosis of loose connective tissue that occludes bronchioles, alveolar ducts, and surrounding alveoli
- Intraluminal polypoid plugs of loose organizing connective tissue (i.e., Masson bodies) within alveolar ducts, alveolar spaces, and frequently bronchioles
 - Intrinsic lymphocytes, plasma cells, and histiocytes in addition to fibroblasts
- Hyperplastic type II pneumocytes lining alveolar septa
- Mild or moderate interstitial thickening consisting of lymphocytes &/or plasma cells
- Foci of endogenous lipoid pneumonia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Fever, malaise
 - Cough and progressive dyspnea
 - o Anorexia, weight loss
- Other signs/symptoms
 - Focal and sparse crackles
 - o Hemoptysis
 - o Chest pain
 - Night sweats
 - Pneumothorax/pneumomediastinum
- Clinical profile
- Pulmonary function tests
 - Mild-to-moderate restrictive pattern (common)
 - Obstructive pattern in 20%
 - Reduced diffusing capacity for carbon monoxide
 - Resting &/or exercise arterial hypoxemia

Natural History & Prognosis

- Diagnosis often delayed (6-12 weeks)
- Overall prognosis is good
- Relapse in 13-58% of affected patients
- Bronchiectasis and greater extent of consolidation (> 10% of parenchyma) associated with residual disease
- Greater extent of consolidation (> 10% of parenchyma) associated with disease relapse
- Reticular opacities at disease onset: Less likely to respond to corticosteroids; may progress to lung fibrosis

Treatment

Corticosteroids

DIAGNOSTIC CHECKLIST

Consider

• OP in patients with migratory pulmonary opacities on radiography and peribronchovascular or perilobular distribution or reversed halo sign on CT

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Organizing Pneumonia





(Left) PA chest radiograph of a 59-year-old woman with dermatomyositis and organizing pneumonia shows bilateral basilar predominant subpleural heterogenous opacities 🔁. (Right) Axial NECT of the same patient shows bilateral subpleural consolidations \supseteq , parenchymal bands Ξ , subpleural curvilinear opacities 🖂, and poorlydefined, arcade-like opacities \blacksquare with the so-called perilobular pattern that spares adjacent secondary pulmonary lobules.





(Left) Axial HRCT of a patient with organizing pneumonia shows well-demarcated right lower lobe peribronchovascular groundglass opacities, at least one of which exhibits the reversed halo sign 🔁. (Right) Axial HRCT of the same patient obtained 6 months after treatment shows a migratory behavior of the right lower lobe ground-glass opacities ∠. The diagnosis of organizing pneumonia is always one of exclusion and commonly warrants

pathologic confirmation.



(Left) Axial NECT of a patient with organizing pneumonia shows a solid lingular mass 🖂 and a small left pleural effusion 🔁. Organizing pneumonia may simulate lung cancer. (Right) Axial fused FDG PET/CT of the same patient shows FDG avidity in the left upper lobe mass 🔁. Organizing pneumonia with focal lung involvement may mimic lung cancer on imaging. Foci of organizing pneumonia, whether cryptogenic or occurring as a secondary lung reaction to several other diseases, typically exhibit moderate to high FDG avidity.

Sarcoidosis

KEY FACTS

TERMINOLOGY

- Sarcoidosis: Systemic chronic granulomatous disease characterized by noncaseating granulomas in multiple organs
 - Lung and mediastinum involved in over 90% of cases

IMAGING

• Radiography

- Bilateral hilar and right paratracheal lymphadenopathy in up to 95% of patients
- ± upper lung zone opacities (reticular, nodular, micronodular, mass-like)
- CT/HRCT
 - Bilateral perilymphatic micronodules (75-90%)
 - Pulmonary nodules and masses (20%); solitary nodule or mass (rare)
 - o Alveolar opacities (10-20%)
 - o Ground-glass opacities (40%)
 - o Pulmonary fibrosis (20%): Upper lobe predominant

TOP DIFFERENTIAL DIAGNOSES

- Silicosis
- Berylliosis
- Lymphangitic carcinomatosis
- Lymphoma

PATHOLOGY

• Diagnosis based on histologic demonstration of noncaseating granulomas + compatible clinical, laboratory, and imaging findings

CLINICAL ISSUES

- Demographics: Adults < 40 years; peak age: 20-29 years
- Symptoms and signs
 - o Asymptomatic, cough, dyspnea, fatigue

DIAGNOSTIC CHECKLIST

• Consider sarcoidosis in patients < 40 years with minimal symptoms and bilateral hilar/mediastinal lymphadenopathy

(Left) PA chest radiograph of a 27-year-old man with sarcoidosis shows bilateral hilar , right paratracheal a, and aortopulmonary window lymphadenopathy. (Right) Composite image with axial CECT of the same patient shows bilateral symmetric hilar , paratracheal , and subcarinal

lymphadenopathy. Although these are classic demographic, radiographic, and CT findings, sarcoidosis is always a diagnosis of exclusion that requires correlation of clinical, imaging, laboratory, and histologic findings.





(Left) PA chest radiograph of a patient with sarcoidosis shows diffuse bilateral reticulonodular opacities slightly more coalescent toward the hila (peribronchovascular distribution). (Right) Coronal CECT of the same patient shows a perilymphatic distribution of profuse peribronchovascular micronodules, which are also located along the subpleural interstitium 🔁. The distribution of micronodules is typical of sarcoidosis but may occur in other perilymphatic processes.





Synonyms

• Sarcoid

Definitions

- Systemic chronic granulomatous disease characterized by noncaseating granulomas in multiple organs
- Lung, hilum, and mediastinum affected in > 90% of patients
 Greatest morbidity/mortality from thoracic involvement
 - o Chronic lung disease in 20% of affected patients

IMAGING

General Features

- Best diagnostic clue
 - Bilateral hilar and right paratracheal lymphadenopathy in up to 95% of cases
- Location
 - Lymphadenopathy: Bilateral hilar (most common)
- Lung: Upper lung zones
- Morphology
 - Lymph node calcification; ↑ incidence with ↑ disease duration

Radiographic Findings

- Radiography
 - Bilateral hilar and symmetric mediastinal lymphadenopathy
 - Multifocal bilateral micronodules, upper lung zone predominant
 - Multifocal nodules, masses, and mass-like consolidations: Nummular or alveolar sarcoid
 - Fibrosis: Upper lung zone predominant reticular opacities, architectural distortion, volume loss
 - Mass-like lesions may mimic progressive massive fibrosis
 - o Pleural effusion is rare

CT Findings

- Lymphadenopathy
 - Bilateral, symmetric: Hilar, paratracheal, aortopulmonary window, subcarinal
 - o Usually "noncompressive" even if bulky
 - o Calcification (20% at diagnosis)
 - Popcorn, amorphous, punctate, or eggshell
 - Atypical: Asymmetric mediastinal, unilateral hilar, internal mammary, paravertebral, retrocrural (unilateral in 5% of cases)
- Nodules and masses
 - Bilateral perilymphatic micronodules (75-90%)
 - Perilymphatic: Peribronchovascular + subpleural interstitial + interlobular septal
 - Upper lobe predominance
 - Rounded or elongate clustered small nodules, close but not confluent: Sarcoid cluster sign
 - Pulmonary nodules and masses (20%)
 - Multifocal
 - Peripheral and perihilar
 - May exhibit air bronchograms (5-10%)
 - Often referred to as nummular sarcoidosis

- Dominant mass-like lesion or large nodules surrounded by small satellite nodules: Galaxy sign
- Cavitary nodules or masses (ischemic necrosis or angiitis)
- o Solitary (rare)
- Consolidations and ground-glass opacities
 - o Consolidations (10-20%)
 - Confluence of micronodules compressing alveoli
 - Bilateral, symmetric, may exhibit air bronchograms
 Upper lobe predominance
 - Ground-glass opacities (40%)
 - Patchy or extensive
 - Usually associated with micronodules
- Small airways disease
 - Mosaic attenuation and air-trapping may occur
- Fibrosis
 - Pulmonary fibrosis
 - Upper lobe predominant reticular opacities, traction bronchiectasis, architectural distortion, volume loss
 - Confluent mass-like opacities may mimic progressive massive fibrosis
 - Peribronchovascular
 - Honeycombing
 - Enlarged pulmonary arteries
- Other findings
 - o Mycetoma formation
 - Fungus balls in preexisting bullae or cysts
 - Pulmonary trunk enlargement in pulmonary
 - hypertensionPericardial involvement: Typically pericardial effusion

MR Findings

- Optimal imaging modality for assessing cardiac involvement
- T1WIC+
 - o Localized or patchy ventricular enhancement
 - o Diffuse subepicardial enhancement

Nuclear Medicine Findings

- Ga-67 scintigraphy
 - Gallium-67 to distinguish fibrotic changes from active disease, but has been replaced by FDG PET/CT
- PET/CT
 - o Valuable in assessing disease extent and activity
 - o Identification of optimal biopsy site
 - Evaluation of response to treatment

Imaging Recommendations

- Best imaging tool
 - Chest radiography is useful for initial evaluation
- Protocol advice
 - HRCT
 - Identification and characterization of micronodules, nodules, and fibrosis

DIFFERENTIAL DIAGNOSIS

Silicosis

- Silica exposure
- Centrilobular and subpleural micronodules; may calcify

Sarcoidosis

Staging of Sarcoidosis Based on Chest Radiography

Stage	Radiographic Abnormalities
Stage 0	Normal
Stage 1	Lymphadenopathy
Stage 2	Lymphadenopathy and pulmonary abnormalities
Stage 3	Pulmonary abnormalities
Stage 4	Pulmonary fibrosis

- Conglomerate nodules and masses in upper lobe posterior segments
- Hilar/mediastinal lymph nodes ± eggshell calcification

Berylliosis

- Exposure to beryllium
- Mediastinal and hilar lymphadenopathy; less common than in sarcoidosis
- Bilateral, peribronchovascular, interlobar, and subpleural micronodules

Lymphangitic Carcinomatosis

- Clinical history of malignancy
- Smooth or nodular bronchovascular and interlobular septal thickening
- Unilateral or bilateral

Lymphoma

- Multicompartment mediastinal and hilar lymphadenopathy (often bulky)
- Micronodules are uncommon

PATHOLOGY

General Features

- Etiology
 - Immune-mediated disease
 - Postulated antigenic stimulation that triggers inflammatory response
 - CD4(+) T-cells interact with antigen-presenting cells to initiate granuloma formation and maintenance
- Diagnosis based on histologic demonstration of noncaseating granulomas + compatible clinical, laboratory, and imaging findings

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic
 - o Cough, dyspnea, fatigue, night sweats, weight loss
 - Ocular involvement
 - Cutaneous involvement: Erythema nodosum, lupus pernio
- Other signs/symptoms
 - Löfgren syndrome (acute presentation)
 - Fever, erythema nodosum, polyarticular arthralgia, bilateral hilar lymphadenopathy
 - Heerfordt syndrome
 - Fever, parotid enlargement, facial palsy, anterior uveitis

Demographics

- Age
 - Young adults, usually < 40 years
 - Peak age: 20-29 years
- Sex
 - o M:F = 1:2
- Ethnicity
 - Higher prevalence in African Americans than in other demographic groups

Natural History & Prognosis

- Patients often present with bilateral hilar lymphadenopathy, pulmonary opacities, and involvement of eyes, skin, and joints
- Most patients go into remission or remain stable within decade of initial diagnosis
 - Up to 20% of patients develop chronic disease and pulmonary fibrosis
 - Sarcoidosis characterized by periods of remission and recurrence
- Factors associated with poor prognosis: Advanced age, stage 2 or 3 at initial diagnosis, extrapulmonary disease, pulmonary hypertension

Treatment

- Stable or improved symptoms with corticosteroid therapy
- Infliximab for refractory sarcoidosis

DIAGNOSTIC CHECKLIST

Consider

• Sarcoidosis in patients < 40 years with minimal symptoms and bilateral hilar and mediastinal lymphadenopathy

Image Interpretation Pearls

• Architectural distortion, traction bronchiectasis, and honeycombing indicate irreversible pulmonary fibrosis

Reporting Tips

- Sarcoidosis is diagnosis of exclusion
- Imaging stage at presentation correlates with prognosis

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Sarcoidosis





(Left) Coronal CECT of a patient with sarcoidosis shows bilateral perihilar mass-like opacities and perilymphatic micronodules along interlobular septa 🔁, $bronchovascular bundles \square$ and subpleural regions 🖂. (Right) Low-power photomicrograph (H&E stain) of a specimen of sarcoidosis shows multiple nodular nonnecrotizing interstitial epithelioid granulomas 🖂 along bronchovascular bundles \square , consistent with a perilymphatic distribution of disease. (From DP: Thoracic.)





(Left) PA chest radiograph of a patient with sarcoidosis shows profuse bilateral pulmonary micronodules and some larger pulmonary nodules \implies (Right) Coronal NECT of the same patient shows profuse bilateral irregular nodules and micronodules involving both lungs. Although sarcoidosis often exhibits a characteristic perilymphatic distribution, disease profusion may make it difficult to differentiate perilymphatic micronodules from random or centrilobular nodules typical of metastases or infection, respectively.





(Left) Axial NECT of a patient with sarcoidosis shows a discrete right upper lobe pulmonary nodule 🔁 with an intrinsic air bronchogram and subtle surrounding perilymphatic micronodules (i.e., the galaxy sign) that produce a slightly spiculated margin. (Right) Axial CECT of a patient with sarcoidosis shows bilateral nodular opacities with air bronchograms \square and without architectural distortion. Multifocal consolidations with or without a nodular morphology are often described as an alveolar pattern.

(Left) Axial CECT of a patient with sarcoidosis shows a dominant spiculated part-solid nodule \supseteq in the posterior segment of the right upper lobe and bilateral mediastinal lymphadenopathy 🔁. Solitary nodules are atypical manifestations that should raise concern for primary lung cancer. (Right) Axial HRCT of a patient with sarcoidosis shows extensive mosaic attenuation and bilateral hilar 🔁 and mediastinal lymphadenopathy ☑ Sarcoidosis may involve the small airways and produce mosaic attenuation and expiratory air-trapping.





(Left) PA chest radiograph of a patient with stage 4 sarcoidosis shows bilateral upper lobe architectural distortion and volume loss. (Right) Axial HRCT of the same patient shows bilateral , peribronchovascular architectural distortion, traction bronchiectasis, posterior hilar retraction, and coalescent opacities that mimic progressive massive fibrosis. This appearance is characteristic of end-stage sarcoidosis but may also occur in fibrotic hypersensitivity pneumonitis and silicosis.





(Left) PA chest radiograph of a patient with end-stage sarcoidosis who presented with hemoptysis shows asymmetric, right greater than left fibrosis, and a right upper lobe mass \boxtimes surrounded by crescentic lucency 🔁. The findings are consistent with saprophytic aspergillosis. (Right) Axial NECT of the same patient shows a right upper lobe aspergilloma 🔁 manifesting as a soft tissue mass with intrinsic lucency surrounded by a nondependent crescent of air ⇒. Note bilateral upper lobe fibrosis 🔁.





Sarcoidosis





(Left) Axial CECT of a patient with end-stage sarcoidosis shows bilateral upper lobe predominant architectural distortion, spiculated perihilar mass-like lesions, and scattered perilymphatic nodules and micronodules. (Right) Low-power photomicrograph (H&E stain) of a specimen of sarcoidosis shows confluent granulomas forming a large nodular mass $\xrightarrow{}$ that could mimic malignancy on imaging. Fibrotic mass-like sarcoid lesions may also mimic progressive massive fibrosis. (From DP: Thoracic.)





(Left) Axial HRCT of a patient with end-stage sarcoidosis shows upper lung zone and peribronchovascular reticulation and honeycombing 🔁. The distribution of disease differs from that of usual interstitial pneumonia in which fibrosis is basilar and subpleural. (Right) Axial CECT shows end-stage sarcoidosis manifesting with bilateral perihilar mass-like lesions \supseteq with intrinsic cavitation or cystic change and a small left pneumothorax 🔁. Cavitation is uncommon in sarcoidosis but may result from necrosis or angiitis.





(Left) Coronal FDG PET of a patient with sarcoidosis shows bilateral hilar, paratracheal, and subcarinal lymphadenopathy with FDG avidity. Based on metabolic activity, FDG PET/CT is very useful for evaluating disease extent and activity as well as response to treatment. (Right) Axial fused FDG PET/CT of a patient with sarcoidosis shows FDG-avid mediastinal and hilar lymph nodes, consistent with active disease. FDG PET/CT is a good tool for evaluation of response to treatment based on temporal decrease &/or increase of metabolic activity.

TERMINOLOGY

- Pleuroparenchymal fibroelastosis (PPFE)
- Rare interstitial pneumonia characterized by upper lobe predominant elastotic fibrosis involving pleura and subpleural lung

o Idiopathic or secondary

IMAGING

• Radiography

- Upper lobe predominant subpleural opacities
- o Apical pleural thickening
- Upper lobe volume loss, hilar elevation
- CT
 - Upper lobe predominant pleuroparenchymal thickening; may be diffuse
 - Subpleural consolidations and ground-glass opacities
 - Traction bronchiectasis/bronchiolectasis
 - Coexisting usual interstitial pneumonia (UIP) or nonspecific interstitial pneumonia (NSIP)

TOP DIFFERENTIAL DIAGNOSES

- Apical fibrosis
- Tuberculosis
- Pneumoconiosis

PATHOLOGY

- Upper thoracic visceral pleura fibrosis
- Subpleural intraalveolar fibrosis with alveolar septal elastosis

CLINICAL ISSUES

- Symptoms: Shortness of breath, cough, weight loss, chest pain
- No sex predilection
- Mean age: 53 years of age
- Disease progression in 60%; 40% die from disease
- No effective treatment
 - o Pirfenidone, corticosteroids, immunosuppressants
 - Lung transplantation

(Left) PA chest radiograph of a woman with pleuroparenchymal fibroelastosis demonstrates upper lobe predominant reticular opacities, upper lobe volume loss, and apical subpleural thickening. (Right) Axial HRCT of the same patient shows biapical pleuroparenchymal thickening 🔁, subpleural reticular and ground-glass opacities 🔁, and traction bronchiectasis and bronchiolectasis 🔁 Pleuroparenchymal fibroelastosis exhibits progression in 60% of affected patients.











Abbreviations

• Pleuroparenchymal fibroelastosis (PPFE)

Synonyms

• Amitani disease

Definitions

• Rare interstitial pneumonia characterized by upper lobe predominant elastotic fibrosis involving pleura and subpleural lung

IMAGING

Radiographic Findings

- Upper lobe-predominant subpleural opacities
- Apical pleural thickening
- Upper lobe volume loss with superior displacement of minor fissure &/or hilar structures

CT Findings

- Upper lobe predominant pleuroparenchymal thickening • Thickness: 4-15 mm
- Architectural distortion and upper lobe volume loss
- Dense subpleural opacities
- Traction bronchiectasis/bronchiolectasis
- Coexistent usual interstitial pneumonia (UIP) or nonspecific interstitial pneumonia (NSIP)
- Subpleural cysts (rare)
- Complications: Pulmonary hypertension, pneumothorax

Imaging Recommendations

- Best imaging tool
 - HRCT

DIFFERENTIAL DIAGNOSIS

Apical Fibrosis

- Difficult to differentiate on imaging; PPFE tends to be more diffuse
- Absence of progression, good prognosis

Tuberculosis

- Biapical architectural distortion and volume loss
- Often chronic and stable; known history of infection

PATHOLOGY

General Features

- Etiology
 - Idiopathic Secondary
 - Lung and bone marrow transplantation (late)
 - Chemotherapy, occupational dust exposure (e.g., asbestos, aluminum), infection (e.g., Aspergillus, Mycobacterium avium-intracellulare), autoimmune disease (e.g., rheumatoid arthritis, ulcerative colitis, ankylosing spondylitis), hypersensitivity pneumonitis
 - Underlying genetic predisposition

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Shortness of breath, cough, weight loss, chest pain
 - Recurrent infection
 - o Pneumothorax

Demographics

- Sex
 - No sex predilection
- Age
 - o Mean: 20-80 years

Natural History & Prognosis

- Disease progression in 60% of patients; 40% die from disease
- 30% overall 5-year survival

Treatment

- No effective treatment
 - Pirfenidone, corticosteroids, immunosuppressants (e.g., tacrolimus and cyclosporine)
 - Lung transplantation

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- Mariani F et al: Pleuroparenchymal fibroelastosis: the prevalence of secondary forms in hematopoietic stem cell and lung transplantation recipients. Diagn Interv Radiol. 22(5):400-6, 2016

Proposed Criteria for Pleuropulmonary Fibroelastosis (PPFE) Diagnosis

Category	Histopathology	HRCT
Definitive PPFE	Upper lobe pleural fibrosis + subjacent intraalveolar fibrosis + alveolar septal elastosis	Pleural thickening + upper lobe subpleural fibrosis without lower lobe involvement
Consistent with PPFE	Intraalveolar fibrosis, but 1. No significant pleural fibrosis, 2. No subpleural predominance, or 3. Not present in upper lobe biopsy	Upper lobe pleural thickening + pleural fibrosis, but 1. No upper lobe distribution, or 2. No characteristic coexistent disease in other sites
Inconsistent with PPFE	Absence of features of definitive and consistent diagnosis	Absence of features of definitive and consistent diagnosis

Adapted from Ricoy J et al: Pleuroparenchymal fibroelastosis: clinical, radiological and histopathological features. Respir Med. 106437, 2021

TERMINOLOGY

- RB: Histopathologic finding in current or former smokers
- RB-ILD: Smoker-associated disease with imaging and histopathological findings of respiratory bronchiolitis and clinical/functional manifestations of interstitial lung disease
- RD and RB-ILD may be indistinguishable on imaging and histopathology

IMAGING

- Radiography
 - Poorly-defined hazy areas of increased density
 - Bronchial wall thickening
 - o Normal in 20-28% of cases
 - Fine reticulonodular opacities
- CT
 - Centrilobular nodules
 - Ground-glass opacity
 - Bronchial wall thickening
 - Upper lobe predominance

TOP DIFFERENTIAL DIAGNOSES

- Desquamative interstitial pneumonia
- Hypersensitivity pneumonitis

PATHOLOGY

- RB: Cellular bronchiolitis is almost invariably an incidental finding in all smokers
- Accumulation of pigmented macrophages (smoker's macrophages) within respiratory bronchioles and alveoli

CLINICAL ISSUES

- RB: Asymptomatic
- RB-ILD: Cough, dyspnea
- Virtually all patients with RB-ILD are heavy smokers

DIAGNOSTIC CHECKLIST

• Consider RB-ILD in symptomatic smoker with upper lung zone predominant centrilobular micronodules and ground-glass opacities on CT

(Left) Axial HRCT of a 29-yearold woman with a history of mixed tobacco and cocaine (known as basuco) use and respiratory bronchiolitis shows ground-glass centrilobular micronodules 🔁, tree-in-bud nodules 🖂, and emphysema 2. (Right) Low-power photomicrograph (H&E stain) shows respiratory bronchiolitis characterized by collections of lightly pigmented macrophages 🔁 within a bronchiole and adjacent alveolar spaces.





(Left) Axial HRCT of a cigarette smoker with respiratory bronchiolitisassociated interstitial lung disease who presented with dyspnea and cough shows patchy ground-glass opacities →, centrilobular ground-glass nodules 🔁, and mild centrilobular 🔁 and paraseptal emphysema. (Right) Axial HRCT of a patient with respiratory bronchiolitisassociated interstitial lung disease shows peripheral ground-glass opacities 🔁 associated with centrilobular emphysema 🖂 and subpleural reticulation 🔁





Abbreviations

- Respiratory bronchiolitis (RB)
- Respiratory bronchiolitis-associated interstitial lung disease (RB-ILD)

Definitions

- RB: Histopathologic finding in current or former smokers
- RB-ILD: Smoker-associated disease with imaging and histopathologic findings of RB and clinical/functional manifestations of interstitial lung disease
- RD and RB-ILD may be indistinguishable on imaging and histopathology

IMAGING

General Features

- Best diagnostic clue
 - Centrilobular nodules and ground-glass opacities with upper lobe predominance

Radiographic Findings

- Normal chest radiograph (20-28%)
- Bronchial wall thickening
- Poorly-defined hazy areas of increased density
- Fine reticulonodular opacities
 - Diffuse or basilar predominance

CT Findings

- HRCT
 - Upper lobe predominance
 - Centrilobular nodules
 - Ground-glass opacities
 - o Bronchial wall thickening
 - Centrilobular emphysema
 - o Intralobular lines/reticulation (20-75%)
 - Honeycombing (uncommon)
 - Tree-in-bud pattern (uncommon)
 - Mosaic attenuation (uncommon)

DIFFERENTIAL DIAGNOSIS

Desquamative Interstitial Pneumonia (DIP)

- Diffuse ground-glass opacities
 Mid and lower zone predominance
- Reticulation and cysts
- Traction bronchiectasis

Hypersensitivity Pneumonitis

- Diffuse ground-glass opacities
- Centrilobular ground-glass micronodules
- Mosaic attenuation and air-trapping
- Decreased risk of developing hypersensitivity pneumonitis in smokers

Aspiration Bronchiolitis

- Centrilobular and tree-in-bud micronodules
- Bronchial wall thickening, bronchiectasis, mosaic attenuation
- Risk factors: Neurological conditions, hiatus hernia, gastroesophageal reflux disease

PATHOLOGY

General Features

- RB: Cellular bronchiolitis almost invariably present as incidental finding in all smokers
- RB has also been demonstrated in lung biopsies of patients with mineral dust exposure (including asbestos)

Gross Pathologic & Surgical Features

• Bronchoalveolar lavage characterized by smoker's macrophages and absence of lymphocytosis

Microscopic Features

- Accumulation of pigmented macrophages (smoker's macrophages) within respiratory bronchioles and alveoli
 - Macrophages contain finely granular golden brown pigment; iron stain (+)
- Mild to moderate chronic inflammation and fibrosis may surround bronchioles and involve adjacent alveolar septa
- Patchy lymphocytic and histiocytic infiltration of peribronchiolar interstitium

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- o RB
 - Asymptomatic patient
- RB-ILD
 - Symptomatic wheezing
 - Persistent cough
 - Exertional dyspnea
 - Chest pain (uncommon)
- Pulmonary function tests
 - Restrictive or mixed (obstructive and restrictive) pulmonary function
 - Decreased diffusing capacity

Demographics

- Age
 - o 22-70 years; median age of 36-54 years
- Epidemiology
 - Virtually all patients with RB-ILD are heavy smokers

Natural History & Prognosis

- RB occurs early after smoking onset
- Progression to fibrotic lung disease exceedingly rare

Treatment

- Smoking cessation
- Corticosteroids

DIAGNOSTIC CHECKLIST

Consider

 RB-ILD in symptomatic smokers with upper lung zone centrilobular micronodules and ground-glass opacities on CT

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TERMINOLOGY

- Desquamative interstitial pneumonia (DIP)
- Interstitial lung disease characterized by accumulation of alveolar macrophages

IMAGING

- Radiography
 - o Ill-defined hazy airspace disease, reticular opacities
 - Mid and lower lung zone involvement
- CT/HRCT
 - o Ground-glass opacities (83-100%)
 - ± associated consolidation
 - Bilateral and moderately symmetric (> 50%)
 - Lower zone (73%), peripheral (59%), patchy (23%), diffuse (18%)
 - o Intralobular lines or reticular opacities (17-63%)
 - Subpleural predominance
 - Associated with ground-glass opacities
 - o Cysts: Small, round, thin-walled (2-4 mm in diameter)

TOP DIFFERENTIAL DIAGNOSES

- Respiratory bronchiolitis-interstitial lung disease
- Nonspecific interstitial pneumonia
- Hypersensitivity pneumonitis

PATHOLOGY

• Diffuse lung involvement by extensive accumulation of alveolar macrophages

CLINICAL ISSUES

- 40-60 years of age; M:F = 2:1; smokers (58-91%)
- Symptoms and signs
 - Dyspnea on exertion
 - Persistent cough

DIAGNOSTIC CHECKLIST

• Consider DIP in patients (particularly smokers) with bilateral lower lung zone predominant ground-glass opacities associated with intralobular lines and thin-walled cysts

(Left) Axial HRCT of a 67-yearold male smoker who presented with dyspnea shows patchy bilateral ground-glass opacities 🔁 and areas of spared normal pulmonary parenchyma. Note the small, thin-walled pulmonary cysts ∠ some of which could represent centrilobular emphysema. (Right) Axial HRCT of the same patient shows patchy ground-glass $opacities \supseteq$, multifocal thinwalled lung cysts 🔁, and subtle subpleural intralobular lines 🔁. Note the absence of fibrosis, architectural distortion, or honeycombing.

(Left) Low-power photomicrograph (H&E stain) of a lung biopsy specimen from a patient with desquamative interstitial pneumonia shows expansion and filling of alveolar spaces by a dense monotonous population of alveolar macrophages 🔁. (Right) Highpower photomicrograph (H&E stain) of the same specimen shows macrophages \implies filling the alveolar lumina and minimal interstitial fibrosis 🔁 or inflammation. The intracellular granular brown pigment 🔁 represents smoker's pigment.









Abbreviations

• Desquamative interstitial pneumonia (DIP)

Definitions

• Interstitial lung disease characterized by accumulation of pigmented macrophages within alveoli and distal pulmonary airspaces

IMAGING

General Features

- Best diagnostic clue
 - Bilateral, lower zone predominant ground-glass opacities ± subpleural intralobular lines

Radiographic Findings

- Normal (22%)
- Ill-defined bilateral airspace opacities
- Bilateral reticular opacities
- Predominant involvement of mid and lower lung zones

CT Findings

- HRCT
 - Ground-glass opacities (83-100%)
 - ± associated consolidation
 - Bilateral and moderately symmetric (> 50%)
 - Lower zone (73%), peripheral (59%), patchy (23%), diffuse (18%)
 - o Intralobular lines or reticular opacities (17-63%)
 - Subpleural predominance
 - Associated with ground-glass opacities
 - o Cysts
 - Small, round, thin-walled (2-4 mm in diameter)
 - o Less common
 - Traction bronchiectasis
 - Honeycombing
 - Emphysema
 - Subpleural nodules
 - Centrilobular nodules

Imaging Recommendations

Best imaging tool
 HRCT

DIFFERENTIAL DIAGNOSIS

Respiratory Bronchiolitis-Interstitial Lung Disease (RB-ILD)

- Ground-glass opacities (upper lobe predominance)
- Centrilobular nodules
- Intralobular lines/reticular opacities
- HRCT findings similar to those of DIP

Nonspecific Interstitial Pneumonia

- Basilar subpleural ground-glass opacities
 May exhibit subpleural sparing
- Basilar reticular opacities
- Traction bronchiectasis and bronchiolectasis

Hypersensitivity Pneumonitis

• Ground-glass opacities

- Centrilobular nodules (more common than in DIP)
- Reticular opacities (upper lobe predominance)
- Cysts (larger than those of DIP)
- Mosaic attenuation

PATHOLOGY

General Features

- Etiology
 - Smokers (58-91%)
 High smoking index (pack-years)
 - Nonsmokers (19%)
 - Occupational exposure to inorganic particles (Si, Mg, Ti, Fe, Ni, Pb)
 - Exposure to mycotoxins (aflatoxin)
 - Connective tissue diseases
 - Infection (cytomegalovirus, Aspergillus)
 - Use of marijuana

Microscopic Features

- Extensive accumulation of alveolar macrophages with intracellular granular brown pigment
- Mild chronic interstitial inflammation
- Mild to moderate fibrotic thickening of alveolar septa

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea on exertion (86%)
 - Persistent cough (65%)
- Other signs/symptoms
 - o Fever (31%)/fatigue (22%)/chest pain (19%)

Demographics

- Age
 - o 40-60 years
- Sex
- o M:F = 2:1

Natural History & Prognosis

- Good outcome (63%)
- Pulmonary fibrosis and death (25%)
- Relapse after cessation of treatment (18%)

Treatment

- Smoking or exposure cessation
- Corticosteroids
- Macrolides

DIAGNOSTIC CHECKLIST

Consider

 DIP in patients (particularly smokers) with bilateral lower lung zone predominant ground-glass opacities associated with intralobular lines and thin-walled cysts

SELECTED REFERENCES

 "Desquamative interstitial pneumonia: a systematic review of its features and outcomes." Merel E. Hellemons, Catharina C. Moor, Jan von der Thüsen, Mariska Rossius, Arlette Odink, Laila Haugen Thorgersen, Johny Verschakelen, Wim Wuyts, Marlies S. Wijsenbeek and Elisabeth Bendstrup. Eur Respir Rev 2020; 29: 190181. Eur Respir Rev. 29(157), 2020 (Left) PA chest radiograph of a patient with desquamative interstitial pneumonia shows multifocal bilateral right upper lung zone predominant hazy airspace disease and fine reticular opacities \implies (Right) Axial HRCT of the same patient shows multifocal bilateral ground-glass 🔁 and reticular → opacities. Reticular opacities have been described in desquamative interstitial pneumonia, often with coexisting ground-glass opacities. Frank honeycombing rarely occurs in patients with desquamative interstitial pneumonia.





(Left) PA chest radiograph of a patient with desquamative interstitial pneumonia not associated with cigarette smoking shows scattered bilateral ill-defined hazy and heterogeneous pulmonary opacities. (Right) Axial CECT of the same patient shows multifocal bilateral groundglass opacities 🔁 Desquamative interstitial pneumonia is , characteristically associated with cigarette smoking but may also develop from exposure to inhaled toxins, drugs, viral infections, and autoimmune diseases.

(Left) High-power

photomicrograph (H&E stain) of a specimen from the same patient shows alveolar filling by a dense and monotonous population of macrophages \square Note that there is only minimal thickening of the alveolar septa 🔁. (Right) Axial HRCT of a patient with desquamative interstitial pneumonia shows multifocal bilateral areas of ground-glass opacity 🔁 and small nodular consolidations 🔁. Note areas of relatively spared lung parenchyma.













(Left) PA chest radiograph of a patient with desquamative interstitial pneumonia shows bilateral ill-defined pulmonary opacities 🔁 slightly more conspicuous in the right upper lung zone. Based on imaging findings alone, the differential diagnosis includes acute processes, such as bacterial pneumonia. (Right) Axial CECT of the same patient shows ground-glass opacities, acinar nodules 🖂, and ill-defined consolidations ➡. Open lung biopsy was performed given persistent imaging abnormalities and confirmed the diagnosis.





(Left) AP chest radiograph of a patient with desquamative interstitial pneumonia shows subtle bilateral ill-defined hazy opacities. Affected patients may have normal or near-normal chest radiographs at presentation (in approximately 20% of cases). (Right) Axial HRCT of the same patient shows bilateral asymmetric ground-glass opacities and associated paraseptal and centrilobular emphysema ⊇. Desquamative interstitial pneumonia typically affects smokers in the 4th through 5th decades of life.





(Left) Axial HRCT of the same patient shows multifocal bilateral ground-glass opacities. While desquamative interstitial pneumonia is usually associated with smoking, the association is less robust than that of respiratory bronchiolitis or pulmonary Langerhans cell histiocytosis. (Right) Low-power photomicrograph (H&E stain) shows desquamative interstitial pneumonia manifesting with uniform intraalveolar macrophages 🔁 and minimal interstitial fibrosis 🔁 or inflammation. (From DP: Thoracic.)

TERMINOLOGY

- Pulmonary Langerhans cell histiocytosis (PLCH)
- Peribronchiolar infiltration by stellate nodules that contain Langerhans cells

IMAGING

- Radiography
 - Normal or increased lung volume
 - Symmetric upper lung zone predominant reticulonodular opacities, nodules, cysts
 - Spares lung bases
- HRCT
 - Irregular, small nodules and cysts with upper/mid lung zone predominance
 - Bronchiolocentric nodules, irregular/stellate borders, 1-10 mm in size
 - Cysts: Variable sizes and bizarre shapes, thin or thick/nodular irregular walls

TOP DIFFERENTIAL DIAGNOSES

- Lymphangioleiomyomatosis
- Silicosis
- Sarcoidosis
- Cystic metastases

PATHOLOGY

• Bronchiolocentric proliferation of Langerhans cells

CLINICAL ISSUES

- Symptoms and signs: Cough, dyspnea, chest pain, fever, weight loss; asymptomatic in 25%
- M = F; 20-40 years of age
- 95% of affected patients are cigarette smokers

DIAGNOSTIC CHECKLIST

• Consider PLCH in adult smokers with upper lung predominant small nodular &/or cystic lung disease

(Left) Graphic shows the morphologic features of the characteristic lung abnormalities in patients with pulmonary Langerhans cell histiocytosis, which include upper lung zone predominant small stellate nodules &/or cysts with relative sparing of the basilar lung parenchyma. (Right) PA chest radiograph of a 35-year-old female smoker with pulmonary Langerhans cell histiocytosis, cough, and dyspnea demonstrates upper and mid lung zone predominant small irregular nodules, some of which exhibit central lucency \implies .





(Left) Axial NECT of the same patient demonstrates upper lung zone predominant small cavitary and noncavitary nodules with normalappearing intervening lung parenchyma. Some nodules 🔁 exhibit a stellate morphology characteristic of pulmonary Langerhans cell histiocytosis lesions. (Right) Axial NECT of the same patient shows relative sparing of the lung bases with decreased profusion of lung cysts and nodules 🔁. The morphology of lung lesions and the disease distribution are characteristic.





Abbreviations

• Pulmonary Langerhans cell histiocytosis (PLCH)

Definitions

• Peribronchiolar infiltration of stellate nodules that contain Langerhans cells

IMAGING

General Features

- Best diagnostic clue
 - HRCT: Nodules + bizarre-shaped pulmonary cysts in upper and mid lung zones in cigarette smokers
- Location
 - Upper and mid lung
 - o Bilateral symmetrical involvement
 - Spares basilar lung near costophrenic angle
- Size
 - Nodules: 1-10 mm in diameter
 - Cysts: 1-3 cm in diameter
- Morphology
 - HRCT: Irregular stellate nodules
 - o Cysts: Variable wall thickness, variable shape

Radiographic Findings

- Radiography
 - Normal or increased lung volume
 - Upper and mid lung zone symmetric **reticulonodular opacities**
 - Multiple ill-defined **nodules**; 1-10 mm in diameter
 - Cysts; 1-3 cm in diameter
 - May not be evident on radiography
 - Upper and mid lung zone predominant involvement
 Spares basilar lung near costophrenic angles
 - Secondary spontaneous pneumothorax
 - Recurrent
 - Unilateral or bilateral
 - Uncommon features
 - Skeletal involvement: Lytic or expansile lesion(s)
 - Lymphadenopathy
 - Airspace disease
 - Solitary nodule
 - Pleural effusion
 - Normal chest radiograph

CT Findings

- NECT
 - Upper and mid lung zone predominance
 - Relative sparing of lung bases
- HRCT
 - Irregular, small nodules and cysts; normal intervening lung
 - Nodules
 - Centrilobular, peribronchial, peribronchiolar
 - Typically irregular/stellate borders; 1-10 mm; occasionally > 1 cm
 - Cavitary nodules with thick nodular walls
 - Range: Few to innumerable lung nodules
 - Nodules may progress to cavitary nodules and cysts

• Cysts

More common than nodules

- 1-10 mm, may be > 1 cm
- Variable sometimes bizarre shapes
- Thin or thick nodular/irregular walls
- Cysts ± nodules
- Ground-glass opacities, reticular opacities, septal lines, irregular bronchovascular bundles
- o Coalescent cysts, fibrosis, honeycomb lung in late disease

Imaging Recommendations

 Best imaging tool
 HRCT is optimal imaging modality for assessment of PLCH

DIFFERENTIAL DIAGNOSIS

Lymphangioleiomyomatosis

- Unique to females, unless related to tuberous sclerosis
- Spherical cysts, thin-walled, uniformly distributed
- Normal intervening lung
- Nodules uncommon
- Chylothorax may occur (pleural effusion rare in PLCH)

Centrilobular Emphysema

- Lung destruction with imperceptible walls and central lobular artery
- May mimic end-stage PLCH

Silicosis and Coal Worker's Pneumoconiosis

- Upper lobe perilymphatic nodules
- Eggshell lymph node calcifications
- Progressive massive fibrosis
- No pulmonary cysts

Sarcoidosis

- Upper lobe, perilymphatic nodules; cavitation very rare
- Hilar/mediastinal lymphadenopathy
- End-stage disease: Upper lobe fibrosis, cysts, honeycomb lung; may resemble end-stage PLCH

Cystic Metastases

- Should be considered in known malignancy
 - Squamous cell cancer
 - o Seminoma
 - o Sarcomas
 - o Transitional cell carcinoma

Pneumocystis jirovecii Pneumonia

- Pneumatoceles may manifest as lung cysts
- Cysts associated with ground-glass opacities

Laryngeal Papillomatosis

- Laryngeal and tracheal mural nodules
- Pulmonary nodules typically cavitate
- Cystic lesions typically in lower lobes and dorsal lungs

Birt-Hogg-Dubé

- Multiple pulmonary cysts with lower lung predominance
- Renal lesions (oncocytoma and renal cell carcinoma)
- Fibrofolliculomas of skin

Hypersensitivity Pneumonitis

- Upper lobe predominant involvement
- Ground-glass centrilobular nodules
- May exhibit cysts, but usually few in number

PATHOLOGY

General Features

- Etiology
 - Pathogenesis incompletely understood; likely myeloid neoplasm with inflammatory properties
 - Childhood PLCH: Clonal cellular process unrelated to smoking
 - Adult PLCH: Immune-mediated proliferation related to smoking: Smoke postulated to stimulate cytokine production and Langerhans cell activation
- PLCH preferred term for isolated pulmonary involvement
- Former terms of LCH variants; usage now discouraged
 - Hand-Schüller-Christian: Young adults and adolescents; lung, bone, pituitary involvement (diabetes insipidus)
 - Letterer-Siwe: Infants, multiorgan involvement, malignant Langerhans cells, poor prognosis
 - Eosinophilic granuloma: Single organ involvement of LCH

Gross Pathologic & Surgical Features

- Majority of affected adults have disease limited to lung
- Cellular and fibrotic lesions with variable cyst formation
 Well-defined, airway-centered nodules with irregular stellate borders
- End-stage: Fibrosis, honeycomb lung, cysts, emphysema

Microscopic Features

- Bronchiolocentric proliferation of granulomas
 - Langerhans cells positive for surface marker CD1a
 - Birbeck granules on electron microscopy are pathognomonic
 - BRAF gene mutation on immunohistochemistry
- Nodules
 - Bronchiolocentric (terminal and respiratory bronchioles), stellate-shaped
 - Typically < 1 cm in diameter; may be 1.5-2 cm
 - Intervening relatively normal or somewhat distorted lung
 - "Cavitary" nodules: Cavity represents enlarged airway lumen
 - o Thick- and thin-walled lung cysts
 - Granulomas destroy and remodel surrounding tissue
- Desquamative interstitial pneumonia (DIP), organizing pneumonia, and respiratory bronchiolitis (RB) may occur in adjacent lung
- Progression from dense cellular nodules to cavitary nodules to increasing fibrosis
 - Fibrotic scars surrounded by enlarged distorted airspaces

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonproductive cough, dyspnea, fatigue, chest pain, fever, weight loss
 - o Asymptomatic (25%)

- Pneumothorax in 25% during course of disease: Unilateral or bilateral; may recur
- Pulmonary function tests: \$\u2264 carbon monoxide diffusing capacity; normal total lung capacity

Demographics

- Age
 - o Typically 20-40 years of age; wide range
 - Sex
- \circ M = F
- Ethnicity
- Caucasian adults, less common in African AmericansEpidemiology
 - Smoking-related lung disease (95% in smokers)
 Only small percentage of smokers develop PLCH
 - Bone involvement, skin lesions, and diabetes insipidus
 <15%

Diagnosis

- Transbronchial lung biopsy
- Bronchoalveolar lavage: > 5% CD1a(+) Langerhans cells
- Open lung biopsy may be required

Natural History & Prognosis

- Early phase predominantly nodular; later phase predominantly cystic
- Disease may regress or resolve, become stable, or progress to advanced cystic disease
 - o 75% of patients with eventual resolution or stability
- May recur up to 7 years after presentation, even with smoking cessation
- May recur in transplanted lung
- End-stage disease may mimic panlobular emphysema or honeycomb lung
- Pulmonary artery hypertension (33%)
- Variable prognosis
 - Complete remission to respiratory failure
 - Mortality < 5%; worse in men, older, patients with recurrent pneumothorax

Treatment

- Smoking cessation
- Corticosteroids for progressive disease
- Chemotherapy and lung transplantation for advanced disease

DIAGNOSTIC CHECKLIST

Consider

• PLCH in adult smokers with upper lung predominant small nodular &/or cystic lung disease

Image Interpretation Pearls

• Characteristic HRCT appearance may be diagnostic in appropriate setting

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- 3. Vassallo R et al: Current understanding and management of pulmonary Langerhans cell histiocytosis. Thorax. 72(10):937-45, 2017





(Left) Coronal NECT of a , patient with pulmonary Langerhans cell histiocytosis shows characteristic small cysts with thick nodular walls and bizarre shapes 乏, which predominantly affect the upper lung zones and spare the lung bases. (Right) Sagittal NECT of a patient with pulmonary Langerhans cell histiocytosis with acute chest pain shows profuse pulmonary cysts ₽, small lung nodules \blacksquare , and a small anterior rightsided pneumothorax 🖂. Affected patients are at risk for secondary spontaneous pneumothorax.





(Left) Axial NECT of a patient with pulmonary Langerhans cell histiocytosis shows multifocal bilateral small cysts with thick irregular walls and centrilobular emphysema. The disease may occur in association with other smoking-related lung diseases, including emphysema. (Right) Axial NECT of a patient with pulmonary Langerhans cell histiocytosis shows thinwalled lung cysts of varying sizes, some with bizarre shapes. Associated cysts may exhibit smooth or irregular cyst walls and may mimic other cystic lung diseases.





(Left) Axial HRCT of a female smoker with end-stage pulmonary Langerhans cell histiocytosis shows profuse coalescent upper lung pulmonary cysts. Pulmonary abnormalities may exhibit regression, stability, or progression on serial imaging studies. (Right) Coned-down PA chest radiograph shows osseous and pulmonary involvement by Langerhans cell histiocytosis manifesting with a pathologic fracture 🔁 of the distal right clavicle through a lytic lesion and small right upper lobe cysts 🖂 and nodules 🔁.

TERMINOLOGY

- Combined pulmonary fibrosis and emphysema (CPFE)
 - Distinct but heterogeneous clinical entity; most often current or former heavy smokers

IMAGING

- Radiography
 - Bilateral upper lobe hyperlucency ± bullae
 - Bibasilar reticulation, honeycomb cysts, volume loss
 - Enlarged pulmonary trunk, right heart
- CT
 - Upper lobe emphysema ± bullae
 - o Bibasilar, subpleural honeycomb cysts
 - o Lower lobe traction bronchiectasis/bronchiolectasis
 - Bibasilar reticulation ± ground glass opacities
 - o Lower lobe volume loss
 - o Dilatation of central pulmonary arteries and right heart

TOP DIFFERENTIAL DIAGNOSES

- Respiratory bronchiolitis interstitial lung disease with fibrosis
- Desquamative interstitial pneumonia with fibrosing nonspecific interstitial lung disease
- End-stage pulmonary Langerhans cell histiocytosis

PATHOLOGY

- Emphysema: Airspace enlargement distal to terminal bronchioles
- Usual interstitial pneumonia pattern; variable features depending on underlying etiology

CLINICAL ISSUES

- Heavy smoking history in older men
- Pulmonary hypertension, lung cancer, acute exacerbation

DIAGNOSTIC CHECKLIST

• CT findings may suggest diagnosis, especially with low diffusing capacity for carbon monoxide

(Left) AP chest radiograph of a 70-year-old smoker shows a left upper lobe thin-walled bulla \bowtie and preserved upper lobe volume. The lower lobes show volume loss, basilar reticular opacities, and fine honeycomb cysts \supseteq that suggest a combination of smoking-related changes and lower lobe fibrosis. (Right) Coronal NECT of the same patient confirms a left upper lobe bulla \bowtie and scattered centrilobular emphysema, along with lower lobe traction bronchiectasis 🔁 and subpleural basilar honeycombing \supseteq .





(Left) Axial NECT of the same patient demonstrates multiple left upper lobe bullae and extensive centrilobular emphysema, consistent with long-term smoking-induced lung injury. (Right) Axial NECT of the same patient shows basilar predominant subpleural honeycomb spaces in multiple layers. Posterior displacement of the left oblique fissure \implies confirms lower lobe volume loss. After lung biopsy and multidisciplinary discussion, the final diagnosis was combined pulmonary fibrosis and emphysema.





Abbreviations

• Combined pulmonary fibrosis and emphysema (CPFE)

Definitions

- Idiopathic pulmonary fibrosis (IPF)/usual interstitial pneumonia (UIP) pattern on background of emphysema
- Other chronic fibrosing interstitial lung disease (ILD) on background of emphysema
- Distinct but heterogeneous clinical entity, most often affects current or former heavy smokers

IMAGING

General Features

- Best diagnostic clue
 - Upper lobe emphysema + basilar honeycombing, traction bronchiolectasis, reticulation

Radiographic Findings

- Upper lobe lucency, bullae, hyperinflation
- Basilar reticulation, honeycombing, volume loss
- Pulmonary hypertension (PH): Pulmonary trunk and right heart enlargement

CT Findings

- HRCT
 - Predominant upper lobe centrilobular emphysema ± bullae
 - Upper lobe cysts, no perceptible margins
 - Thin-walled cysts, bullae; may mimic honeycombing
 - Lower lobes: IPF/UIP pattern
 - Subpleural basilar predominant honeycombing
 - Traction bronchiectasis/bronchiolectasis
 - Basilar predominant reticulation
 - Lower lobes: Other fibrosing ILD patterns
 - Chronic (fibrotic) hypersensitivity pneumonitis
 - Connective tissue disease (CTD)-related ILD
 - Nonspecific interstitial pneumonia (NSIP)
 - PH
 - Dilatation of central/segmental pulmonary arteries
 - Right heart chamber enlargement
 - Progressive lower lobe volume loss
 - New ground-glass opacities: Acute exacerbation
 - New/enlarging nodule or mass: Lung cancer

Imaging Recommendations

- Best imaging tool
 - HRCT for optimal characterization of coexistent emphysema and progressive fibrotic lung disease

DIFFERENTIAL DIAGNOSIS

Respiratory Bronchiolitis-Associated ILD (RB-ILD)

- Upper lobe centrilobular hazy nodules in smokers
- Subpleural reticular opacities, upper lobe air-trapping

Desquamative Interstitial Pneumonia (DIP) With Fibrosing NSIP

- Smokers with diffuse or patchy ground-glass opacities
- Reticulation, traction bronchiectasis/bronchiolectasis
- Extensive honeycombing atypical; no basilar predominance

Pulmonary Langerhans Cell Histiocytosis (PLCH)

- Earlier onset: Young to middle-aged adult smokers
- Upper lobe nodules and cysts; coexist with emphysema
- End-stage PLCH (unusual): Fibrotic scars, cysts, bullae

PATHOLOGY

General Features

- Etiology
 - Smoking ± gastroesophageal reflux may potentiate fibrosis
 - Smoking-related lung injury with limited pulmonary fibrosis; varied expressions and nomenclature
 - CPFE: Diffuse and progressive fibrosis in smokers

Microscopic Features

- Emphysema: Airspace enlargement ± RB, DIP
- UIP: Fibroblastic foci, honeycomb cysts, lobular collapse

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Smoker with worsening cough and progressive dyspnea
- Other signs/symptoms
 - Finger clubbing, hypoxemia
 - o PH, right heart strain

Demographics

- Mean age; ~ 70 years
- Sex: M > F (~ 4:1)

Natural History & Prognosis

- Clinical course and prognosis varies per type of fibrosing ILD
- Increased risk of PH (WHO Group 3): 50-90%
- Increased risk of lung cancer: 30-47%

Treatment

- Smoking cessation limits ongoing lung inflammation
- Antifibrotic therapy may slow progression

Diagnosis

- May require multidisciplinary discussion
- HRCT findings strongly suggest diagnosis
- Impaired diffusion capacity for carbon monoxide (DLCO)
 - Coexisting obstruction and restriction may deceptively "normalize" lung function tests
- Lung biopsy ± bronchoalveolar lavage (BAL) may be required for confirmation

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Timely recognition of characteristic CPFE imaging findings impacts treatment and prognosis

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Asbestosis

KEY FACTS

TERMINOLOGY

 Asbestosis: Interstitial lung disease caused by inhalation of asbestos fibers

IMAGING

- Radiography
 - o Pleural plaques (25%)
 - o Late disease: Basilar reticular opacities, honeycombing

• CT/HRCT

- Reticular opacities most common manifestation
- Subpleural dot-like (centrilobular) or branching opacities, earliest manifestation
- o Subpleural curvilinear lines: Parallel adjacent chest wall
- Parenchymal bands: Perpendicular to pleura
- Lower lobe predominant subpleural fibrosis, traction bronchiectasis, and honeycombing in advanced disease
- Mosaic attenuation from small airways disease
- Pleural plaques (80%-95%): Most reliable finding for differentiation of asbestosis from IPF

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic pulmonary fibrosis
- Systemic sclerosis
- Rheumatoid arthritis
- Hypersensitivity pneumonitis
- Drug-induced lung disease
- Lymphangitic carcinomatosis

PATHOLOGY

• Lung fibrosis + asbestos bodies = asbestosis

CLINICAL ISSUES

- Slowly progressive dyspnea and nonproductive cough
- Asbestos is potent carcinogen: Multiplicative risk factor for lung cancer in cigarette smokers

DIAGNOSTIC CHECKLIST

Consider asbestosis in patients with basilar interstitial lung • disease and pleural plagues

(Left) PA chest radiograph of a 55-year-old man with asbestosis and progressive dyspnea shows low lung volume and diffuse bilateral reticular opacities. Note bilateral calcified pleural $plaques \supseteq$ over the central diaphragmatic pleura. (Right) Axial HRCT of the same patient shows multifocal bilateral subpleural reticular opacities times with associatedtraction bronchiolectasis \implies and basilar subpleural honeycombing 🔁. Note calcified and noncalcified bilateral paravertebral pleural plaques 🔁.

(Left) Low-power

of a specimen of asbestosis shows numerous asbestos bodies \supseteq within airspaces.

background is virtually replaced by dense fibroconnective tissue 🖂

subpleural ground-glass

The latter is a common CT

asbestosis.









Definitions

• Fibrosing interstitial lung disease caused by inhalation of asbestos fibers

IMAGING

General Features

Best diagnostic clue
 Basilar subpleural reticulation (fibrosis) + pleural plaques

Radiographic Findings

- Radiography
 - o May be normal (10-20%)
 - o Pleural plaques (25%)
 - International Labor Office (ILO) classification compared to standard radiograph "B" reading
 - Asbestosis: s, t, or u opacities
 - o Late disease: Basilar reticular opacities, honeycombing
 - Lung cancer: Nodule or mass ± lymphadenopathy
 - Predilection for lower lungs in contrast to upper lung zone predominance in general population of smokers

CT Findings

- Reticular opacities most common manifestation
 o Interlobular septal thickening &/or intralobular lines
- Subpleural dot-like (centrilobular) or branching opacities earliest manifestation
 - Fibrosis around small airways related to asbestos fiber deposition
- Subpleural curvilinear lines
 - Parallel chest wall within 1 cm of pleura; 5-10 cm long
 - Peribronchial confluent fibrosis or atelectasis associated with obstructed respiratory bronchioles
 - Not specific for asbestosis
- Parenchymal bands perpendicular to pleura
 - o 2-5 cm long
 - Fibrosis along interlobular septa or bronchovascular bundles
- Small airways disease from fibrosis related to asbestos fiber deposition
 - May produce mosaic attenuation pattern
- Fibrosis with traction bronchiectasis and honeycombing in advanced disease
 - o Reflects initial location of deposited asbestos fibers
 - Peripheral basilar lung most commonly affected
 - May exhibit usual interstitial pneumonia (UIP) pattern
- Pleural plaques (80-95%); for reliable differentiation of asbestosis from idiopathic pulmonary fibrosis (IPF)
 - Honeycombing and traction bronchiectasis less common than in IPF
- Nodule or mass regarded as suspicious for lung cancer
- Imaging Recommendations
- Best imaging tool
 - CT: Identification of fibrosis; evaluation of nodules, pleural plaques, and rounded atelectasis
 - Screening of asbestos-exposed workers
 - 10% of asbestos-exposed workers screened on CT for asbestosis have lung mass

- Patients with clinical asbestosis: Abnormal chest radiographs in 80%; abnormal HRCT in 96%
- 33% of patients without clinical or radiographic evidence of asbestosis have abnormal HRCT
 False-negatives for early asbestosis (25%)
- False-negatives for early aspestosi
- Protocol advice
 - Prone imaging to differentiate interstitial lung disease from dependent atelectasis

DIFFERENTIAL DIAGNOSIS

Idiopathic Pulmonary Fibrosis

- Basilar subpleural reticulation and honeycombing with traction bronchiectasis/bronchiolectasis
- Band-like opacities and mosaic attenuation less common
- No pleural plaques

Progressive Systemic Sclerosis

- Basilar subpleural opacities
- No pleural plaques; pleural thickening and pseudo-plaques common
- Dilated esophagus

Rheumatoid Arthritis

- Arthritis and joint erosions
- Basilar subpleural ground-glass opacities and reticulations
- No pleural plaques

Hypersensitivity Pneumonitis

- Mosaic attenuation, air-trapping
- Upper lung zone fibrosis, less severe in lung bases
- No pleural plaques

Drug-Induced Lung Disease

- Various patterns of interstitial fibrosis
- No pleural plaques

Lymphangitic Carcinomatosis

- Nodular or smooth interlobular septal and peribronchovascular thickening
- Pleural effusion and lymphadenopathy common
- No pleural plaques

PATHOLOGY

General Features

- Associated abnormalities
 - Asbestos-related pleural disease
 - Multifocal discontinuous pleural thickening ± calcification
 - Characteristic involvement of pleura over central tendinous portion of hemidiaphragms
 - Benign exudative pleural effusion
 - Diffuse pleural thickening
 - Rounded atelectasis
 - Lung cancer
 - o Malignant pleural mesothelioma
- General
 - Asbestos: Heat resistant, high tensile strength, flexible, durable
 - Serpentine (chrysotile or white asbestos, 90% of commercial asbestos)
 - □ Wavy fiber, long (> 100 μm), diameter (20-40 μm)

- Amphibole
 - □ Crocidolite (blue asbestos), amosite (brown asbestos), anthophyllite, tremolite, actinolite
 - □ Straight rigid fiber; length:width = 3:1 (aspect ratio)
- Retention: Long, thin fibers > short, thick fibers
- Pathophysiology
 - Increased lower lung zone fiber deposition from gravitational ventilatory gradient
 - Fiber deposition in respiratory bronchioles
 - No fiber removal by lymphatics; largest most harmful fibers too large to be removed by macrophages
- Epidemiology
 - Long-term exposure: Asbestos mills, insulation, shipyards, construction
 - Dose-response relationship
 - Usually high dust concentrations
 - Typically 20 years following initial exposure, but latency period could be as short as 3 years
 - 1% risk of asbestosis with cumulative dose of 10 fiberyear/mL: Calculation of cumulative dose; years of exposure x fibers/mL (fibers/mL = measurement of ambient airborne asbestos)

Staging, Grading, & Classification

- Histologic grading of asbestosis: Asbestosis Committee of College of American Pathologists and Pulmonary Pathology Society
 - Grade 0: No peribronchiolar fibrosis or fibrosis confined to bronchiolar walls
 - Grade 1: Fibrosis confined to wall of respiratory bronchioles and first tier of adjacent alveoli
 - o Grade 2: Extension of fibrosis to alveolar ducts or ≥ 2 tiers of alveoli adjacent to respiratory bronchiole; sparing of some alveoli between adjacent bronchioles
 - Grade 3: Fibrosis of all alveolar walls between ≥ 2 adjacent respiratory bronchioles
 - Grade 4: Honeycombing

Gross Pathologic & Surgical Features

- Volume loss
- Coarse basilar predominant honeycombing

Microscopic Features

- Asbestosis
 - Early fibrosis: Centered on respiratory bronchioles with centrifugal spread
 - Patchy distribution, severe honeycombing uncommon
 Fibrosis associated with > 1 million fibers/g lung tissue
- Asbestos (ferruginous) bodies: Fibers coated with ferritin
 - Hemosiderin-coated fiber (mostly amphibole)
 Incompletely phagocytized by macrophages
 - Not pathognomonic for asbestosis
 - Coated fibers fewer than uncoated fibers
 - No correlation with fibrosis
- Fibrosis + asbestos bodies = asbestosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Gradual onset of dyspnea on exertion, nonproductive cough

- Rales (end-inspiratory crackles)
- o Clubbing in 1/3 of affected patients
- Other signs/symptoms
 - Pulmonary function tests
 - Restrictive physiology, decreased diffusion capacity
 - Decreased small airway flow rates

Demographics

- Sex
 - o Men, typically due to occupational exposure

Diagnosis

- Asbestos bodies in bronchoalveolar lavage fluid highly specific for diagnosis of asbestosis
- Poor transbronchial biopsy yields
- American Thoracic Society 2003 general criteria for diagnosis
 - Evidence of structural pathology consistent with asbestosis as documented by imaging or histology
 - Evidence of causation as documented by occupational and exposure history
 - Includes pleural plaques and asbestos bodies
 - Exclusion of alternative plausible causes for findings

Natural History and Prognosis

- Latency period: 20-30 years
- Slowly progressive disease; does not regress
- Mortality increases with increasing severity of fibrosis
- Asbestos is potent carcinogen
 - Multiplicative risk factor for lung cancer in cigarette smokers; high proportion of smokers with asbestosis (1 in 4) die of lung cancer
- Increased risk of malignant pleural or peritoneal mesothelioma
- Increased risk of oropharyngeal, laryngeal, renal, and gastrointestinal cancers, and leukemia

Treatment

- No treatment
- Smoking cessation
- Control and regulation of asbestos in workplace
- Occupationally exposed affected individuals eligible for worker's compensation
 - Pathologic tissue not required to gain compensation

DIAGNOSTIC CHECKLIST

Consider

- Asbestosis in patients with basilar interstitial lung disease and pleural plaques
- Lung cancer screening in cigarette smokers with asbestosis

Reporting Tips

• Asbestosis may be reportable disease in some states

- 1. Bhandari J et al: Asbestosis 2021
- Musk AW et al: Asbestos-related diseases. Int J Tuberc Lung Dis. 24(6):562-7, 2020
- 3. Walkoff L et al: Chest imaging in the diagnosis of occupational lung diseases. Clin Chest Med. 41(4):581-603, 2020
- Arakawa H et al: Asbestosis and other pulmonary fibrosis in asbestosexposed workers: high-resolution CT features with pathological correlations. Eur Radiol. 26(5):1485-92, 2016

Asbestosis





(Left) Axial HRCT of an 83year-old man with occupational exposure to asbestos and progressive dyspnea shows bilateral subpleural reticular opacities \square with interlobular septal thickening and intralobular lines, traction bronchiectasis 🔁, mosaic attenuation, and calcified pleural plaques 🔁. (Right) Prone axial HRCT of the same patient shows subpleural reticulation \supseteq and traction bronchiolectasis 🔁 The combination of subpleural fibrosis and pleural plaques is virtually diagnostic of asbestosis.





(Left) Axial HRCT of a patient with asbestosis shows bilateral posterior pleural thickening with calcifications \square , subpleural reticulations , and a spiculated left lower lobe mass 🔁 with volume loss, which exhibited the comet-tail sign (not shown) of rounded atelectasis. (Right) Axial CECT of a patient with asbestosis shows a right lower lobe primary lung cancer 🖾 manifesting as a mass. Note bilateral discontinuous calcified pleural plaques 🖂 Asbestos exposure is a risk factor for both lung cancer and malignant mesothelioma.





(Left) Coronal CECT of a patient with asbestosis shows subpleural reticulations and honeycombing, pleural plaques 🔁, a left upper lobe mass 🔁 representing a primary lung cancer, and solid left apical pleural metastases □ (Right) Coronal FDG PET/CT of the same patient shows the FDG avid left upper lobe lung cancer 🔁, left apical solid pleural metastases $\overline{\rightarrow}$, and bilateral metastatic hilar 🔁 and mediastinal 🄁 lymphadenopathy. Asbestos exposure multiplies the risk of primary lung cancer in cigarette smokers.

KEY FACTS

TERMINOLOGY

- Coal worker's pneumoconiosis (CWP)
- Progressive massive fibrosis (PMF)
- Silicosis and CWP: Lung diseases due to inorganic mineral dust inhalation

IMAGING

• Radiography

- o 1- to 3-mm nodules; may calcify
- Upper lung zone predominant
- PMF: Upper lobe aggregation of nodules into masses
- Acute silicoproteinosis: Central alveolar opacities with air bronchograms; mimics alveolar proteinosis

• HRCT

- Perilymphatic micronodules
- Upper lobe masses
- Hilar/mediastinal lymphadenopathy; may calcify (eggshell Ca++)

TOP DIFFERENTIAL DIAGNOSES

- Sarcoidosis
- Tuberculosis
- Hypersensitivity pneumonitis
- Lung cancer

CLINICAL ISSUES

- Occupations: Sandblasting, quarrying, mining, glassblowing, pottery
- Simple silicosis: Asymptomatic
- Complicated silicosis (PMF)
- o Symptomatic
- Death from respiratory failure, pneumothorax, tuberculosis

DIAGNOSTIC CHECKLIST

• Consider thorough occupational history review in any patient with upper lobe nodular interstitial lung disease

(Left) PA chest radiograph of a patient with simple silicosis shows bilateral upper lung zone predominant pulmonary micronodules. (Right) Axial NECT of the same patient shows diffuse predominantly peribronchovascular 🔁 micronodules and nodules disposed along the interlobar fissures 🔁. This combination of peribronchovascular and subpleural nodules is characterized as perilymphatic. Sarcoidosis and lymphanaitic carcinomatosis exhibit a similar distribution.





(Left) PA chest radiograph of a patient with complicated silicosis (i.e., progressive massive fibrosis) shows bilateral upper lobe peribronchovascular masses \square with irregular borders. (Right) Axial HRCT of the same patient shows bilateral upper lobe predominant soft tissue masses and peribronchovascular micronodules. The masses result from coalescence of peribronchovascular nodules. These masses may cavitate and may exhibit FDG uptake, thus mimicking malignancy.





Abbreviations

• Coal worker's pneumoconiosis (CWP)

Synonyms

 Simple pneumoconiosis, complicated pneumoconiosis, progressive massive fibrosis (PMF), anthracosis, anthracosilicosis

Definitions

- Silicosis and CWP: Lung diseases due to inhalation of crystalline silicon dioxide or silica and inorganic mineral dusts
- **Simple or chronic pneumoconiosis**: Lung nodules < 1 cm, profuse in upper lung zones, often with hilar/mediastinal lymphadenopathy
- **Complicated pneumoconiosis** (PMF): Coalescence of nodules into larger lesions > 1 cm
- Acute silicoproteinosis: Resembles alveolar proteinosis, develops within weeks after heavy dust exposure
- **Caplan syndrome**: CWP + rheumatoid arthritis + necrobiotic nodules
- Chronic interstitial pneumonia: Pulmonary fibrosis

IMAGING

General Features

- Best diagnostic clue
 - Perilymphatic micronodules with upper lung zone predominance ± PMF
- Location
 - Spherical dusts predominantly affect upper lungs
 - Coal dust accumulates about respiratory bronchioles
 Silica accumulates along lymphatics: Centrilobular and
 - peripheral secondary pulmonary lobule
- Size
 - o Nodule 1-3 mm

Radiographic Findings

- Abnormalities seen 10-30 years after exposure
- Silicosis and CWP are similar; but less severe lung disease in CWP
- Hilar and mediastinal lymphadenopathy; may calcify (eggshell Ca++)
- Simple pneumoconiosis
 - 1- to 3-mm nodules with upper lobe predominance; may calcify
- Complicated pneumoconiosis (PMF)
 - Nodule > 1-cm diameter
 - Location: Usually bilateral, right > left, dorsal lung, central migration over time
 - May be lenticular (wide on PA, narrow on lateral radiography)
 - Lateral PMF margin roughly parallels chest wall and is sharply-defined; medial inner edge less well-defined
 - Decreased nodule profusion due to nodule aggregation into PMF
 - ± amorphous calcification
 - May cavitate; ± mycetoma formation in cavities
 - Paracicatricial emphysema peripheral to PMF; risk for pneumothorax

- Acute silicoproteinosis
 - o Central "butterfly" alveolar opacities + air bronchograms
 - Frequent hilar/mediastinal lymphadenopathy
 - Rapid progression over months
 - Evolution to fibrosis with severe architectural distortion, bullae, pneumothorax
- Caplan syndrome: Association of rheumatoid arthritis with pneumoconiosis
 - Multiple large nodules/masses, < 5 cm (may cavitate or calcify)
 - o Nodules are peripheral and subpleural
 - Cavitation may lead to pneumothorax
 - o Nodules may evolve quickly or resolve
 - o Nodules enlarge faster than silicotic PMF
 - Findings of rheumatoid arthritis: Humeral or clavicular erosions; lung abnormalities may precede bone disease

CT Findings

• HRCT

- More sensitive than radiography
- Perilymphatic micronodules, nodules < 7 mm
- More profuse in dorsal upper lobes, right > left
- Silicotic nodules more sharply-defined than those of CWP
- ± calcification
- Aggregate subpleural nodules may produce pseudoplaques
- Intralobular lines and interlobular septal thickening uncommon
- Mass (aggregation of micronodules into PMF)
 - Irregular elliptical shape; emphysema peripheral to mass
 - > 4 cm; low-attenuation areas secondary to necrosis
- Hilar/mediastinal lymphadenopathy; may calcify (eggshell Ca++ in 5%)
- Chronic interstitial pneumonia (12%)
 - Honeycombing and traction bronchiectasis
 - Usual interstitial pneumonia (UIP) or inconsistent with UIP pattern
 - Reticulation &/or honeycombing; subpleural or peribronchovascular
 - □ Ground-glass opacities

Nuclear Medicine Findings

- PET/CT
 - PMF may exhibit FDG avidity and mimic lung cancer

Imaging Recommendations

- Best imaging tool
 - HRCT more sensitive than radiography for detection of lung disease and detection/evaluation of PMF

DIFFERENTIAL DIAGNOSIS

Sarcoidosis

- Absence of occupational exposure, PMF less frequent
- Clustered nodules (galaxy sign)

Tuberculosis

• Centrilobular or miliary nodules; do not aggregate as masses

Pulmonary Langerhans Cell Histiocytosis

- Subpleural nodules unusual; no PMF
- Cysts, often irregular; absent in pneumoconiosis

Hypersensitivity Pneumonitis

- Ground-glass centrilobular nodules; no PMF; primarily mid lung involvement
- Air-trapping common; less likely in pneumoconiosis

Talcosis

- Nodules generally smaller, < 1 mm in diameter
- Panlobular emphysema, more common in lower lobes

Lung Cancer

- May be indistinguishable from PMF; may cavitate and exhibit FDG avidity on PET/CT
- Follow-up imaging or tissue sampling often required

PATHOLOGY

General Features

- Etiology
 - Inhaled silica dust, silicon dioxide (SiO₂), or coal dust deposited in respiratory bronchioles; removed by macrophages and lymphatics
 - Slow removal, half-time of single dust burden ~ 100 days
- Silica more fibrogenic than coal
- Increased risk of tuberculosis

Gross Pathologic & Surgical Features

- Primarily involves upper lung zones
- PMF may progress to end-stage fibrosis
- Silica content in affected lung 2-3% (up to 20%); silica content in normal dried lung 0.1%

Microscopic Features

- Silica
 - Silica particles centered within concentric lamellae of collagen along bronchioles, small vessels, and lymphatics
 - Birefringent silica crystals (1-3 μ) on polarized microscopy
 - Silica-laden macrophages carry particles to hilar/mediastinal lymph nodes and form granulomas
 - Silicoproteinosis: High silica concentrations, alveoli filled by lipoproteinaceous material, similar to alveolar proteinosis
- Coal
 - Coal macule: Stellate collection of macrophages containing black particles (1-5 μ) in terminal/respiratory bronchioles and pleural lymphatics; little or no collagen
 - Macule surrounded by focal emphysema

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Symptoms
 - None with simple silicosis
 - Miners commonly smoke and may have bronchitis or emphysema
 - Cough, dyspnea, ↑ sputum in complicated disease
 - Black sputum in coal workers
- Other signs/symptoms
 - Cor pulmonale in advanced disease

- o Caplan syndrome: Features of rheumatoid arthritis
- Clinical profile
 - Typical occupations: Sandblasting, quarrying, mining, glassblowing, pottery
 - Coal mines usually contain silica
 - Acute silicoproteinosis: Massive exposure to silica dust, usually in sandblasters
 - Recent attention to artificial stone workers (i.e., quartz) with higher content of silica and other fibrinogenic metals such as iron, zirconium, titanium, and aluminium; known to induce sarcoid-like reactions; may exhibit faster disease progression
- Pulmonary function tests
 - Simple pneumoconiosis: Usually normal
 - **Complicated pneumoconiosis**: ↓ diffusion capacity, ↓ lung volume, restrictive defect
 - Often mixed obstruction and restriction: Combined effects of cigarette smoking and interstitial fibrosis
 - Functional impairment correlates more closely with degree of emphysema (as determined by CT) than with nodule profusion

Demographics

- Age
 - Simple and complicated pneumoconiosis rare in patients < 50 years of age
- Sex
 - More common in men due to occupational exposure
- Epidemiology
 - Risk related to dose (intensity of exposure) and time (length of exposure)
 - o ~15% of miners may develop interstitial fibrosis

Natural History & Prognosis

- Typically > 20 years of exposure
- Simple pneumoconiosis: Normal longevity
- Complicated PMF: Death from respiratory failure, pneumothorax, tuberculosis
- Silicoproteinosis: Death within 2-3 years
- Debatable increased risk of lung cancer

Treatment

- Prevention: Respirators in dusty environments, reduction of ambient dust concentrations
- Removal from work environment exposure
- Smoking cessation
- No specific treatment for pneumoconiosis available
- At risk for tuberculosis: Cavitation in PMF requires culture
 Tuberculosis skin tests

DIAGNOSTIC CHECKLIST

Consider

• Thorough review of occupational history in any patient with upper lobe nodular lung disease

- Hoy RF: Artificial stone silicosis. Curr Opin Allergy Clin Immunol. 21(2):114-20, 2021
- Jones CM et al: Silicosis in artificial stone workers: spectrum of radiological high-resolution CT chest findings. J Med Imaging Radiat Oncol. 64(2):241-9, 2020





(Left) Axial HRCT of a patient with complicated silicosis (i.e., progressive massive fibrosis) shows bilateral perilymphatic micronodules. While nodules are more profuse centrally (i.e., peribronchovascular), there is also nodularity along the interlobar fissures 🔁. (Right) Coronal NECT of the same patient shows bilateral upper lobe predominant soft tissue masses \implies representing coalescent progressive massive fibrosis. While endstage sarcoidosis may mimic these imaging findings, affected patients do not have a history of silica exposure.





(Left) Axial FDG PET/CT of a patient with complicated silicosis (i.e., progressive massive fibrosis) shows FDGavid upper lobe predominant masses 🖂 amid a background of emphysema and perilymphatic micronodules. (Right) Axial HRCT of a patient with chronic interstitial pneumonia due to silicosis shows bilateral subpleural ground-glass opacities, reticulation \supseteq , and traction bronchiolectasis 🔁. Chronic interstitial pneumonia may be a manifestation of silicosis and may mimic idiopathic interstitial pneumonia.





(Left) Axial CECT of a patient with complicated silicosis shows bilateral upper lobe soft tissue masses. Note cavitation \supseteq within the left upper lobe mass and intrinsic dependent soft tissue, consistent with mycetoma. Cavitation may occur in complicated silicosis. (Right) Coronal CECT of the same patient shows upper lobe masses with cavitation 🔁 on the left and calcified bilateral hilar and mediastinal lymph nodes 🔁 Peripheral lymph node calcifications are referred to as eggshell calcifications.

KEY FACTS

TERMINOLOGY

- Giant cell interstitial pneumonia (GIP)
- Pneumoconiosis resulting from inhalation of hard metals
- Hard metals: Cobalt and cobalt alloys (e.g., tungsten)
- Hypersensitivity reaction with histologic GIP

IMAGING

- CT
 - Ground-glass opacities
 - Lower lobe predominance
 - May improve on serial imaging
 - Reticular opacities
 - No change on serial imaging
 - o Consolidations
 - Centrilobular nodules (rare)
 - Honeycombing (rare); similar morphology and distribution as usual interstitial pneumonia pattern
 - o Mediastinal lymphadenopathy

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic pulmonary fibrosis
- Fibrotic nonspecific interstitial pneumonia
- Lymphoid interstitial pneumonia
- Pulmonary alveolar proteinosis
- Pneumocystis jirovecii pneumonia

PATHOLOGY

- Constrictive bronchiolitis (earliest manifestation)
- Interstitial thickening with fibrous tissue deposition and mononuclear inflammatory cell infiltration
- Subacute fibrosing alveolitis: Accumulation of macrophages and multinucleated giant cells in alveolar spaces

CLINICAL ISSUES

- Cough, exertional dyspnea
- \$\product diffusing capacity for carbon monoxide
- Treatment: Avoid exposure, bronchodilators, corticosteroids

(Left) PA chest radiograph of a 47-year-old man with hard metal pneumoconiosis shows bilateral lower lobe predominant patchy airspace opacities 🔁. (Right) Axial HRCT of the same patient shows diffuse bilateral centrilobular ground-glass micronodules \square and patchy ground-glass opacities 🔁 Ground-glass and reticular opacities are considered classic findings of hard metal pneumoconiosis, but consolidations, centrilobular nodules, honeycombing, and lymphadenopathy have also been described.





(Left) Axial HRCT of the same patient shows right lower lobe patchy ground-glass opacities 🔁 and subtle reticulations 🔁. (Right) Axial HRCT of the same patient shows centrilobular ground-glass micronodules 🖂, patchy ground-glass opacities 🔁, and mild subpleural reticulation 🔁. Affected patients often present after 10-12 years of exposure with cough, shortness of breath, weight loss, and fatigue and classically exhibit impaired diffusing capacity and restrictive physiology. Biopsy showed giant cell interstitial pneumonia.





Synonyms

• Giant cell interstitial pneumonia (GIP)

Definitions

- Pneumoconiosis resulting from hard metal inhalation
 Hard metals: Cobalt and cobalt alloys (e.g., tungsten)
 - Hypersensitivity reaction with histologic features of GIP

IMAGING

General Features

- Best diagnostic clue
 - Exposure to hard metal
 - HRCT findings of bilateral reticulation ± ground-glass opacity
- Location
 - Bilateral, lower lung zone predominance

Radiographic Findings

- Reticular opacities ± hazy opacities
- Lower lung zone predominant reticular opacities
- Random distribution of hazy opacities

CT Findings

- HRCT
 - Lower lobe ground-glass opacities
 - May demonstrate improvement on serial imaging
 - Reticular opacities do not change on serial imaging
 - Consolidations
 - Centrilobular nodules (rare)
 - Honeycombing (rare); similar morphology and distribution as usual interstitial pneumonia (UIP) pattern
 - o Mediastinal lymphadenopathy

Imaging Recommendations

 Best imaging tool o HRCT

DIFFERENTIAL DIAGNOSIS

Idiopathic Pulmonary Fibrosis

- Basilar subpleural honeycombing; UIP pattern
- Absence of occupational exposure

Fibrotic Nonspecific Interstitial Pneumonia

- Basilar subpleural fibrosis
- Absence of occupational exposure

Lymphoid Interstitial Pneumonia

- Lung cysts, ground-glass opacities
- History of autoimmunity (e.g., Sjögren syndrome, rheumatoid arthritis)

Pulmonary Alveolar Proteinosis

• Ground-glass opacities on background of interlobular septal thickening and intralobular lines; so-called crazy-paving pattern

Pneumocystis Jirovecii Pneumonia

- Acute or subacute presentation
- History of immunosuppression (e.g., human immunodeficiency virus infection)

PATHOLOGY

General Features

• GIP represents a hypersensitivity reaction

Staging, Grading, & Classification

• Progression of disease may produce parenchymal remodeling and honeycombing

Microscopic Features

- Constrictive bronchiolitis (earliest manifestation)
- Interstitial thickening with fibrous tissue deposition and mononuclear inflammatory cell infiltration
- Subacute fibrosing alveolitis: Accumulation of macrophages and multinucleated giant cells in alveolar spaces
- Interstitial fibrosis and cysts rare; may occur after many years of exposure
- Increased concentration of hard metals compared to normal population (10x) on atomic absorption spectrophotometry or ionic coupled plasma emission spectrometry

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Cough, exertional dyspnea, fatigue, weight loss
- Other signs/symptoms
 - $\circ \downarrow$ diffusing capacity for carbon monoxide
 - Restrictive or mixed restrictive and obstructive pattern on pulmonary function tests
- Clinical profile
 - Exposure: Hard metal and diamond polishing industries
 - Source of cobalt may not always be clear
 - Association with cobalt exposure from e-cigarette use

Demographics

- Low prevalence in exposed workers
 - ~ 11% of 1,039 workers have work-related wheezing;
 0.7% have radiographic evidence of interstitial lung disease
 - 45% of patients with radiographic interstitial abnormalities show progressive disease over time

Natural History & Prognosis

 Manifests after 10-12 years of exposure (latency period as short as 2 years)

Treatment

- Acute and subacute phases
 - Avoidance of exposure
 - o Bronchodilators and inhaled corticosteroids
- Fibrotic phase
 - Systemic corticosteroids

- Fels Elliott DR et al: Giant cell interstitial pneumonia secondary to cobalt exposure from e-cigarette use. Eur Respir J. 54(6), 2019
- Adams TN et al: Cobalt related interstitial lung disease. Respir Med. 129:91-7, 2017
- Khoor A et al: Giant cell interstitial pneumonia in patients without hard metal exposure: analysis of 3 cases and review of the literature. Hum Pathol. 50:176-82, 2016

Berylliosis

KEY FACTS

TERMINOLOGY

- Chronic beryllium disease (CBD)
- Beryllium used in multiple industries
- Inhalation produces 2 types of lung injury
 - Acute chemical pneumonitis (uncommon) Chronic granulomatous disease
- Diagnosis requires
 - History of beryllium exposure
 - Positive beryllium-specific lymphocyte proliferation test (in blood or bronchoalveolar lavage fluid)
 - Noncaseating granulomas on histology

IMAGING

- Imaging findings similar to those of sarcoidosis
 - Parenchymal nodules and interlobular septal thickening
 Mediastinal and hilar lymphadenopathy
- Lymphadenopathy is always associated with lung disease
- Chronic fibrosis with upper lobe predominance

TOP DIFFERENTIAL DIAGNOSES

- Sarcoidosis
- Silicosis
- Tuberculosis
- Hypersensitivity pneumonitis (fibrotic)

PATHOLOGY

- Noncaseating pulmonary granulomas
- May be indistinguishable from sarcoidosis except for demonstration of beryllium-specific immune response

CLINICAL ISSUES

- CBD develops ~ 10-20 years after 1st exposure
 CBD occurs in 2-5% of beryllium-exposed workers
- Lung is primarily affected
- Extrapulmonary disease is rare
 - Dermatitis, ulcers, dermal granulomas, hepatosplenomegaly (granulomatous infiltration)

(Left) Axial CECT of a 57-yearold man with exposure to beryllium for 8 years shows multiple micronodules along interlobular septa 🔁 and interlobar fissures 🖂 consistent with chronic beryllium disease, which results from an inflammatory reaction in individuals with chronic exposure and sensitivity to beryllium. (Right) Coronal CECT of the same patient confirms micronodules along interlobular septa 🖂 and interlobar fissures 🔁 present in up to 50% of cases of patients with chronic beryllium disease.





(Left) PA chest radiograph of a 62-year-old man with over 15 years of exposure to beryllium shows characteristic findings of chronic beryllium disease, including bilateral small nodules (ILO category q) and hilar lymphadenopathy 🔁. The radiographic findings mimic those of sarcoidosis. (Right) Axial CECT of a 70year-old man who worked for more than 20 years in the beryllium ceramics industry shows conglomerate nodular opacities 🔁 similar to those seen in sarcoidosis and silicosis.





Abbreviations

- Acute beryllium exposure (ABE)
- Chronic beryllium disease (CBD)
- Delayed-type hypersensitivity to beryllium (BES)

Synonyms

- Salem sarcoidosis
 - Seen in young women in the fluorescent light industry in Salem, Massachusetts in 1940s

Definitions

- Beryllium: Gray, lightweight metal with high thermal stability and conductivity
 - Aerospace, telecommunication, defense, computer, medical, glass blowing, and nuclear industries
- Inhalation of dust, aerosol, or fumes produces 2 types of lung injury
 - Acute chemical pneumonitis (uncommon)
 - Chronic granulomatous disease
- Diagnosis requires
 - History of beryllium exposure
 - Positive beryllium-specific lymphocyte proliferation test (in blood or bronchoalveolar lavage fluid)
 - o Nonnecrotizing granulomas on histology

IMAGING

General Features

- Best diagnostic clue
 - Hilar and mediastinal lymphadenopathy + parenchymal abnormalities
 - Imaging findings similar to those of sarcoidosis
 - Parenchymal micronodules (57%) (most common)
- Location
 - Mid lung zone perilymphatic micronodules (i.e., peribronchovascular, interlobular, and subpleural)
 Upper lung zone fibrosis (advanced disease)
- Size
 - Micronodule coalescence \rightarrow conglomerate masses (7%)
- Morphology
 - Imaging pattern resembles that of sarcoidosis
 - Micronodules (57%)
 - Interlobular septal thickening (50%)
 - Ground-glass opacities (32%)

Radiographic Findings

- Radiography
 - Acute exposure (ABE)
 - Usually secondary to single intense exposure
 Diffuse alveolar opacities due to acute
 - noncardiogenic pulmonary edema □ Slow resolution of abnormalities
 - Chronic disease (CBD)
 - Normal chest radiographs in early stage (~ 50%)
 - Radiographic abnormalities should be characterized using International Labor Office (ILO) reading classification
 - Upper and mid lung zone diffuse nodular opacities: ILO categories p (1.5 mm), q (1.5-3.0 mm), and r (3-10mm)

- □ Irregular opacities: ILO categories s (width: 1.5 mm), t (width: 1.5-3.0 mm) and u (3-10mm)
- Lung nodules may be calcified
- Mediastinal and hilar lymphadenopathy
 May exhibit eggshell calcification
- Peribronchovascular fibrosis and conglomerate masses
- Spontaneous pneumothorax (up to 10%)

CT Findings

- HRCT
 - o Lung
 - Parenchymal micronodules and interlobular septal thickening (most common)
 - □ Parenchymal micronodules (57%)
 - Subpleural micronodules may coalesce as pseudoplaques
 - Interlobular septal and peribronchovascular thickening (50%)
 - Conglomerate masses
 - Ground-glass opacities (32%) more common than in sarcoidosis
 - Honeycombing (late stage)
 - Emphysema
 - o Hilar and mediastinal lymphadenopathy (25-40%)
 - May exhibit amorphous or eggshell calcification
 - Dilated pulmonary trunk (pulmonary hypertension)

Imaging Recommendations

- Best imaging tool
 - HRCT

DIFFERENTIAL DIAGNOSIS

Sarcoidosis

- May be indistinguishable from berylliosis on imaging
 Bilateral, symmetric hilar (90%), and right paratracheal lymphadenopathy (60%)
 - o Perilymphatic micronodules
- Peripheral lymphadenopathy (30%): Cervical, axillary, inguinal
- Multiorgan disease
 - Bone involvement (30%); hands and feet (osteolytic or sclerotic)
 - o Ocular (uveitis) and neurologic manifestations

Silicosis

- Occupational exposure to silica
- Centrilobular and subpleural micronodules (may be calcified)
 - Upper lobe predominance
- Nodules may progress to progressive massive fibrosis
- Calcified mediastinal and hilar lymph nodes
- Paracicatricial emphysema

Tuberculosis

- Scattered centrilobular micronodules and tree-in-bud opacities
- Consolidation
- Cavitation
- Miliary tuberculosis: Diffuse evenly distributed 1- to 3-mm micronodules

Idiopathic Pulmonary Fibrosis

- Irregular reticular opacities
- Traction bronchiectasis/bronchiolectasis
- Subpleural honeycombing
- Subpleural, lower lung predominance

Hypersensitivity Pneumonitis

- Persistent or recurrent exposure to antigen/hapten
- Upper and mid lung zone predominance
- Nonfibrotic: Ground-glass opacities and centrilobular nodules
- Fibrotic: Reticulation, architectural distortion, bronchiectasis, honeycombing
- Air-trapping

PATHOLOGY

General Features

- Etiology
 - Exposure to beryllium dust, fumes, or aerosols
- Short exposure time (9 weeks) may result in sensitization
- Genetics
 - HLA-DPB1 (Glu 69) present in 97% of patients with CBD
 - Not useful for screening given ↑ prevalence in general population (> 30%)

Staging, Grading, & Classification

- ABE: Acute chemical pneumonitis
- CBD: Chronic granulomatous disease

Gross Pathologic & Surgical Features

- Exposure to beryllium: Cell-mediated immune response; T-cells become sensitized to beryllium
- Subsequent exposure: Macrophages, CD4(+) helper Tlymphocytes and plasma cells accumulation in lungs, noncaseating granulomas that may evolve to fibrosis
- Indistinguishable from sarcoidosis except for demonstration of beryllium-specific immune response

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - ABE (single intense exposure)
 - Conjunctivitis
 - Pharyngitis
 - Laryngotracheobronchitis
 - Dermatitis
 - Lung primarily affected
 - Dyspnea
 - Cough
 - Chest pain
 - End-stage lung disease
 - Systemic: Fever, fatigue, anorexia, night sweats, weight loss
 - o Arthralgias, myalgias
- Other signs/symptoms
 - Extrapulmonary disease rare
 - Skin manifestations: Dermatitis, ulcers, dermal granulomas
 - Lymphadenopathy, hepatosplenomegaly (granulomatous infiltration)

– Hypercalcemia, renal stones

Demographics

- Epidemiology
 - o Beryllium-exposed workers
 - Ceramics manufacture
 - Glass blowers
 - Electronic industries
 - Nuclear weapon production
 - Aerospace industry
 - ABE is rare today given strict industrial control measures

Natural History & Prognosis

- Latency ranges from few months to 40 years after 1st exposure
- CBD typically develops approximately 10-20 years after 1st exposure
 - Susceptible workers exposed to beryllium may develop BES
 - Beryllium stimulates pulmonary proliferation and accumulation of beryllium-specific T-cells
 - Small percentage of BES progresses to CBD (2-5%)
- Variable clinical course
 - Asymptomatic patient with normal chest radiographs and pulmonary function
 - Symptomatic patient with abnormal chest radiographs and abnormal pulmonary function
 - Pulmonary function tests: Restrictive pattern; ↓ vital capacity, lung capacity, and diffusing lung capacity
 - □ ↑ alveolar-arterial oxygen gradient during exercise is highly sensitive
- Acute exposure (very rare)
 - o Mortality (10%)
 - Well-recognized cause of lung cancer

Treatment

- Cessation of beryllium exposure
 - Improvement of pulmonary function
 - May be definitive treatment for patients with early stage disease
- Corticosteroids for symptomatic patients or abnormal pulmonary function tests
- Lung transplantation for end-stage lung disease

DIAGNOSTIC CHECKLIST

Consider

• Excluding history of beryllium exposure in patients with sarcoid-like imaging findings

Image Interpretation Pearls

• Consider diagnosis of berylliosis in patients with mediastinal/hilar lymphadenopathy and perilymphatic micronodules

- 1. Sizar O et al: Berylliosis 2021
- MacMurdo MG et al: Chronic beryllium disease: update on a moving target. Chest. 158(6):2458-66, 2020
- 3. Martínez González C et al: Berylliosis: a granulomatosis to remind us of the importance of occupational history. Arch Bronconeumol. 56(7):470-1, 2020

Berylliosis





(Left) PA chest radiograph of a 55-year-old man with more that 15 years of exposure to beryllium shows bilateral irregular nodular opacities 🔁 that are larger than 1 cm. (Right) Axial CECT of the same patient shows bilateral . irregular solid nodules 乏 in the upper lobes that result from confluent granulomatous lesions similar to those present in sarcoidosis. Hilar and mediastinal lymphadenopathy is usually a delayed finding of chronic beryllium disease.





(Left) Axial CECT of a 50-yearold man with sarcoidosis shows multiple coalescent micronodules 🔁 in a peribronchovascular distribution as well as subpleural 🔁 and perifissural micronodules, CT findings indistinguishable from those of berylliosis. (Right) Axial CECT of a 49-year-old woman with sarcoidosis shows perilymphatic pulmonary micronodules and peribronchovascular thickening 🔁. Correlation with occupational history is critical to differentiate sarcoidosis from berylliosis.





(Left) PA chest radiograph of a 61-year-old man with longterm exposure to silica dust shows diffuse micronodules, subpleural pseudoplaques 🔁, and bilateral hilar lymphadenopathy 🔁. (Right) Axial NECT of the same patient shows bilateral small well-defined centrilobular 🔁 and subpleural \boxtimes pulmonary nodules of uniform size. Subpleural nodules can become confluent and resemble pleural plaques. The antecedent of previous exposure to silica is of great value to establish the correct diagnosis.

Silo-Filler's Disease

KEY FACTS

TERMINOLOGY

- Occupational lung disease resulting from exposure to nitrogen dioxide (NO₂)
- Inhalation of toxic gases from freshly stored silage

IMAGING

- Radiography
 - Initial chest radiograph may be normal
 - Early findings: Noncardiogenic pulmonary edema, normal heart size, pleural effusions uncommon
 - Late findings: Hyperinflation from constrictive bronchiolitis, diffuse ill-defined small/miliary nodules
- HRCT
 - Early: Bilateral consolidations and ground-glass opacities, organizing pneumonia
 - Late: Constrictive bronchiolitis
- Chest radiography for assessment and monitoring
- HRCT for assessment of late complications

TOP DIFFERENTIAL DIAGNOSES

- Agricultural lung diseases
 - o Dung lung, anhydrous ammonia inhalation
 - Organic dust toxicity syndrome
 - Pesticide exposure
- Hypersensitivity pneumonitis (farmer's lung)
- Smoke inhalation

CLINICAL ISSUES

- Symptoms/signs
 - Cough, lightheadedness, dyspnea, fatigue
 - Severity based on exposure duration/concentration
 - Late: Relapse of dyspnea and cough
- Presentation usually in September and October

DIAGNOSTIC CHECKLIST

 Consider silo-filler's disease in any breathless farmer presenting at harvest time

(Left) PA chest radiograph of a patient who developed acute dyspnea within hours of working in a freshly filled silo shows dense bilateral perihilar consolidations, consistent with pulmonary edema. Note absence of cardiomegaly or pleural effusion. (Right) PA chest radiograph of a man with silo-filler's disease who presented with chronic dyspnea shows numerous bilateral small pulmonary nodules. Silo-filler's disease should be suspected in farmers who present with dyspnea, particularly during harvest time.





(Left) Axial CECT of a patient with silo-filler's disease who presented with dyspnea shows patchy bilateral ground-glass opacities and findings of mild paraseptal emphysema. (Right) HRCT of a patient with late-stage silo-filler's disease shows mosaic attenuation from constrictive bronchiolitis. Note paucity of vascular structures in areas of lung hyperlucency and dilated airways with mildly thickened walls 🛃. Silo-filler's disease is a recognized etiology of constrictive bronchiolitis.





Abbreviations

• Nitrogen dioxide (NO₂)

Definitions

- Occupational lung disease resulting from exposure to NO₂
- Inhalation of toxic gases from freshly stored silage

IMAGING

General Features

- Best diagnostic clue
 - Early: Pulmonary edema within hours of inhalation
 - Late: Mosaic attenuation on HRCT from constrictive bronchiolitis

Radiographic Findings

- Initial chest radiograph may be normal
- Early findings
 - Parenchymal injury immediately within first 48 hours
 - Noncardiogenic edema 6-12 hours post exposure
 - Ill-defined opacities, nonspecific pulmonary edema pattern
 - Resolution over 3-5 days
 - Progression of consolidation after 48 hours; consider superinfection
 - Normal heart size
 - o Pleural effusions uncommon
- Late findings
 - o 2-4 weeks post exposure (range: weeks to months)
 - Hyperinflation from constrictive bronchiolitis
 - Diffuse ill-defined small or miliary nodules

CT Findings

- HRCT
 - Early: Bilateral airspace and ground-glass opacities
 - Organizing pneumonia
 - Late: Constrictive bronchiolitis with mosaic attenuation

Imaging Recommendations

- Best imaging tool
 - Chest radiographs suffice for initial assessment and disease monitoring
- Protocol advice
 - Early: Serial radiography
 - Late: HRCT

DIFFERENTIAL DIAGNOSIS

Agricultural Lung Diseases

- Other toxic gases: Hydrogen sulfide (H₂S), ammonia, carbon dioxide, methane
 - Toxic manure exposure (dung lung)
 - Anhydrous ammonia inhalation
- Organic dust toxicity syndrome
 - o Usually seen in spring from moldy dust silage
 - Radiographs usually normal, HRCT may show ill-defined centrilobular nodules
- Pesticide exposure
 - Paraquat lung: Usually skin absorption
 - Rapid pulmonary fibrosis, often fatal

Hypersensitivity Pneumonitis (Farmer's Lung)

- Exposure to dust (not gas)
 Allergic reaction to fungi (typically *Actinomycetes*) in hay
- CT: Centrilobular ground-glass nodules, mosaic attenuation
- May result in chronic fibrosis

Smoke Inhalation

- Acutely, bronchial wall thickening and subglottic edema
- Perihilar and upper lung zone pulmonary edema

PATHOLOGY

General Features

- Etiology
 - NO₂ in top-unloading silo
 - Silage is product of anaerobic bacterial fermentation of grass crops, used to feed livestock
 - $\circ~$ Inhalation of NO2 leads to cellular damage

Microscopic Features

- Acute: Diffuse alveolar damage with hyaline membrane formation
- Late: Small airway damage, constrictive bronchiolitis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Severity based on exposure duration and NO₂ concentration
 - Acute: Minutes to hours after exposure
 - Most exposures mild/self-limited (cough, dyspnea)
 - High concentration: Bronchospasm, sudden death
 - Pulmonary edema due to cellular damage
 - o Late: Relapse of dyspnea, cough
- Other signs/symptoms
 - Methemoglobinemia

Demographics

- Epidemiology
 - o 5 cases/100,000 silo-associated farm workers/year
 - September and October (harvest months)

Natural History & Prognosis

- Variable, depends on extent of initial injury
- 1/3 with severe exposure die from pulmonary edema or constrictive bronchiolitis

Treatment

- Preventive: Avoid freshly filled silo for 14 days
- Monitor those exposed for 48 hours, steroids
- Supportive, mechanical ventilation to maintain oxygenation
- Serial cultures for infectious surveillance

DIAGNOSTIC CHECKLIST

Consider

• Silo-filler's disease in any breathless farmer presenting at harvest time

SELECTED REFERENCES

1. Amaducci A et al: Nitrogen Dioxide Toxicity 2021

KEY FACTS

TERMINOLOGY

- Allergic inflammatory response of lung parenchyma and airways to inhaled organic antigens or haptens
- New classification proposes 2 clusters that incorporate clinical, imaging, and pathologic findings
 - Nonfibrotic: Symptoms occur hours after exposure and may be recurrent
 - Fibrotic: Chronic symptoms (e.g., clubbing, hypoxemia, inspiratory crackles)

IMAGING

Radiography

- Nonfibrotic: Normal versus nonspecific opacities
- Fibrotic: Upper lobe peribronchovascular reticular opacities &/or honeycombing
- HRCT/CT
 - Nonfibrotic: Diffuse ground-glass opacities, interlobular septal thickening, and pleural effusions
 - Ground-glass centrilobular nodules

- Mosaic attenuation, air-trapping; head cheese sign
- Fibrotic: Peribronchovascular &/or subpleural reticulation ± honeycombing
 - Thin-walled, air-filled cysts (rare)
 - Acute exacerbation: Preexistent reticular opacities or honeycombing + new diffuse opacities ± new traction bronchiectasis/bronchiolectasis

TOP DIFFERENTIAL DIAGNOSES

- Respiratory bronchiolitis
- Idiopathic pulmonary fibrosis
- Nonspecific interstitial pneumonia

CLINICAL ISSUES

- Nonfibrotic: Recurrent systemic symptoms (e.g., chills, fever, sweats, myalgias)
- Fibrotic: Chronic symptoms (e.g., dyspnea, cough), clubbing, hypoxemia, inspiratory crackles
- Treatment: Removal from exposure; corticosteroids

(Left) AP chest radiograph of a 57-year-old man with nonfibrotic hypersensitivity pneumonitis (bird fancier's lung) demonstrates bilateral ill-defined heterogenous airspace opacities 🖂. (Right) Axial CECT of the same patient shows bilateral ground-glass opacities and interlobular septal thickening amid low-attenuation areas (mosaic attenuation). Groundglass opacities are a nonspecific finding of nonfibrotic hypersensitivity pneumonitis. A high index of suspicion is required to suggest the diagnosis.

(Left) Axial HRCT of a patient with nonfibrotic hypersensitivity pneumonitis shows diffuse, centrilobular ground-glass nodules and focal lobular air-trapping 🖂 Centrilobular ground-glass nodules are characteristic of nonfibrotic hypersensitivity pneumonitis, although other entities exhibit similar findings (e.g., respiratory bronchiolitis). (Right) Low-power photomicrograph (H&E) stain of a specimen of nonfibrotic hypersensitivity pneumonitis shows peribronchiolar interstitial inflammation and lymphocytic infiltration 🔁









Abbreviations

- Hypersensitivity pneumonitis (HP)
- Idiopathic pulmonary fibrosis (IPF)

Synonyms

• Extrinsic allergic alveolitis

Definitions

- Immune-mediated disease that manifests as interstitial lung disease (ILD) in susceptible individuals after exposure to identified or unidentified factor
- Type of cellular bronchiolitis
- HP: Transitory pulmonary opacities or irreversible pulmonary fibrosis
- Classification: Nonfibrotic and fibrotic HP
 - Two clusters that incorporate clinical, imaging, and pathologic findings
 - Nonfibrotic: Symptoms occur hours after exposure; may be recurrent
 - Fibrotic: Chronic symptoms (e.g., clubbing, hypoxemia, inspiratory crackles)

IMAGING

General Features

- Best diagnostic clue
 - Nonfibrotic: Centrilobular ground-glass nodules and airtrapping
 - Fibrotic: Upper lobe peribronchovascular fibrosis

Radiographic Findings

- Nonfibrotic
 - Chest radiographs frequently normal
 - o Nonspecific findings: Ill-defined opacities
- Fibrotic
 - o Chest radiographs frequently abnormal
 - Upper lobe peribronchovascular reticular opacities &/or honeycombing
 - Subpleural honeycombing with apicobasal gradient identical to usual interstitial pneumonia (UIP)
 - Acute exacerbation of HP similar to acute exacerbation of IPF (i.e., diffuse opacities amid preexistent reticular opacities; exclusion of cardiogenic pulmonary edema)

CT Findings

- Nonfibrotic
 - May simulate exudative phase of diffuse alveolar damage (acute interstitial pneumonia)
 - Acute HP in Richerson classification
 - Diffuse ground-glass opacities
 - Interlobular septal thickening
 - Pleural effusions
 - Ground-glass centrilobular nodules
 - Subacute HP in Richerson classification
 - Mosaic attenuation
 - Air-trapping
 - Three-density pattern (formerly known as headcheese sign)
 - Combination of ground-glass opacities, air-trapping, and normal lung

- Fibrotic
 - Chronic HP in Richerson classification
 - Peribronchovascular &/or subpleural reticulation ± honeycombing
 - Architectural distortion
 - Traction bronchiectasis
 - Superimposed findings of nonfibrotic HP
 - Subpleural abnormalities identical to those of nonspecific interstitial pneumonia (NSIP) or UIP
 - o Thin-walled, air-filled cysts (rare)
 - Emphysema (rare): May occur in never smokers
 - Organizing pneumonia (OP) (rare): Patchy peripheral opacities (may be migratory on serial imaging), reversed halo &/or atoll signs
 - Acute exacerbation of HP
 - Preexistent reticular opacities or honeycombing + new diffuse opacities ± new traction bronchiectasis/bronchiolectasis

Imaging Recommendations

- Best imaging tool
- HRCT/CT
- Protocol advice
 - Expiratory HRCT critical for identification of air-trapping
 - Prone HRCT critical for differentiating subtle subpleural abnormalities from dependent atelectasis

DIFFERENTIAL DIAGNOSIS

Acute Interstitial Pneumonia

- Nonfibrotic HP may be indistinguishable
- Diffuse ground-glass opacities
- Diagnosis often established histologically

Respiratory Bronchiolitis

- Nonfibrotic HP may be indistinguishable
- Centrilobular ground-glass micronodules and air-trapping more severe in nonfibrotic HP
- Differentiation may require tissue sampling

Idiopathic Pulmonary Fibrosis

- Fibrotic HP may be indistinguishable
- Appropriate clinical history is critical
- Diagnosis supported by UIP pattern on CT/HRCT

Nonspecific Interstitial Pneumonia

- Fibrotic HP may be indistinguishable
- Honeycombing is uncommon
- Appropriate clinical history is critical
- Diagnosis often established histologically

Lymphoid Interstitial Pneumonia

- Mimic: Nonfibrotic HP with cysts
- History of Sjögren syndrome
- Differentiation typically requires histologic assessment

Sarcoidosis

- Upper lobe predominant peribronchovascular fibrosis
- HP and sarcoidosis may be indistinguishable
- Characteristic perilymphatic nodules (i.e., along fissures)

PATHOLOGY

General Features

- Etiology
 - Inhaled antigens &/or haptens deposited along bronchiolar and alveolar epithelium elicit alveolitis and cellular bronchiolitis through type III and type IV immune hypersensitivity reactions
 - Bacterial, yeast, or avian antigens
 - Spores from macroscopic fungi
 - Chemical haptens: Isocyanates, zinc, inks, dyes
 - Other antigens: Viruses, endotoxins, β-glucan, anthrax vaccination
 - Other: Colistin, catechin (green tea extract), and methylmethacrylate

Staging, Grading, & Classification

- Historically classified as acute, subacute, and chronic (Richerson classification) based on clinical factors with imaging and pathologic findings not statistically validated
 - Richerson classification
 - Acute
 - □ Clinical presentation: Flu-like symptoms; 6-24 hours after exposure
 - □ HRCT: Diffuse ground-glass opacities, interlobular septal thickening, pleural effusions
 - Subacute
 - Clinical presentation: Cough, dyspnea; gradual onset (days to weeks)
 - HRCT: Specific findings; ground-glass centrilobular nodules and patchy (lobular) air-trapping
 - Chronic
 - Clinical presentation: Cough, dyspnea, fatigue, weight loss, clubbing
 - HRCT: Nonspecific findings; similar to those of pulmonary fibrosis with honeycombing and traction bronchiectasis
- New classification to incorporate clinical, imaging, and histologic findings
 - Nonfibrotic (most former acute and subacute HP)
 - Fibrotic (includes most chronic HP)

Microscopic Features

- Nonfibrotic
 - Neutrophil and eosinophil infiltration of alveolar spaces and small vessel vasculitis
 - Lymphocytic interstitial infiltration, poorly-formed nonnecrotizing granulomas, cellular bronchiolitis
 - Diffuse alveolar damage
- Fibrotic
 - Poorly-formed peribronchial noncaseating granulomas ± multinucleated giant cells
 - Bronchiolocentric lymphocytic and plasmatic alveolar wall infiltration
 - Peribronchiolar fibrosis
 - Constrictive bronchiolitis
 - Histologic features of UIP, NSIP, OP, and centrilobular fibrosis or bridging fibrosis (continuous fibrosis between centrilobular and subpleural locations)
 - Acute exacerbation of HP demonstrates features of diffuse alveolar damage and superimposed fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonfibrotic
 - Symptoms occur hours after exposure and may be recurrent
 - Systemic or influenza-like symptoms: Chills, fever, sweats, myalgias
 - Chest tightness, cough, dyspnea
 - Recurrent systemic symptoms
 - o Fibrotic
 - Chronic symptoms: Dyspnea, cough
 - Other: Clubbing, hypoxemia, inspiratory crackles
- Other signs/symptoms
 - Bronchoalveolar lavage (BAL) fluid: ↑ lymphocytes and predominance of CD8 cells over CD4 cells
 - Pulmonary function tests: Restrictive physiology, ↓ DLCO
 - Hot tub lung: Clinical, histopathologic, and imaging features of nonfibrotic HP
 - BAL fluid culture shows nontuberculous mycobacteria
 - Acute exacerbation of fibrotic HP
 - Rapidly progressive dyspnea (days to weeks)
 - Cough, fever, flu-like symptoms
 - o Summer-type HP
 - Most prevalent HP in Japan, occurs in summer with recurrent episodes for several years
 - Symptoms elicited in home environment; demonstrates familial occurrence
- Clinical predictors for diagnosis of HP
 - Exposure to known offending antigen
 - Positive precipitating antibodies
 - Recurrent symptoms
 - Inspiratory crackles
 - o Symptoms 4-8 hours after antigenic exposure
 - o Weight loss

Demographics

- 4-15% of all ILDs
- 0.5-3% of all farmers develop HP

Natural History & Prognosis

- May progress to fibrosis and death within few years
- Factors associated with worse prognosis in fibrotic HP
 - Long period of antigenic exposure (bird fancier's lung)
 - Histologic pattern of either fibrotic NSIP or UIP
 - Digital clubbing
 - o Olderage
 - Extensive bronchiectasis or honeycombing on CT
- ↑ mortality among farmers and individuals in agricultural industries

Treatment

• Usually responds to treatment: Removal from exposure; corticosteroids

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(Left) Axial HRCT of a patient with nonfibrotic hypersensitivity pneumonitis shows mosaic attenuation and lobular air-trapping **⊡**. While a nonspecific finding, lobular air-trapping is very common in hypersensitivity pneumonitis. (Right) Composite image with axial inspiratory (left) and expiratory (right) HRCT of a patient with nonfibrotic hypersensitivity pneumonitis shows mosaic attenuation and the three-density pattern. While nonspecific, the latter is a common CT finding of hypersensitivity pneumonitis.





(Left) PA chest radiograph of a patient with fibrotic hypersensitivity pneumonitis shows low lung volume and extensive mid and upper lung zone reticular opacities. (Right) Axial HRCT of the same patient shows peribronchovascular groundglass and reticular opacities and associated traction bronchiectasis \supseteq . Hypersensitivity pneumonitis is a classic example of lung disease leading to peribronchovascular fibrosis, which may progress to honeycombing.





(Left) Axial HRCT of a patient with fibrotic hypersensitivity pneumonitis demonstrates upper lobe predominant peribronchovascular and subpleural reticular opacities \square and honeycombing as well as scattered traction bronchiectasis 2. (Right) Composite image with axial inspiratory HRCT at baseline (left) and 5 years later (right) of a patient with hypersensitivity pneumonitis shows evolution from subtle subpleural ground-glass opacities \supseteq to frank fibrosis with traction bronchiectasis 🔁.

KEY FACTS

TERMINOLOGY

• Inhalation injury to upper and lower respiratory tract from thermal, chemical, and particulate matter (products of combustion)

IMAGING

- Severity of injury depends on concentration and length of exposure: Airways primarily affected on 1st day, lung affected over next 2 days
- Acute: Up to 48 hours
 - Initial radiograph often normal
 - Diffuse bronchial wall thickening (85%)
 - Conical narrowing of subglottic trachea
- Subacute: 3 days to end of hospitalization
 - Superimposed pneumonia
 - Cardiogenic edema, large IV fluid volume
- Delayed: Weeks to months after hospital discharge
 Bronchiectasis, mosaic attenuation, air-trapping

TOP DIFFERENTIAL DIAGNOSES

- Hydrostatic pulmonary edema
- Pneumonia
- Aspiration
- Neurogenic pulmonary edema
- Mitral regurgitant pulmonary edema

PATHOLOGY

- Friable airway mucosa with ulceration and charring
- Acute: Diffuse alveolar damage with hyaline membrane formation
- Delayed: Constrictive bronchiolitis

CLINICAL ISSUES

- Symptoms and signs
 - Dyspnea, wheezing, carbonaceous sputumSinged nasal hairs, burns
- Smoke inhalation is primary cause of death in 75% of patients with burn injuries

(Left) Initial AP chest radiograph of an intubated patient rescued from a house fire shows subtle central bronchial wall thickening \Longrightarrow . Chest radiographs are often normal at initial presentation following acute inhalational lung injury. (Right) AP chest radiograph of the same patient obtained 5 hours later shows bilateral coalescent consolidations with a slight upper lobe predominance. Pulmonary edema may complicate the appearance of acute lung injury in severe cases of smoke inhalation.





(Left) AP chest radiograph of a 21-year-old man who sustained 30% skin burns and smoke inhalation injury during a house fire shows multifocal upper lung zone predominant airspace opacities with confluent right upper lung and perihilar consolidations. (Right) Coronal CECT of the same patient shows bilateral upper lobe consolidations \supseteq and patchy ground-glass opacities 🔁. Bronchoscopy revealed tracheal edema, erythema, and ulceration, consistent with smoke inhalation injury.





TERMINOLOGY

Definitions

• Inhalation injury to upper and lower respiratory tract from thermal, chemical, and particulate matter (products of combustion)

IMAGING

General Features

- Best diagnostic clue
 - Upper lung zone predominant multifocal airspace disease + subglottic tracheal narrowing in patient with appropriate history

Radiographic Findings

- Radiography
 - Severity of injury depends on concentration and length of exposure
 - Airways primarily affected on 1st day
 - Lung parenchyma affected over next 2 days
 - Acute: Up to 48 hours
 - Initial radiograph often normal
 - Diffuse bronchial wall thickening (85%)
 - Conical narrowing of subglottic trachea from edema
 - Subsegmental atelectasis: Airway lumina narrowed by mucosal edema
 - Perihilar and upper lung predominant consolidation
 - Mild/uncomplicated: Resolves over 3-5 days
 - Pleural effusions may develop without parenchymal involvement, may relate to hypoproteinemia from skin burns
 - Soft tissue thickening from edema related to skin burns
 - Subacute: 3 days to end of hospitalization
 - Barotrauma from positive pressure ventilation
 - Superimposed pneumonia; especially with cutaneous burns
 - □ Suspect pneumonia if lung abnormalities progress after first 48 hours: Up to 40%
 - Cardiogenic edema commonly superimposed
 - □ Large volume of administered fluid, especially with cutaneous burns
 - Acute respiratory distress syndrome (ARDS)
 - Pulmonary emboli after first 3 days
 - **Delayed**: Weeks to months after hospital discharge
 - Hyperinflation and small nodules in previously affected lung (constrictive bronchiolitis)

CT Findings

- Acute
 - Bronchial wall thickening
 - Ground-glass opacities: Edema or mosaic attenuation from small airway edema
- Subacute
 - Evaluation of suspected complications, such as pulmonary embolus
 - Assessment of lung abnormalities, especially in patients with complicated clinical course
- Delayed
 - Mosaic attenuation

- Bronchiectasis
- Expiratory air-trapping

Other Modality Findings

- Xenon-133 ventilation scanning
 - Delayed washout, incomplete washout within 120 seconds, or segmental hang-up
 - May be abnormal when chest radiograph is normal; rarely used

Imaging Recommendations

- Best imaging tool
 - Chest radiography for initial assessment and monitoring disease course
 - CT: Problem-solving tool or evaluation of unexplained radiographic abnormalities

DIFFERENTIAL DIAGNOSIS

Hydrostatic Pulmonary Edema

- Smoke inhalation has proclivity for upper lung zones
- Fluid overload common in smoke inhalation due to massive fluid administration for burns

Pneumonia

- Similar imaging findings, but clinical history suggests diagnosis
- Pneumonia common in smoke inhalation; develops > 48 hours post admission

Aspiration

- Similar radiographic findings
- Hypoxic neurologically impaired victims of smoke inhalation at high risk for aspiration

Neurogenic Pulmonary Edema

- Central nervous system insult with resultant increased intracranial pressure
- Hypoxic neurologically impaired victim; head CT often required to exclude intracranial pathology

Mitral Regurgitant Pulmonary Edema

- Pulmonary edema: Heart failure in patient with incompetent mitral valve
- Diffuse involvement, more severe in right upper lobe; directional backflow via right superior pulmonary vein
- Enlarged heart; usually normal in smoke inhalation
- Rapid response to diuretic and inotropic support

PATHOLOGY

General Features

- Etiology
 - Nitric oxide (NO)
 - Smoke-induced release from epithelial cells and alveolar macrophages
 - NO: Loss of hypoxic vasoconstriction and increased vascular permeability
 - o Bronchial blood flow markedly increased (up to 20x)
 - May contribute to pulmonary edema
 - Animal models: Bronchial artery occlusion lessens severity of smoke injury

- Smoke consists of gases and fine particles: Carbonaceous particles (soot) absorb noxious substances in gas; act as delivery vehicles to respiratory mucosa
- Water solubility of combustion products determines site of action
 - Highly water-soluble products irritate and affect upper airways
 - Ammonia, hydrogen chloride, sulfur dioxide
 - Less water-soluble products are nonirritating, primarily affect distal airways
 - Chlorine, nitrogen oxides, phosgene
- Severity of chemical pneumonitis depends on smoke composition and concentration and length of exposure
 - Injury anywhere from upper airways to pulmonary capillary bed
- Airway wall
 - Spectrum of findings: Edema and inflammatory cells → hemorrhage, necrosis, ulceration, charring
- Airway casts commonly cause widespread bronchial plugging
 - Casts: Neutrophils, shed bronchial epithelium, mucin, fibrin
 - Mean reduction in cross-sectional area: Bronchi (30%), bronchioles (10%) 48 hours after injury

Pathophysiology

- General
 - Gas concentrations in lung determined by ventilation perfusion ratio (V:Q)
 - Normal upright lung: V:Q ratio highest in upper lung zone; inhaled gas concentrates in nondependent lung
- Thermal injury
 - Rare, inhaled gases rapidly cooled by upper respiratory tract
 - Injury limited to upper respiratory tract and larynx
 - Seen primarily with superheated steam and explosions
- Asphyxiation from carbon monoxide and carbon dioxide
 - Carbon monoxide displaces oxygen, produces profound hypoxemia (50% of fire-related fatalities)
- Carbon dioxide reduces ambient oxygen concentration
- Pyrolysis
 - Cyanide gas from natural and synthetic fabric and plastics especially polyvinyl chloride (PVC)
 - Hydrogen chloride from PVC combustion combines with water to produce hydrochloric acid

Gross Pathologic & Surgical Features

• Diffusely friable airway mucosa with ulceration and charring

Microscopic Features

- Acute: Diffuse alveolar damage with hyaline membrane formation
- Delayed: Constrictive bronchiolitis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dyspnea
 - o Wheezing
 - Carbonaceous sputum
 - Singed nasal hairs

- o Burns
- Other signs/symptoms
 - Elevated carboxyhemoglobin (from carbon monoxide inhalation)
 - Increased mixed venous PO₂ and decreased arteriovenous oxygen difference; suggests either carbon monoxide or hydrogen cyanide poisoning
 - Wheezing common due to airway narrowing
- Bronchoscopy (typically used acutely for diagnosis)
 Laryngeal edema, airway ulceration, charring
- Delayed symptoms months later: Dyspnea, nonproductive cough
- Pulmonary function tests
- Decreased maximum expiratory flow volume and forced vital capacity

Demographics

- Age
 - Any age; favors those who are physically unable to escape fire
- Epidemiology
 - 23,000 injuries and 5,000 deaths per year in USA
- Firefighters
 - Long-term risk of obstructive lung disease

Natural History & Prognosis

- Smoke inhalation is primary cause of death in 75% of patients with burn injuries
- Mortality rate range; 50-80%
- Abnormal chest radiograph within 48 hours of exposure is poor prognostic sign
- Despite advances in cutaneous burn care, mortality from smoke inhalation has not improved over past 2 decades

Treatment

- Supportive, intubation and ventilation with supplemental oxygen to counter hypoxia
- Fluid management critical to support cardiac and urine output
- Serial cultures for infectious surveillance
- Steroids may be detrimental; prophylactic antibiotics do not influence survival
- Promising: Aerosolized acetylcysteine and heparin

DIAGNOSTIC CHECKLIST

Consider

• Hydrogen cyanide exposure in patients with unexplained respiratory failure or persistent anion gap metabolic acidosis

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(Left) AP chest radiograph of a 28-year-old man who was intubated on admission following smoke inhalation during a house fire shows multifocal bilateral airspace disease with dense right upper lobe consolidation. (Right) Axial CECT of the same patient obtained 5 years later shows mosaic attenuation with areas of hyperlucency, scattered bronchiectasis, and mild bronchial wall thickening. The central airway abnormalities are distributed in regions of prior inhalational injury.





(Left) AP chest radiograph of the same patient obtained 4 weeks later shows clearing of the upper lobe airspace disease and a new right lower lobe consolidation. Pneumonia commonly develops in patients with smoke inhalation injury, which is the cause of death in 75% of burn patients. (Right) AP chest radiograph (coned down to the upper trachea) of a patient who sustained 70% skin burns in a house fire shows subglottic narrowing \blacksquare that required intubation for airway protection.





(Left) AP chest radiograph of a 35-year-old man trapped in a nightclub fire shows hyperinflated but clear lungs. A normal initial chest radiograph is commonly seen in patients with smoke inhalation injury. (Right) Axial expiratory HRCT of a patient who was trapped in a nightclub fire 4 years previously shows diffuse mosaic attenuation due to airtrapping. Chronic dyspnea related to smoke inhalation may be the result of constrictive bronchiolitis or asthma.

KEY FACTS

TERMINOLOGY

- E-cigarette or vaping product use-associated lung injury (EVALI)
- Lung injury from use of e-cigarette or vaping device in absence of infection or alternative plausible diagnosis

IMAGING

- Radiography: Bilateral pulmonary opacities
- CT
 - Diffuse ground-glass opacities, perilobular
 - Nodular ground-glass opacities

TOP DIFFERENTIAL DIAGNOSES

- Atypical pneumonia
- Eosinophilic pneumonia
- Hypersensitivity pneumonitis
- Inhalational lung injury
- Drug toxicity
- Diffuse alveolar hemorrhage

PATHOLOGY

- Etiology: Tetrahydrocannabinol (THC): Most commonly vaped substance (> 90%) followed by nicotine (70%) and cannabidiol (8%)
- Histology
 - Nonspecific acute lung injury pattern (100%)
 - Lipid-laden macrophages on bronchoalveolar lavage (> 80%)

CLINICAL ISSUES

- Leukocytosis, dyspnea, cough
- Fever, gastrointestinal symptoms
- Median age: 24 years, most patients < 35 years
- Men (77%)
- Nearly all reported cases in North America

DIAGNOSTIC CHECKLIST

• Consider EVALI in young patient with nonspecific respiratory symptoms after weeks or months of vaping

(Left) AP chest radiograph of a 39-year-old woman with ecigarette or vaping product use-associated lung injury (EVALI) and acute hypoxic respiratory failure shows bilateral ground-glass opacities and consolidations. Bronchoalveolar lavage demonstrated lipid-laden macrophages. Extensive workup for infection was negative. (Right) Axial NECT of a 32year-old man with EVALI who presented with cough and hypoxemia shows bibasilar ground-glass opacities \square that demonstrate subpleural sparing *⊡*.





(Left) Axial CECT of a 24-yearold man with EVALI who presented with cough and hemoptysis shows multifocal bilateral nodular acinar ground-glass opacities. (Right) Coronal CECT of an 18-yearold man with EVALI with cough and chest pain shows pneumomediastinum ➡, subcutaneous air, and multifocal peribronchovascular groundglass opacities ➡ in the midand lower lung zones.





Abbreviations

• E-cigarette or vaping product use-associated lung injury (EVALI)

Synonyms

• Vaping-associated or induced lung injury

Definitions

• Lung injury from use of of e-cigarettes or vaping devices in absence of infection or alternative plausible diagnosis (e.g., cardiac, rheumatologic, or neoplastic process)

IMAGING

General Features

- Best diagnostic clue
 - Bilateral symmetric ground-glass opacities, subpleural sparing
- Location
 - Variable: Upper lung, midlung, or lower lung zone
 - Upper lung zone predominant distribution in 50%
- Morphology
 - Abnormal radiographs at presentation (> 90%)
 - Pulmonary abnormalities on CT in 100%

Radiographic Findings

• Bilateral pulmonary opacities

CT Findings

- Diffuse ground-glass opacities with perilobular distribution (most common)
- Nodular ground-glass opacities
- Patchy consolidations
- Pleural effusion
- Pneumomediastinum and pneumothorax (rare)

Imaging Recommendations

Best imaging tool
 Unenhanced thin-section chest CT

DIFFERENTIAL DIAGNOSIS

Atypical Pneumonia With Acute Lung Injury

- Influenza, COVID-19, mycoplasma
- Ground-glass opacities, centrilobular nodules/tree-in-bud opacities, organizing pneumonia

Eosinophilic Pneumonia

- Peripheral ground-glass opacities/consolidations, interlobular septal thickening
- Peripheral eosinophilia

Hypersensitivity Pneumonitis

 Ground-glass opacities, mosaic attenuation/air-trapping, headcheese sign

Inhalational Lung Injury

- Initially normal radiograph
- Bronchial wall thickening, subglottic edema
- Airspace disease: Pneumonia, edema
- Delayed: Mosaic attenuation, air-trapping, bronchiectasis

Drug Toxicity

• Various imaging patterns: Organizing pneumonia, hypersensitivity pneumonitis, eosinophilic pneumonia, alveolar hemorrhage

Diffuse Alveolar Hemorrhage

- Focal or diffuse ground-glass opacities ± hemoptysis
- Recurrent episodes may lead to fibrosis

PATHOLOGY

General Features

- Etiology
 - Tetrahydrocannabinol (THC): Most commonly vaped substance (> 90%) followed by nicotine (70%) and cannabidiol (8%)
- Histologic features
 - Nonspecific acute lung injury (100%): Combination of diffuse alveolar damage, organizing pneumonia, foamy macrophages, interstitial inflammation, fibrinous exudates, hyaline membranes; acute eosinophilic pneumonia rarely described
 - Lipid-laden macrophages in bronchoalveolar lavage (> 80%); controversial whether related to lipoid pneumonia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Leukocytosis, dyspnea, cough
- Other signs/symptoms
 Fever, gastrointestinal symptoms

Demographics

• Median age: 24 years, most patients < 35 years

• Men (77%)

• Nearly all reported cases in North America

Natural History & Prognosis

- Most (95%) patients require hospitalization
- > 1/4 (27%) of admitted patients require intubation
- Most (95%) of patients survive to hospital discharge

Treatment

• Support measures, corticosteroids

DIAGNOSTIC CHECKLIST

Consider

• EVALI (diagnosis of exclusion) in young patient with nonspecific respiratory symptoms after weeks or months of vaping

Image Interpretation Pearls

• Ground-glass opacities, consolidations, nodular opacities with bilateral distribution, often with subpleural sparing

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Aspiration

KEY FACTS

TERMINOLOGY

- Synonyms
 - Aspiration pneumonia, aspiration pneumonitis, aspiration bronchiolitis

IMAGING

- Radiography
 - Bronchopneumonia more common than pneumonia
 - Unilateral or bilateral consolidations (gravitational)
 - Atelectasis (segmental/lobar)
- NECT
 - Focal/multifocal consolidation(s); gravitational
 - o Atelectasis: Endobronchial aspirated material
 - Centrilobular nodules and tree-in-bud opacities
 - Pneumatoceles
- CECT
 - Assessment of complications
 - Necrotizing pneumonia, abscess, empyema, pulmonary embolus

TOP DIFFERENTIAL DIAGNOSES

- Multifocal consolidations
 - Organizing/eosinophilic pneumonia
- Tuberculosis
- Atelectasis
 - Endobronchial tumor
 - o Broncholithiasis
- Focal mass
 - Lipoid pneumonia
 - Organizing pneumonia
 - Lung cancer

CLINICAL ISSUES

- Symptoms related to amount/type of aspirated material, frequency, and host response
- Acute: Cough, wheezing, cyanosis, tachypnea
- Subacute/chronic aspiration may mimic asthma
- Common cause of hospital-acquired infections

(Left) Axial NECT of a 68-yearold woman with achalasia shows a dilated esophagus with an air-fluid level \supseteq and patchy left upper lobe groundalass acinar and tree-in-bud opacities. Aspiration cellular bronchiolitis is a common complication of achalasia. (Right) Coronal NECT of a patient with acute aspiration pneumonia shows bilateral perihilar acinar opacities and a distended stomach with intrinsic heterogeneous material 🖾. Aspiration pneumonia is the etiology of most hospital-acquired infections.





(Left) Axial NECT of a 46-yearold man with severe periodontal disease shows a left lower lobe cavitary mass with ill-defined borders. Aspiration-related lung abscess may occur in patients with poor oral hygiene. (Right) AP chest radiograph obtained 24 hours after surgery shows extensive bilateral consolidations secondary to aspiration while under anesthesia. Acute pneumonitis due to aspiration of sterile gastric content (Mendelson syndrome) is associated with a high mortality rate.





Abbreviations

- Tracheoesophageal fistula (TEF)
- Bronchoesophageal fistula (BEF)

Synonyms

- Aspiration pneumonia: Lung infection caused by aspiration of colonized oropharyngeal secretions
- Aspiration pneumonitis: Acute lung injury caused by aspiration of material inherently toxic to lungs
- Aspiration bronchiolitis: Chronic inflammatory reaction to recurrent aspirated foreign particles in bronchioles

Definitions

- Inhalation of oropharyngeal or gastric content into larynx or lower respiratory tract with resultant various types of aspiration syndromes
 - Aspiration pneumonia: Most hospital-acquired infections
 - Lentil aspiration pneumonia: Leguminous material (lentils, beans, peas)
 - Fistulas between esophagus and trachea, bronchi or lung
 - □ Congenital TEF
 - □ Esophageal cancer (5-10%)

• Aspiration pneumonitis

Mendelson syndrome

- □ Aspirated sterile gastric content with pH < 2.5
- Peripartum, anesthesia, decreased level of consciousness
- □ Severity depends on aspirate pH and volume
- Exogenous lipoid pneumonia
 Mineral oil or related substances
- Hydrocarbon aspiration pneumonia
 - □ Children: Accidental poisoning
 - □ Fire-eaters: Hydrocarbon-containing fluids (petroleum)
- Aspiration of inert fluids or particulates
 - Foreign bodies: Food particles (children); tooth fragments (older adults)
 - Foreign body aspiration commonly associated with atelectasis
 - Near drowning: Massive amount of fresh or salt water
- Aspiration bronchiolitis
 - Often referred to as diffuse aspiration bronchiolitis
 - Obliterative bronchiolitis and gastroesophageal reflux (mimics asthma)
 - Common, often overlooked

IMAGING

General Features

- Best diagnostic clue
 - Gravity-dependent opacities
 - Radiopaque material within airways
- Location
 - Recumbent patients: Diffuse perihilar consolidation
 Upper lobe superior segments
 - Lower lobe posterior basilar segments
 - Upright patients: Lower lobe basilar segments

Radiographic Findings

- Radiography
 - Initial chest radiographs are often negative
 - Normal chest radiographs in > 25% of patients with confirmed pneumonia on CT
 - Bronchopneumonia more common than pneumonia (70% versus 15%)
 - Unilateral or bilateral air-space consolidation (gravitational distribution)
 - Focal/multifocal consolidation
 - o Abscess
 - Atelectasis (segmental/lobar): Endobronchial radiopaque material

CT Findings

NECT

- Air-space consolidation, solitary or multiple; gravitational distribution
- o Atelectasis: Endobronchial aspirated material
- Aspiration bronchiolitis
 - Centrilobular ill-defined nodules and tree-in-bud opacities
 - Bronchiectasis
 - Mosaic attenuation, expiratory air-trapping
 - Same findings as infectious bronchiolitis
 Hiatus hernia

 - Ancillary findings
 - Achalasia or dilated esophagus (e.g., scleroderma)
 - Gastroparesis
 - Clinical and neurological conditions that affect deglutition
- Pneumatoceles common in hydrocarbon aspiration
- Lipoid pneumonia
 - Spiculated mass or consolidation; may mimic lung cancer
 - May exhibit low attenuation > 10 HU
 - May exhibit fat attenuation
- CECT
 - Evaluation of complications: Necrotizing pneumonia, abscess, empyema, pulmonary embolus

Nuclear Medicine Findings

- PET/CT
 - Lipoid pneumonia exhibits high FDG avidity similar to lung cancer

Imaging Recommendations

- Best imaging tool
 - Chest radiography for initial diagnosis and follow-up
 - Chest CT for identification of esophageal mass, dilated esophagus ± air-fluid level, hiatal hernia; assessment of complications

DIFFERENTIAL DIAGNOSIS

Multifocal Consolidations

- Organizing/eosinophilic pneumonia
- Tuberculosis
- Vasculitis
- Sarcoidosis

Aspiration

Atelectasis

- Endobronchial tumor: Lung cancer, carcinoid, metastases
- Broncholithiasis

Focal Mass

- Lipoid pneumonia
- Organizing pneumonia
- Lung cancer

PATHOLOGY

General Features

- Etiology
 - Responsible for up to 15% of community acquired pneumonias
 - Common cause of hospital-acquired infection
 - Silent microaspiration in normal healthy adults is common during sleep
 - Aspiration pneumonia results from aspiration of large volume (macroaspiration) of colonized infected oropharyngeal or gastrointestinal content
 - Large volume aspiration
 - Dysphagia
 - Head and neck cancer
 - Esophageal cancer
 - Esophageal stricture
 - Esophageal dilatation
 - Motility disorders
 - Additional causes of aspiration
 - Alcoholism
 - Loss of consciousness
 - Neuromuscular disorders
 - Dementia
 - Stroke
 - Impaired consciousness
 - Cardiac arrest
 - Poor dental hygiene and advanced periodontal disease
 → increased likelihood of bacterial colonization
 - Exogenous lipoid pneumonia: Aspiration of mineral or vegetable lipoid material
 - o TEF and BEF
 - Most fistulas between esophagus and tracheobronchial tree in adults are acquired
 - Esophageal cancer and lung cancer are most common etiologies (> 50%)
 - 15% of patients with esophageal cancer and 1% of patients with lung cancer develop esophagorespiratory fistula
 - Benign causes: Prolonged mechanical ventilation, trauma, caustic ingestion, infection, and inflammation

Gross Pathologic & Surgical Features

- Necrotizing acute bronchopneumonia: Edema, hemorrhage, polymorphonuclear leukocytes, foreign body granulomas
- **Obliterative bronchiolitis**: Bronchiolar mucosal injury with subsequent airflow obstruction
- Granulomatous pneumonitis: Typical lentil aspiration pneumonia
- Lipoid pneumonia: Lipid-laden macrophages, fibrosis, histiocytic reaction

• Organizing pneumonia: Chronic aspiration with fibroblastic response and granulation tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Symptoms and signs vary with amount/type of aspirated material, frequency, host response
 - o Acute
 - Cough, wheezing, cyanosis, tachypnea
 - Acute meat aspiration: "café coronary syndrome" (mimics myocardial infarction)
 - Pneumonia: Fever, cough, purulent sputum
 - Subacute/chronic
 - Mimics asthma
- Other signs/symptoms
- Pleuritic chest pain
 - Occasionally hemoptysis
- Clinical profile
 - Aspiration pneumonia is associated with higher mortality than other forms of community acquired pneumonia (30% versus 11%)
 - Microbiology of aspiration pneumonia has shifted away from anaerobes to traditional community-acquired pneumonia organisms
- Barium aspiration
 - Barium sulfate is often used to evaluate swallowing disorders
 - Barium sulfate: Heavy inorganic inert metal, which is neither absorbed nor metabolized
 - No pharmacologic activity; chemical pneumonitis related to barium aspiration is rare
 - Microaspiration of small amount of barium sulfate is common and usually asymptomatic
 - Because of high viscosity, massive barium aspiration may induce bronchial and alveolar obstruction leading to alveolar dead space with shunt effect
 - Respiratory complications more common in older patients with comorbidities
 - Dysphagia and head and neck cancer are common risk factors for high volume aspiration
 - Complications more likely to occur with large volume aspiration of high concentration barium preparation (250% weight/volume)
 - Aspiration of lower concentration barium preparation (< 200% weight/volume) less likely to be produce serious complications

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Aspiration





(Left) Axial CECT MIP reformatted image of a patient with aspiration bronchiolitis shows patchy ground-glass and centrilobular micronodules 🔁 in association with a dilated esophagus 🔁. (Right) Axial CECT of a patient with achalasia and aspiration bronchiolitis shows multiple bilateral lower lobe posterior centrilobular nodules, tree-inbud opacities 🖂, and small nodular consolidations 🖂 with an intrinsic air-fluid level.





(Left) Axial CECT of a patient with aspiration due to esophageal cancer with esophago-respiratory fistula shows frothy secretions \supseteq in the left lower lobe bronchus with near-complete luminal obstruction and left lower lobe centrilobular nodules and ground-glass opacities 🛃. (Right) Axial NECT of a patient with altered mental status and massive aspiration shows a large amount of lowattenuation material
attenuation materialfills the bilateral lower lobe bronchi and associated bilateral lower lobe postobstructive atelectasis 🚬





(Left) Axial NECT of a patient with with esophagorespiratory fistula and miliary tuberculosis shows a fistula \supseteq between the esophagus and the left lower lobe bronchus, left lower lobe consolidation and volume loss \blacksquare , and profuse bilateral miliary nodules. (Right) Frontal chest radiograph of a patient with an esophago-respiratory fistula obtained after fluoroscopic evaluation shows a large amount of high-density barium sulfate aspiration within the airways and the alveolar spaces.

Excipient Lung Disease

KEY FACTS

TERMINOLOGY

- Excipient lung disease
- Occlusion of pulmonary arterioles and capillaries by insoluble foreign body particles from intravenous (IV) injection of crushed tablets intended for oral use only, which leads to acute or chronic cor pulmonale

IMAGING

- Talc/cellulose
 - Diffuse centrilobular micronodules &/or tree-in-bud opacities
 - Fissural sparing
 - Absence of signs of airways disease
 - Dilated pulmonary trunk (> 3 cm) indicating pulmonary hypertension
 - Dilated right heart (right ventricular strain)
- Ritalin
 - Lower lobe predominant panlobular emphysema
 - Mimics α-1 antitrypsin deficiency

TOP DIFFERENTIAL DIAGNOSES

- Cellular bronchiolitis
- Miliary infection
- Pulmonary hypertension
- Pulmonary capillary hemangiomatosis
- a-1 antitrypsin deficiency
- Sarcoidosis

PATHOLOGY

- Foreign bodies produce angiocentric granulomas
- Birefringent rod-like cellulose crystals, 20-200 µm
- Birefringent needle-like or plate-like talc crystals, 5-15 µm

CLINICAL ISSUES

- Patients almost always deny injection, even when confronted
- Frequent evolution to pulmonary hypertension and cor pulmonale, which may lead to sudden death
- Treatment: Discontinuation of IV injection

(Left) AP chest radiograph of a 37-year-old patient with talc granulomatosis shows bilateral, ill-defined, micronodular opacities and enlarged bilateral pulmonary arteries 🔁 concerning for pulmonary hypertension, a very common ancillary finding. (Right) Axial CECT of the same patient shows diffuse, bilateral, centrilobular micronodules with a tree-inbud pattern. Note that these nodules spare the subpleural aspects \supseteq of the lungs and are diffusely and evenly distributed.





(Left) Composite image with coronal CECT MIP reformatted images of the same patient obtained at baseline (left) and months later (right) shows progression of tree-in-bud opacities as the patient continued to intravenously inject crushed tablets intended for oral use. (Right) Lowpower photomicrograph (H&E stain) of a specimen from the same patient shows innumerable small nodular lesions 🔁 centered about the bronchovascular bundles. While some nodules are nearly subpleural, the pleura itself 🔁 is free of nodules.





Excipient Lung Disease

TERMINOLOGY

- Abbreviations
- Excipient lung disease (ELD)

Synonyms

- Angiocentric systemic granulomatosis
- Pulmonary angiothrombotic granulomatosis
- Pulmonary granulomatous vasculitis
- Pulmonary foreign body angiogranulomatosis
- Pulmonary mainline granulomatosis
- Talc embolism
- Foreign body microembolism
- Foreign body granulomatosis
- Intravascular talcosis
- Ritalin lung

Definitions

- Occlusion of pulmonary arterioles and capillaries by insoluble foreign body particles from intravenous (IV) injection of crushed tablets intended for oral use only → acute or chronic cor pulmonale
- Oral tablets contain active and inactive components
 o Inactive components (excipients)
 - Also referred to as binders or fillers
 - Provide stabilization, bulk, substance, or therapeutic enhancement
 - Cellulose (most common)
 - Talc (common but decreasing in frequency)
 - Other (less common)
 - Corn starch
 - □ Cotton fibers
 - □ Crospovidone
- Ritalin (methylphenidate) contains talc
 - Associated with panlobular emphysema
 - Likely triggered by drug itself with talc coadjuvancy
 Definite association of emphysema with IV Ritalin use
 - Association of long-term appropriate oral Ritalin use with emphysema has been postulated

IMAGING

General Features

- Best diagnostic clue
 - Diffuse centrilobular micronodules &/or tree-in-bud opacities
 - Fissural sparing
- Location
 - Cellulose granulomatosis: Diffuse
 - Ritalin (methylphenidate) lung: Lower lobe predominance
- Size
 - o Micronodules (1-2 mm)

Radiographic Findings

- Radiography commonly normal
- Cellulose and talc: Diffuse micronodules
- Ritalin (methylphenidate): Lower lobe-predominant emphysema and bullae

CT Findings

- Cellulose
 - Centrilobular nodules &/or tree-in-bud opacities common
 - Diffuse, bilateral, and evenly distributed
 - Sparing of pleura and interlobar fissures
- Talc
 - Centrilobular nodules &/or tree-in-bud opacities common
 - Diffuse, bilateral, evenly distributed
 - Sparing of pleura and interlobar fissures
 - Conglomerate masses (similar to progressive massive fibrosis) on background of pulmonary micronodules
 - Ground-glass attenuation
 - Panlobular emphysema
- Absence of features of airways disease
 - Bronchial wall thickening
 - Bronchiectasis
 - Mucus plugging
 - Mosaic attenuation
 - Air-trapping
- Dilated pulmonary trunk (> 3 cm) indicates pulmonary hypertension
- Dilated right heart (right ventricular strain)
 - Right ventricular:left ventricular diameter ratio > 1.0
 - Flattening of interventricular septum or septal bowing toward left ventricular lumen
- If serial studies available
 - Progression and increased conspicuity of centrilobular nodules
 - Progressive dilatation of pulmonary trunk and right heart
- Ritalin (methylphenidate)
 - Lower lobe predominant panlobular emphysema (most common)
 - Similar to α-1 antitrypsin deficiency
 - o Conglomerate masses (progressive massive fibrosis)
 - Centrilobular micronodules (uncommon)

Imaging Recommendations

- Best imaging tool
 - MIP reformations help differentiate centrilobular from miliary and perilymphatic micronodules
 - Miliary and perilymphatic micronodules involve fissures

DIFFERENTIAL DIAGNOSIS

Cellular Bronchiolitis

- Principal cause of tree-in-bud nodules
 - Infectious bronchiolitis
 - Diffuse aspiration bronchiolitis
- Tree-in-bud pattern may be diffuse; not typically evenly distributed
- Other findings of airways disease
 Bronchial wall thickening
 - o Bronchiectasis
 - Mucus plugging
 - Mosaic attenuation
 - Air-trapping (expiratory imaging)

Miliary Infection

- Hematogenous dissemination of infection
 Tuberculosis: Dyspnea, cough, hypoxemia
 Histoplasmosis
- Some nodules along pleura and fissures

Pulmonary Hypertension

- Plexogenic arteriopathy
 - o May exhibit diffuse centrilobular nodules on CT
- Cholesterol granulomas in 25%
 May exhibit diffuse centrilobular nodules on CT
 May be indistinguishable from cellulose granulomatosis

Pulmonary Capillary Hemangiomatosis

- Ground-glass centrilobular nodules correlate with angiomatoid proliferation
- May be indistinguishable from cellulose granulomatosis

a-1 Antitrypsin Deficiency

- Differential diagnosis for Ritalin lung
- Lower lobe predominant and panlobular
- Differentiation based on history, serum α-1 antitrypsin levels, and pathology

Sarcoidosis

- Affected patients frequently asymptomatic
- Perilymphatic distribution of micronodules
 Abundant nodules along pleura and fissures
- Hilar and mediastinal lymphadenopathy common

PATHOLOGY

General Features

- Foreign bodies produce angiocentric granulomas
- Cellulose
 - Crystals within granulomas
 - Translucent and colorless, or pale blue-gray on H&E
 - Birefringent rod-like crystals; 20-200 μm
 - Occluded and recanalized pulmonary arterioles
 - Intravascular and perivascular foreign body granulomas with giant cells
- Talc
 - Intravascular birefringent talc crystals
 - Colorless to pale yellow on H&E
 - Strongly birefringent needle-like or plate-like crystals;
 5-15 µm
 - Perivascular foreign body giant cells
 - Interstitial granulomas lead to fibrosis (similar to progressive massive fibrosis) with surrounding cicatricial emphysema
 - Small talc particles may pass through capillaries into pulmonary veins and lodge in retina, kidneys, liver, spleen, lymph nodes, bone marrow, spinal cord

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Affected patients may be asymptomatic
 - Dyspnea, sputum production
 - o Fever
 - o Arrhythmia and sudden death

- Other signs/symptoms
 - Funduscopy may reveal talc crystals in retinal arterioles
 - Echocardiography: Pulmonary hypertension, dilated right heart chambers
- Clinical profile
 - Risk factors
 - IV drug user
 - Chronic use of analgesics, stimulants, and antihistamines
 - Chronic treatment with opioid tablets (e.g., codeine, hydrocodone)
 - IV injection of methadone tablets produces severe symptoms
 - Common clinical features: Chronic pain, malignancy, multiple sclerosis, migraine, psychiatric disorder
 - Chronic Ritalin (methylphenidate) use
 - Healthcare workers
 - Long-term central intravascular catheters [e.g., central lines, peripherally inserted central catheters (PICC)], implanted vascular ports, hemodialysis catheters
 - After discontinuation of IV talc injection
 - Progression of lung fibrosis (progressive massive fibrosis) and pulmonary hypertension over months and years: 1 dyspnea, respiratory failure, and death

Natural History & Prognosis

- Patients almost always deny injection, even when confronted
 - Diagnosis requires high index of suspicion
 - Diagnosis frequently requires pathologic confirmation
 - Most cases result from repetitive injection
 - Recurrent episodes of shortness of breath, fever, arrhythmia
 - Patients may have needle tracks or history of IV drug use
- Few cases result from single massive injection
- Whether massive, acute, or recurrent injection, frequent evolution to pulmonary hypertension and cor pulmonale may lead to sudden death

Treatment

- If suspicion is high based on imaging, patient should be closely monitored until disclosure of injection &/or pathologic confirmation
- Discontinuation of IV injection

DIAGNOSTIC CHECKLIST

Consider

- Cellulose granulomatosis in any patient with diffuse, evenly distributed tree-in-bud nodules
 - o Denial of IV injection of crushed tablets is common
 - Very high risk of sudden death

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Excipient Lung Disease





(Left) Axial CECT of the same patient shows a dilated pulmonary trunk 🖂, consistent with pulmonary hypertension. Normally, the pulmonary trunk exhibits a diameter similar to that of the , adjacent ascending aorta. (Right) Axial oblique CTA of the same patient shows dilatation of the right ventricle \supseteq , inversion of interventricular septum \supseteq , and a small pericardial effusion 🔁 indicating increased right heart pressures resulting from mechanical obstruction of the pulmonary arteriolar tree.





(Left) PA chest radiograph of a 65-year-old woman with Ritalin (methylphenidate) lung shows hyperinflation and lower lung zone band-like opacities. (Right) Coronal CECT of the same patient shows panlobular emphysema predominantly involving the lower lobes. While centrilobular micronodules related to talc may be present, the predominant finding is typically lower lobe panlobular emphysema.





(Left) Axial NECT of a patient with excipient lung disease from crospovidone shows faint centrilobular micronodules 🖂, lower lobe consolidations \square , and trace bilateral pleural effusions 🖂. (Right) Intermediate-power photomicrograph (Movat pentachrome stain) of a specimen from the same patient shows yellow corallike particles 🖻 in a muscular pulmonary artery. Crospovidone exhibits unique features including coral-like particles up to 100 μm in length and absence of birefringence.

KEY FACTS

TERMINOLOGY

- Acute eosinophilic pneumonia (AEP)
- Acute rapidly progressive lung disease with bronchoalveolar lavage (BAL) eosinophilia

IMAGING

- Diffuse or patchy parenchymal opacities (ground-glass &/or consolidation) associated with bilateral septal thickening and pleural effusion
- Ground-glass opacities (100%); consolidation (55%)
- Interlobular septal thickening (90 %)
- Centrilobular nodules (31%)
- Cephalocaudal and axial random distribution
- Pleural effusions (76%)

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary edema
- Diffuse alveolar hemorrhage
- Diffuse alveolar hemorrhage

PATHOLOGY

• AEP can represent acute type I hypersensitivity reaction triggered by a variety of causes (inhalational exposure, drugs, and infections)

CLINICAL ISSUES

- Acute onset of fever (often high) and rapidly progressing shortness of breath
- Pleuritic chest pain in 75%
- BAL: Higher eosinophil count (> 25%)
- Peripheral eosinophil count usually normal at presentation, may become elevated with disease progression

DIAGNOSTIC CHECKLIST

 Consider AEP in patient with acute respiratory illness, parenchymal opacities on imaging, and pulmonary eosinophilia on BAL in the absence of specific causes of eosinophilic lung disease

(Left) Axial NECT of a 61-yearold woman with acute eosinophilic pneumonia shows diffuse bilateral ground-glass opacities on a background of thick interlobular septal and intralobular lines 🖂, the socalled crazy-paving pattern. (Right) Coronal NECT of the same patient shows diffuse bilateral ground-glass opacities, ᠫ thick interlobular septa 🔁, and intralobular lines. Acute eosinophilic pneumonia is characterized by rapid onset of respiratory failure, fever, and eosinophilia.





(Left) AP chest radiograph of a patient with acute eosinophilic pneumonia shows bilateral parenchymal opacities and interlobular septal thickening that mimic pulmonary edema. Note the normal heart size. (Right) Axial HRCT of a patient with acute eosinophilic pneumonia shows patchy ground-glass opacities, interlobular septal thickening \square , and small pleural effusions 🔁. The findings mimic cardiogenic pulmonary edema, but the non-gravitationallydependent distribution of airspace disease should suggest other possibilities.





Abbreviations

• Acute eosinophilic pneumonia (AEP)

Definitions

• Acute rapidly progressive lung disease with eosinophilia on bronchoalveolar lavage (BAL)

IMAGING

General Features

- Best diagnostic clue
 - Diffuse or patchy parenchymal opacities (ground-glass &/or consolidation) associated with bilateral septal thickening and pleural effusion

Radiographic Findings

- Radiography
 - o Ground-glass opacity &/or consolidation
 - Bilateral, diffuse or patchy
 - Rapid progression (hours to days) similar to pulmonary edema
 - Interlobular septal thickening
 - Pleural effusion
 - Heart size usually normal

CT Findings

- Ground-glass opacities (100%)
- Consolidation (55%)
- Centrilobular nodules (31%)
- Interlobular septal thickening (90 %)
- Crazy-paving pattern (28%)
- Bronchovascular bundle thickening (66%)
- Random distribution in cephalocaudal and axial planes
- Pleural effusions (76%)
 o Bilateral (96%)
 - Small to moderate size
- Lymph node enlargement (45%)

DIFFERENTIAL DIAGNOSIS

Pulmonary Edema

- Hydrostatic/cardiogenic edema
 - Wide vascular pedicle
 - Cardiomegaly
 - Edema is usually gravity-dependent compared to variable distribution of AEP
- Permeability pulmonary edema
 - ARDS with diffuse alveolar damage (DAD)
 - Identification of etiology (pulmonary or extrapulmonary)
 - Exudative phase: Bilateral heterogeneous opacities
 - Proliferative phase: Coarse reticular opacities
 - Fibrotic phase: Slow resolution of reticular opacities

Diffuse Alveolar Hemorrhage

- Patchy or diffuse ground-glass opacities &/or consolidation
- Ill-defined centrilobular nodules
- Crazy-paving pattern
- Anemia / hemoptysis

PATHOLOGY

General Features

- AEP may represent acute type I hypersensitivity reaction triggered by variable causes (inhalational exposure, drugs, infections)
- Infectious pathogens may cause eosinophilic pneumonia via interaction with cells that have the capacity to produce cytokines and chemokines
- Drugs may cause AEP by binding to human pulmonary surfactant

Microscopic Features

• Eosinophilic infiltration in alveolar spaces and interstitium

• DAD in severe AEP

- Bronchoalveolar Lavage
- High eosinophil count (> 25%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Acute onset of fever (often high) and rapidly progressive shortness of breath
 - o Mvalgias in 50%
 - Pleuritic chest pain in 75%

Demographics

- Age
 - Young adults; mean age of 29 years
- Sex
 - No sex predominance
 - Epidemiology
 - o Incidence: 9/100,000 persons/year
 - Starting to smoke is a recognized risk factor for AEP

Laboratory Data

• Peripheral eosinophil count usually normal at presentation, may become elevated with disease progression

Natural History & Prognosis

- Good prognosis even in patients with acute respiratory failure
- Spontaneous disease regression reported

Treatment

- Remove exposure to triggering agent
- Systemic glucocorticoid therapy

DIAGNOSTIC CHECKLIST

Consider

• AEP in patient with acute respiratory illness, parenchymal opacities (radiography or CT), and pulmonary eosinophilia on BAL in the absence of specific causes of eosinophilic lung disease

- Suzuki Y et al: Eosinophilic pneumonia: a review of the previous literature, causes, diagnosis, and management. Allergol Int. 68(4):413-9, 2019
- De Giacomi F et al: Acute eosinophilic pneumonia. causes, diagnosis, and management. Am J Respir Crit Care Med. 197(6):728-36, 2018
KEY FACTS

TERMINOLOGY

- Chronic eosinophilic pneumonia (CEP)
- Idiopathic lung disease characterized by respiratory symptoms > 2 weeks, parenchymal opacities, and marked tissue and peripheral blood eosinophilia

IMAGING

- Radiography
 - o Peripheral upper lobe consolidation
- CT
 - Homogeneous consolidation &/or ground-glass opacities
 Peripheral, upper lobe predominant &/or migratory
 - o Crazy-paving pattern (8%)
 - Band-like opacities parallel to chest wall
 - Interlobular septal thickening (uncommon)

TOP DIFFERENTIAL DIAGNOSES

- Cryptogenic organizing pneumonia
- Simple pulmonary eosinophilia

• Eosinophilic granulomatosis with polyangiitis

PATHOLOGY

- Postulated autoimmune mechanisms or hypersensitivity reaction in CEP pathophysiology
- CEP diagnosis does not generally require lung biopsy

CLINICAL ISSUES

- 2/3 of patients have prior history of asthma
- 1/2 of patients have history of atopy
- Insidious clinical course with average of 7-8 months between onset of symptoms and diagnosis
- Symptoms: Productive cough, fever, dyspnea, weight loss
 Usually no extrathoracic manifestations
- Rapid and dramatic response to corticosteroid therapy
- Most patients relapse after steroid withdrawal (80%)

DIAGNOSTIC CHECKLIST

• Consider CEP in patient with chronic symptoms and peripheral upper lung zone consolidations

(Left) AP chest radiograph of a patient with chronic eosinophilic pneumonia shows bilateral peripheral mass-like consolidations that predominantly affect the upper lungs. (Right) AP chest radiograph of the same patient obtained several days later shows new dense middle lobe consolidation \blacksquare and hazy left upper lobe 🛃 and right basilar opacities. Note residual right upper lobe hazy opacity 🛃. The peripheral distribution and migratory nature of the airspace disease are characteristic of chronic eosinophilic pneumonia.





(Left) Axial CECT of a patient with chronic eosinophilic pneumonia shows peripheral ground-glass opacities \blacksquare with exquisite demonstration of subpleural sparing 🖾, a finding that can also be seen in nonspecific interstitial pneumonia and alveolar hemorrhage. (Right) Axial NECT of a patient with chronic eosinophilic pneumonia shows peripheral left lung consolidation with intrinsic air $bronchograms \supseteq and$ surrounding ground-glass opacity 🔁





Abbreviations

• Chronic eosinophilic pneumonia (CEP)

Definitions

• Idiopathic lung disease characterized by respiratory symptoms > 2 weeks, parenchymal opacities, and marked tissue and peripheral blood eosinophilia

IMAGING

General Features

Best diagnostic clue
 Peripheral upper lobe consolidation

Radiographic Findings

- Consolidation
 - Nonsegmental peripheral
 - Photographic negative of pulmonary edema (25% of patients)
 - Upper lobe predominant
 - Spontaneous migration (wax and wane)

CT Findings

- Homogeneous consolidation &/or ground-glass opacities
 Peripheral
 - Upper lobe predominant
 - o Migratory
- Crazy-paving pattern
- Band-like opacities parallel to chest wall
 > than 2 months after symptom onset
- Interlobular septal thickening (uncommon)
- Nodule or mass (uncommon)
- Mediastinal lymphadenopathy (uncommon)
- Pleural effusion (< 10%)

DIFFERENTIAL DIAGNOSIS

Cryptogenic Organizing Pneumonia (COP)

- Basilar predominance
- Bronchial dilatation more common in COP
- COP more likely to exhibit nodules and masses
- Reversed halo sign (common)

Simple Pulmonary Eosinophilia

- Patchy ground-glass opacities &/or consolidations
- Patchy subpleural nodules ± halo sign
- Usually self-limited process

Eosinophilic Granulomatosis with Polyangiitis

- Patchy ground-glass opacities &/or consolidations
- Bronchial wall thickening
- ANCA(+)

Acute Lung Injury Due to Covid-19

• May be indistinguishable based solely on imaging

E-Cigarette or Vaping Product Use-Associated Lung Injury (EVALI)

• May be indistinguishable based solely on imaging

PATHOLOGY

General Features

- Postulated autoimmune mechanisms or hypersensitivity reaction in CEP pathophysiology
- IL5-mediated eosinophil overproduction and lung infiltration may play integral role
- Diagnosis does not generally require lung biopsy

Microscopic Features

- Infiltration of lung interstitium and alveolar spaces by eosinophils
- Fibrinous exudate with preservation of lung architecture
- Lung biopsy may show evidence of other processes, such as organizing pneumonia

Laboratory Findings

- Peripheral blood eosinophilia (usually > 1,000/mL)
- Bronchoalveolar lavage (BAL) eosinophil count almost always > 25%
- Serum IgE levels elevated (50% of cases)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Productive cough, fever, dyspnea, weight loss
 - Usually no extrathoracic manifestations
- Clinical profile
 - o 2/3 of patients have prior history of asthma
 - o 1/2 of patients have history of atopy

Demographics

- Age
 - o Mean age of 45 years at diagnosis
 - Wide age range (18-80 years)
- Sex
- o M:F = 1:2
- Epidemiology
 - o Incidence of 0.23 cases/100,000 people
 - 3% of cases of various interstitial lung diseases

Natural History & Prognosis

- Insidious clinical course with average 7-8 months between onset of symptoms and diagnosis
- < 10% spontaneous resolution</p>
- Rapid and dramatic response to corticosteroid therapy
- Most patients relapse after steroid withdrawal (80%)

DIAGNOSTIC CHECKLIST

Consider

• CEP in patient with chronic symptoms and peripheral upper lung zone consolidations

- Crowe M et al: Chronic eosinophilic pneumonia: clinical perspectives. Ther Clin Risk Manag. 15:397-403, 2019
- Suzuki Y et al: Eosinophilic pneumonia: a review of the previous literature, causes, diagnosis, and management. Allergol Int. 68(4):413-9, 2019
- Allen J et al: Eosinophilic pneumonias. J Allergy Clin Immunol Pract. 6(5):1455-61, 2018

Hypereosinophilic Syndrome

KEY FACTS

TERMINOLOGY

- Hypereosinophilia (HE)
- Hypereosinophilic syndrome (HES)
- HE: Absolute eosinophil count > 1.5 × 10⁹/L on 2 examinations (interval > 1 month) &/or tissue HE
- HES: Organ damage &/or dysfunction attributable to tissue HE

IMAGING

- Patchy ground-glass opacities &/or consolidation
- Nodules (random distribution)
- Interlobular septal thickening
- Radiological manifestations of pulmonary edema secondary to heart failure

TOP DIFFERENTIAL DIAGNOSES

- Eosinophilic pneumonia
- Cardiogenic pulmonary edema
- Eosinophilic granulomatosis with polyangiitis

PATHOLOGY

- Primary or neoplastic HES
- Secondary or reactive HES
- Idiopathic HES
- Eosinophilic infiltration of affected organ

CLINICAL ISSUES

- Cardiac manifestation (> 50%)
 - Endocardial fibrosis, restrictive cardiomyopathy, valvular damage, mural thrombus
- Lung involvement (40%)
 - Chronic dry cough, dyspnea, wheezing
 - Fatigue, weight loss
- Neurologic disease
 - Cerebral thromboemboli, encephalopathy, peripheral neuropathy
- Arterial embolism
- Overall prognosis poor

(Left) PA chest radiograph of a patient with hypereosinophilic syndrome shows patchy peribronchial ⊇ and peripheral opacities. (Right) Axial CECT of a patient with hypereosinophilic syndrome shows patchy bilateral ground-glass opacities ⊇ and bronchovascular thickening ⊇. Imaging findings both on radiography and CT are nonspecific and need to be evaluated within the appropriate clinical context.





(Left) Axial NECT of a 14-yearold adolescent boy with primary hypereosinophilic syndrome shows centrilobular $micronodules \supseteq$ and groundglass opacities 🔁. (Right) Axial CECT of a 42-year-old man with idiopathic hypereosinophilic syndrome who presented with dyspnea, an erythematous rash over his entire body, and persistent eosinophilia of 8 months duration shows nonspecific diffuse bilateral ground-glass opacities 🔁 and consolidations.





Abbreviations

- Hypereosinophilia (HE)
- Hypereosinophilic syndrome (HES)

Definitions

- HE: Absolute eosinophil count > 1.5 × 10⁹/L (> 1,500 cells/µL) on 2 examinations (interval > 1 month) &/or tissue HE
- HES
 - o HE
 - Organ damage &/or dysfunction attributable to tissue HE
 - Exclusion of other causes of eosinophilia

IMAGING

Radiographic Findings

- Radiography
 - Parenchymal opacities (ground-glass &/or consolidation)
 Bilateral, diffuse or patchy
 - o Nodules
 - Random distribution
 - Radiological manifestations of pulmonary edema secondary to heart failure
 - o Cardiomegaly

CT Findings

- HRCT
 - o Ground-glass opacities &/or consolidation
 - Patchy
 - Random distribution in cephalocaudal and axial planes
 - o Nodules
 - With or without halo sign
 - Random distribution
 - o Interlobular septal thickening
 - Bronchovascular bundle thickening
 - Bronchial wall thickening
 - Pleural effusion in < 50%
 - o Intrathoracic lymphadenopathy (12%)
- Other CT manifestations
 - o Cardiomegaly
 - o Pulmonary edema secondary to heart failure

DIFFERENTIAL DIAGNOSIS

Eosinophilic Pneumonia

- May exhibit blood eosinophilia
 Does not meet criteria for HES
- Upper lobe peripheral predominance (chronic eosinophilic pneumonia)
- New-onset cigarette smoking (acute eosinophilic pneumonia)

Cardiogenic Pulmonary Edema

- No blood eosinophilia
- Ischemic heart disease most common cause

Eosinophilic granulomatosis With polyangiitis

- May exhibit blood eosinophilia
- History of asthma

PATHOLOGY

General Features

- Primary or neoplastic HES
 - Underlying myeloid/lymphoid/stem cell neoplasm with HE and rearrangement of *PDGFRA*, *PDGFRB*, *FGFR*, or with *PCM1-JAK2* translocation
- Secondary or reactive HES
 - Associated with inflammatory or neoplastic disease, parasitic infection, or adverse drug reaction
 - Expansion of non-clonal eosinophils driven by cytokines (such as IL-5) produced by other cell types
 - Lymphocytic variant (L-HES)
 IL-5-producing cells are aberrant clonal population of lymphocytes
- Idiopathic HES
 Patient meets criteria for HES but does not fit definitions of primary or reactive HES
- Cardiac manifestation (> 50%)
 Endocardial fibrosis, restrictive cardiomyopathy, valvular damage, mural thrombus
- Neurologic disease
- Cerebral thromboemboli, encephalopathy, peripheral neuropathy
- Other organs involved by HES
 Gastrointestinal tract, kidney, joints, skin

Gross Pathologic & Surgical Features

• Bronchoalveolar lavage (BAL) fluid eosinophilia as high as 73%

Microscopic Features

- Eosinophilic infiltration of affected organ
- Tissue necrosis

CLINICAL ISSUES

Presentation

- Lung involvement (40%)
 - Chronic dry cough, dyspnea, wheezing
 - Fatigue, weight loss
- Cardiac involvement
- Heart failure
- Arterial embolism

Demographics

- Age
- Most patients between 20-50 years (mean: 33 years)
- Sex
 - Old studies show predominance of HES in men (M:F = 9:1)
 - Recent studies show equal distribution of HES (M:F = 1:1)

Natural History & Prognosis

- Overall prognosis poor
- Cardiac disease is main cause of morbidity and mortality
- 5% of patients with HE eventually develop hematologic malignancy

SELECTED REFERENCES

. Kahn JE et al: (A critical appraisal of) classification of hypereosinophilic disorders. Front Med (Lausanne). 4:216, 2017

KEY FACTS

TERMINOLOGY

• Pulmonary alveolar microlithiasis (PAM): Rare autosomal recessive disorder characterized by intraalveolar calcium phosphate deposits (microliths or calcospherites)

IMAGING

• Imaging findings related to disease stage

• Radiography

- Early stage: Micronodular (sand-like) pattern
- o Advanced stage: Dense, irregular and reticular opacities
 - May obscure heart and diaphragm
 - "White lungs" (lungs are almost completely opaque)
 - Black pleura sign: Thin subpleural lucent line

• HRCT

- Dense nodules < 1 mm; random, septal, bronchovascular
- Ground-glass opacity, consolidation: Confluent micronodules
- Crazy paving: Calcification along interlobular septa
- Subpleural cysts: Correlate with black pleura sign

TOP DIFFERENTIAL DIAGNOSES

- Metastatic pulmonary calcification
- Dendriform pulmonary ossification
- Silicosis

PATHOLOGY

- Autosomal recessive disorder: Mutation of SLC34A2 gene
- Intraalveolar microliths: Round, concentrically laminated nodules

CLINICAL ISSUES

- Slight male predominance
- All ages; 2nd- and 3rd-decade predominance
- Signs and symptoms
 - Asymptomatic (early stage)
 - Dyspnea on exertion, dry cough (late stage)
 - Disease progression to cor pulmonale and respiratory failure in most patients
 - Disease may be stable in some patients

(Left) PA chest radiograph of a 36-year-old man with alveolar microlithiasis shows diffuse bilateral micronodular sandlike opacities and basilar parenchymal opacities that obscure the heart borders. (Right) Axial HRCT of the same patient shows ground-glass opacities ⊇, subpleural linear calcification ⊇, calcified micronodules ⊇, and tiny subpleural cysts ⊇.





(Left) High-power photomicrograph (H&E stain) of a specimen of alveolar microlithiasis demonstrates preserved lung architecture and small laminar calcifications (microliths or calcospherites) 🔁 in virtually all alveolar spaces. (Right) Axial HRCT of a patient with alveolar microlithiasis shows a diffuse high-attenuation crazypaving pattern with extensive calcifications along interlobular septa 🖂 on a background of alveolar calcification and tiny subpleural cysts 🖂.





Abbreviations

• Pulmonary alveolar microlithiasis (PAM)

Definitions

• Rare autosomal recessive lung disorder characterized by intraalveolar accumulation of calcium phosphate deposits (microliths or calcospherites)

IMAGING

General Features

- Best diagnostic clue
 - Calcified pulmonary micronodules
- Location
 - Bilateral distribution
 - Predominant mid and lower lung zone involvement
- Size
 - o <1mm
- Imaging manifestations are related to disease stage and profusion and distribution of calcified micronodules

Radiographic Findings

- Early stage
 - Micronodular pattern (sand-like)
 - Basilar predominance
- Advanced stage
 - Dense, irregular nodular and reticular opacities related to confluence of micronodules
 - May obscure heart (vanishing heart phenomenon) and diaphragm borders
 - o "White lungs" (lungs are almost completely opaque)
 - Black pleura sign: Thin lucent line between chest wall and alveolar calcifications

CT Findings

- HRCT
 - o Nodules
 - Dense, < 1 mm in size
 - Random, septal, bronchovascular
 - Ground-glass opacity
 - Related to confluence of micronodules
 - Consolidation
 - Related to confluence of micronodules
 - Air bronchograms
 - Interlobular septal thickening
 - High concentrations of calcified micronodules in secondary pulmonary lobule periphery
 - Crazy-paving pattern from calcifications along interlobular septa
 - Subpleural lines: Subpleural calcifications
 - Thick bronchovascular bundles
 - Traction bronchiectasis: < 10 mm
 - Subpleural cysts (dilated alveolar ducts, < 10 mm): Produce black pleura sign; subpleural lucency highlighted by adjacent calcified micronodules
 Bullae: Upper lobes (1-8 cm)

Nuclear Medicine Findings

Tc-99m MDP bone scintigraphy
 Diffuse bilateral radionuclide uptake

DIFFERENTIAL DIAGNOSIS

Metastatic Pulmonary Calcification

- Associated with chronic renal failure
- Ground-glass opacities and centrilobular nodules

Dendriform Pulmonary Ossification

- Associated with advanced pulmonary fibrosis and chronic aspiration
- Dendriform (branch-like lesions along terminal airways)

Silicosis

- Soft tissue &/or small calcified nodules
- Hilar/mediastinal lymphadenopathy; may exhibit egg-shell calcification

PATHOLOGY

General Features

- Autosomal recessive disorder with high penetrance
 Mutation of *SLC34A2* gene; encodes sodium-phosphate cotransporter NPT2b in alveolar type II cells
- Normal serum calcium and phosphorus
- Absence of any systemic disease of calcium metabolism

Microscopic Features

- Alveoli filled with calcospherites
 - Microliths: Round, concentrically laminated intra-alveolar nodules,
- Ossification and minimal inflammation may occur

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic (early stage)
 - Dyspnea on exertion, dry cough (late stage)
- Other signs/symptoms
 Chost pain homophysic
- Chest pain, hemoptysis, pneumothorax, digital clubbing
 Clinical manifestations often less severe than imaging abnormalities (clinical-radiologic dissociation)
- Microlith deposition in male genitalia (testicles and seminal vesicles) associated with infertility

Demographics

- Age
- All ages; 2nd- and 3rd-decade predominance
- Epidemiology
 - > 1/2 of reported cases (52.5%) in Turkey, China, Japan, India, and Italy

Natural History & Prognosis

- Disease may be stable in some patients
- Progression to cor pulmonale and respiratory failure in most patients

Treatment

• Lung transplantation

- Bendstrup E et al: Pulmonary alveolar microlithiasis: no longer in the stone age. ERJ Open Res. 6(3), 2020
- Shaw BM et al: Pulmonary alveolar microlithiasis. Semin Respir Crit Care Med. 41(2):280-7, 2020

Metastatic Pulmonary Calcification

KEY FACTS

TERMINOLOGY

- Calcium deposition in normal lung parenchyma
 - Abnormal calcium metabolism
 - Predisposing factors: Chronic renal failure, hypercalcemia, increased tissue alkalinity

IMAGING

- Radiography: Calcification rarely detected unless severe
- CT
 - o Ground-glass opacities (most common)
 - Typically centrilobular location, forming small rosettes
 - Dense consolidation
 - Multiple small calcified nodules
- Associated findings: Small vessel calcification in chest wall, heart, or pulmonary vasculature

TOP DIFFERENTIAL DIAGNOSES

- Sarcoidosis
- Silicosis

- Talcosis
- Alveolar microlithiasis
- Amyloidosis

PATHOLOGY

- Hypercalcemic conditions: Chronic renal failure (most common cause)
- High V:Q ratio in upper lobes leads to alkaline pH (7.51) (also in gastric wall and renal medulla), and upper lobe predilection in some reports

CLINICAL ISSUES

- Frequently asymptomatic, benign course
- Several systemic and pulmonary conditions
- Pulmonary function tests usually normal

DIAGNOSTIC CHECKLIST

- Consider MPC in patients with pulmonary abnormalities and known specific causative conditions
- Diagnosis may require CT and Tc-99m MDP

(Left) PA chest radiograph of a patient with metastatic pulmonary calcification shows bilateral peripheral, nodular, hyperdense pulmonary consolidations 🔁. Most metastatic calcification lesions are not dense enough to be identifiable on radiography. (Courtesy N. L. Müller, MD, PhD.) (Right) Axial NECT of the same patient shows multifocal left upper lobe peripheral nodular calcifications 🔁. CT is more sensitive than radiography for the identification of calcification. (Courtesy N. L. Müller, MD, PhD.)





(Left) Coned-down frontal chest radiograph of a patient with secondary hyperparathyroidism and metastatic pulmonary calcification shows multiple nodular airspace opacities that spare the subpleural lung 🔁. Note chest wall small vessel calcifications \square , a very common and specific ancillary finding. (Right) Axial NECT of the same patient shows highattenuation pulmonary nodular lesions forming rosettes with relative subpleural sparing \square , reflecting the centrilobular nature of the disease.





Abbreviations

• Metastatic pulmonary calcification (MPC)

Synonyms

• Pulmonary calcinosis

Definitions

- Pulmonary calcification
 - Dystrophic calcification
 - Calcium deposition in **injured** pulmonary parenchyma
 - Absence of ↑ serum calcium levels
 - Metastatic calcification
 - Calcium deposition in **normal** lung parenchyma
 - Abnormal calcium metabolism
 - Predisposing factors: Chronic renal failure,
 - hypercalcemia, increased tissue alkalinity
- Calciphylaxis
 - o Small vessel calcification leading to end-organ ischemia
 - o May result in rapidly fatal noncardiogenic edema

IMAGING

General Features

- Best diagnostic clue
 - Centrilobular ground-glass nodules or dense consolidations ± chest wall vascular calcification in setting of hypercalcemia
- Location
 - Variable, may be upper lung zone predominant: Tropism for tissues with relatively alkaline pH

Radiographic Findings

- Radiography
 - o Calcification rarely detected unless severe
 - Conventional high kVp technique not optimal for detection of calcification
 - Dual-energy digital radiography more sensitive than conventional radiography
 - Confluent or patchy airspace opacities
 - May mimic pulmonary edema or pneumonia
 - Intrinsic calcification seldom identified
 - Discrete or confluent nodules ± calcification
 - Diffuse interstitial process

CT Findings

- More sensitive than radiography for calcium identification
 - Very small nodules may not appear calcified despite presence of microscopic calcifications
 - Calcification may not be seen in up to 40% of cases
 - Some series report predilection for upper lung zones due to increased alkalinity in apices; other studies report no zonal predilection
- Variable appearances, three main patterns
 - Ground-glass opacities (most common)
 - Typically centrilobular; small rosettes with normal subpleural lung
 - Mulberry-shaped or miniature "cotton balls"
 - May exhibit punctate internal calcification

• Dense consolidation

- Most of abnormal lung shows calcification

- Wedge-shaped, usually peripheral consolidation of variable size
- Possibly due to vascular occlusion, which may be identified on CT angiography

• Multiple small nodules

- 3- to 10-mm, predominantly calcified
- Diffuse distribution
- Associated findings
 - Peripheral reticulation described
 - Small vessel calcification involving chest wall, heart, pulmonary arteries
 - Parathyroid masses representing parathyroid adenomas
 - Lytic bone lesions and "rugger-jersey" spine from hyperparathyroidism
- Dual-energy CT with calcium suppression shown to aid detection

Nuclear Medicine Findings

- Imaging with technetium-99m-methylene diphosphonate (Tc-99m MDP)
 - Most sensitive technique for early detection
 - o Increased radioactive isotope uptake
 - Symmetric and sufficiently dense to obliterate rib outlines

MR Findings

- Option for characterizing lung calcium accumulation caused by metabolic disorder
 - Hyperintense signal on T1WI, low calcium concentration of lesion

Imaging Recommendations

- Best imaging tool
 - CT is readily available and optimal for lesion detection and characterization

DIFFERENTIAL DIAGNOSIS

Sarcoidosis

- Nodule calcification is rare, upper lobes primarily involved
- Associated hypercalcemia (↑ production of calcitriol) may increase risk of MPC
 - o Seasonal hypercalcemia due to UV light sensitivity

Silicosis

- Silicotic nodules may calcify; upper lobes primarily involved
- History of occupational exposure

Talcosis

- History of intravenous drug use
- Upper lobe micronodules (< 1 mm) smaller than those in MPC: tend to coalesce into perihilar fibrotic masses

Alveolar Microlithiasis

- Small (~ 1 mm), punctate calcifications
- Diffuse involvement, more severe in lower lobes

Tuberculosis

- Upper lobes primarily involved, not associated with extensive calcification unless healed
- Prior granulomatous disease more likely to result in traction bronchiectasis and lung scarring

Mitral Stenosis

- Left atrial enlargement and vascular redistribution (pulmonary venous hypertension)
 - Generalized cardiomegaly and chronic edema common in patients with MPC
- Ossification primarily affects lower lobes

Amyloidosis

- Large nodules; small nodules generally do not calcify
- Often associated with interlobular septal thickening

Dendriform Pulmonary Ossification

- Dendritic calcification in lower lobes
 - May be isolated or associated with interstitial lung disease
 - o If isolated, likely related to chronic gastric acid aspiration
- Typically incidental finding in older men

Amiodarone Lung Toxicity

- Mass-like consolidations ± increased attenuation
- Basilar subpleural reticulation and fibrosis
- Increased attenuation in liver and spleen

PATHOLOGY

General Features

- Etiology
 - MPC rarely develops in patients with normal calcium metabolism
 - Hypercalcemic conditions
 - Benign causes of hypercalcemia
 - Chronic renal failure
 - Steroid and phosphate therapy
 - Chronic immobilization
 - Hyperparathyroidism
 - Hypervitaminosis D
 - Milk-alkali syndrome
 - Sarcoidosis
 - Liver transplantation
 - Malignant causes of hypercalcemia
 - Skeletal metastases (particularly breast carcinoma)
 - Multiple myeloma
 - Lymphoma and leukemia
 - Head and neck squamous cell carcinoma
 - Choriocarcinoma
 - Parathyroid carcinoma
 - Pathophysiology
 - Chronic acidosis leaches calcium from bone
 - Hyperparathyroidism causes bone resorption
 - Decreased renal function causes hyperphosphatemia and elevated calcium phosphate product
 - Calcium is less soluble in alkaline environment
 - High V:Q ratio in upper lobes leads to alkaline pH (7.51) (alkaline pH also in gastric wall and renal medulla)
 - Favors diffuse upper lung zone calcium deposition in some case series
 - Focal calcification suggests vascular occlusion to supplied area (focally increased V:Q ratio)
- Associated abnormalities
 - Lung, stomach, kidney, and heart (most common) metastatic calcification

- General pathology
 - MPC represents calcium deposition in normal tissue in contrast to dystrophic calcification, which affects abnormal tissue

Gross Pathologic & Surgical Features

• Rigid and gritty on cut section, preserved lung architecture

Microscopic Features

- Interstitial location
 - Interstitial abnormalities on CT are rare
 - CT abnormalities mimic airspace disease
- Alveolar septal and vascular deposition (50x > normal)
 Tropism for elastic tissues (small and medium-sized)
 - vessels)
- Organization and calcification of intraalveolar exudates
- Calcium stains positive with Alizarin red and von Kossa stains
- Fibrosis develops in more severe or longstanding cases

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Frequently asymptomatic, benign course
 - Gradual-onset dyspnea; some have sudden onset of symptoms and rapid fulminant course

Natural History & Prognosis

- Pulmonary function tests usually normal
 - With severe disease, restrictive pulmonary function and decreased diffusion capacity
 - Inverse correlation between pulmonary function and hypercalcemia
- Varies from incidental finding that remains stable for years to fulminant life-threatening course within days
- Death from cardiac involvement (alteration of conducting pathways)
- MPC may be reversible with correction of hypercalcemia • Irreversible in setting of fibrosis

Treatment

- Correction of hypercalcemia and treatment of underlying cause
- MPC may progress despite renal transplantation
- Promising preliminary response to sodium thiosulfate

DIAGNOSTIC CHECKLIST

Consider

- MPC in patients with pulmonary abnormalities and known specific causative conditions
- Diagnosis may require CT and Tc-99m MDP scintigraphy

Image Interpretation Pearls

• Lymph node calcification, interlobular septal thickening, and tree-in-bud opacities not seen in patients with MPC

- Fehrmann A et al: Metastatic pulmonary calcification: first report of pulmonary calcium suppression using dual-energy CT. Radiol Case Rep. 15(7):900-3, 2020
- 2. Lakshmana Perumal N et al: An unusual cause of pulmonary calcification. BMJ Case Rep. 12(6), 2019





(Left) Axial HRCT of a patient with metastatic pulmonary calcification shows right upper lobe peripheral, subpleural, clustered, high-attenuation nodular calcifications \supseteq with intrinsic air bronchograms 🖾 (Right) Composite image with axial NECT in lung (left) and soft tissue (right) window of a 46-year-old man with chronic renal disease and metastatic pulmonary calcification shows a right upper lobe heterogeneous consolidation with instrinsic calcification \supseteq (optimally visualized on soft tissue window) that exhibits subpleural sparing 🖂





(Left) AP chest radiograph of a 53-year-old man on hemodialysis shows metastatic pulmonary calcification that manifests as a right upper lobe consolidation initially diagnosed as pneumonia. Because of lack of improvement on follow-up chest radiography, a chest CT was obtained for further evaluation. (Right) Axial CECT of the same patient shows a calcified right upper lobe subsegmental consolidation ∠ Calcification is seldom identified on radiography and is more easily visualized on CT.





(Left) Axial NECT of a 54-yearold woman with metastatic calcification in the setting of chronic renal disease shows subtle bilateral upper lobe $ground-glass opacities \supseteq$ and mild reticulation. Note absence of noticeable calcification, which makes definitive diagnosis extremely difficult. (Right) Axial NECT MIP reformatted image of the same patient, obtained 18 months later, shows clustered punctate upper lobe peribronchovascular calcifications 🔁. Calcification is visible on CT in up to 60% of affected patients.

KEY FACTS

TERMINOLOGY

- Lymphangioleiomyomatosis (LAM)
- Tuberous sclerosis complex (TSC)
- LAM: Proliferation of neoplastic smooth muscle-like cells
 Sporadic LAM (S-LAM)
 - LAM associated with tuberous sclerosis (TSC-LAM)

IMAGING

Radiography

- Normal or increased lung volume
- Diffuse thin curvilinear opacities (cyst walls)
- Pneumothorax, pleural effusion
- CT/HRCT
 - Diffuse bilateral thin-walled cysts; normal intervening lung parenchyma
 - Ground-glass opacities related to hemorrhage
 - Septal thickening related to interstitial edema
 - Pneumothorax, pleural effusion
 - Lymphadenopathy, renal angiomyolipomas

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary Langerhans cell histiocytosis
- Birt-Hogg-Dubé syndrome
- Lymphoid interstitial pneumonia
- Light-chain deposition disease

PATHOLOGY

• Neoplastic smooth muscle cell proliferation around vessels, bronchioles, alveolar walls, lymphatics, and cyst walls

CLINICAL ISSUES

- Women of childbearing age; mean age: 34 years
- Progressive dyspnea, chest pain, cough, wheezing, hemoptysis
- Acute dyspnea and chest pain from spontaneous pneumothorax

DIAGNOSTIC CHECKLIST

• Consider LAM in young women with diffuse bilateral thinwalled lung cysts ± pneumothorax or pleural effusion

(Left) PA chest radiograph of a woman with lymphangioleiomyomatosis and progressive dyspnea shows normal lung volume and diffuse bilateral subtle

curvilinear opacities 🗁 with intrinsic lucencies that correspond to profuse pulmonary cysts. (Right) Coronal CECT of the same patient shows profuse bilateral thin-walled round pulmonary cysts of uniform sizes, characteristic of lymphangioleiomyomatosis. Note normal appearing intervening lung parenchyma.





(Left) Coronal NECT of a patient with

lymphangioleiomyomatosis shows profuse bilateral thinwalled pulmonary cysts of variable sizes and a large left lower lobe cyst 🔁. Large cysts measuring up to 30 mm may occur in patients with lymphangioleiomyomatosis. (Right) High-power photomicrograph (H&E stain) of a specimen of lymphangioleiomyomatosis shows atypical smooth muscle cell proliferations \square in the wall of a pulmonary cyst and foci of pulmonary hemorrhage Image: Example: E





Abbreviations

- Lymphangioleiomyomatosis (LAM)
- Tuberous sclerosis complex (TSC)

Definitions

- Rare neoplastic cystic lung disease; proliferation of atypical smooth muscle cells
 - o Sporadic LAM (S-LAM)
 - o LAM associated with tuberous sclerosis (TSC-LAM)
 - TSC: Neurocutaneous syndrome of multiorgan hamartomas, seizures, and cognitive disorders

IMAGING

General Features

- Best diagnostic clue
 - Premenopausal woman with diffuse thin-walled lung cysts, spontaneous pneumothorax, &/or chylothorax

Radiographic Findings

- Normal (in spite of diffuse cystic disease) or hyperinflation
- Diffuse thin curvilinear opacities and central lucencies (cysts)
- Pneumothorax
- Pleural effusion (chylous) in ~ 1/3; unilateral or bilateral

CT Findings

- Diffuse bilateral thin-walled cysts; normal intervening lung
 2-5 mm; may be as large as 25-30 mm
 - Spherical or ovoid cysts; polygonal cysts in severe disease
 - Perceptible smooth thin cyst walls
 - Progression from mild to severe lung involvement
- Ground-glass opacities from alveolar hemorrhage
- Septal thickening due to lymphatic obstruction/edema
- Multifocal micronodular pneumocyte hyperplasia (MMPH): Solid or ground-glass nodules (1-10 mm); more common in TSC-LAM
- Pneumothorax, pleural effusion (chylous), hydropneumothorax
- Thoracic duct enlargement
- Pericardial effusion (chylous)
- Lymphadenopathy (with low attenuation areas): Retrocrural region, abdomen, pelvis
- Lymphangioleiomyomas: Thorax, abdomen, pelvis
 Encapsulated masses with cystic components
- Renal angiomyolipomas (AML) in 32% of S-LAM
- Other: Hepatic/splenic AML, ascites (chylous)

Imaging Recommendations

- Best imaging tool
 - CT/HRCT is imaging modality of choice
- Protocol advice
- Coronal reformations to document diffuse involvement
- Screening recommendations (CT)
 - Women with TSC: Once after age 18; then every 5-10 years
 - Young/middle-aged non-smoking women with pneumothorax
 - Women with incidental AML, basilar lung cysts on abdomen CT, or chylous pleural effusion/ascites

o Women with unexplained progressive dyspnea

DIFFERENTIAL DIAGNOSIS

Pulmonary Langerhans Cell Histiocytosis

- M = F; smokers
- Upper lung zone predominant involvement
- Small cysts, bizarre shapes, nodular cyst walls
- Small irregular lung nodules (≤ 10 mm)

Birt-Hogg-Dubé Syndrome

- Autosomal dominant: Lung cysts, renal and skin lesions
- Irregular cysts; basilar, medial, subpleural
- Cysts may abut septa and encircle vessels

Lymphoid Interstitial Pneumonia

- Adult women; 50-60 years of age
- Immunosuppression, Sjögren syndrome
- Few large cysts, ground-glass opacities, nodules

Light-Chain Deposition Disease

- Association with lymphoproliferative disorders
- Light-chain deposition in alveolar walls, small airways, and vessels
- Diffuse lung cysts of variable sizes

Centrilobular Emphysema

- Males and females; smokers
- Upper lobe predominant involvement
- Centrilobular lucencies with imperceptible walls; visualization of central lobular artery

PATHOLOGY

General Features

- Etiology
 - Classified as low-grade malignant neoplasm by World Health Organization
 - LAM cells may metastasize via lymphatics
- Genetics
 - Inactivating mutations in *TSC* genes
 - TSC genes inhibit mechanistic mammalian target of Rapamycin complex 1 (*mTORC1*)
 - Hyperactivated *mTORC1* leads to extensive pulmonary lymphangiogenesis
 - S-LAM: Acquired mutations in *TSC2* gene confined to LAM lesions
 - TSC: Inherited autosomal dominant disorder
 - Genetic and acquired mutations in TSC1 (encodes hamartin) or TSC2 (encodes tuberin) genes in all cells
 - TSC-LAM: ~ 40% of women and 15% of men with TSC
- Associated abnormalities
 - Chylous ascites
 - o Abdominal lymphadenopathy
 - Renal, hepatic, splenic AMLs
 - Abdominal and pelvic lymphangioleiomyomas
 - Uterine leiomyomas, lymphaticoureteric and lymphaticovenous communications

Staging, Grading, & Classification

- LAM histology score (LHS)
 - Based on percent of lung involvement by cysts
 - o LHS-1: < 25%; LHS-2: 25-50%; LHS-3: > 50%

- Interstitial, Diffuse, and Inhalational Lung Disease
- LHS correlates with survival; worse prognosis with higher scores

Gross Pathologic & Surgical Features

- Lung enlargement; diffusely distributed lung cysts
- Thoracic, abdominal, and pelvic lymphadenopathy
- Enlarged thoracic duct and lymphatic channels
 - LAM cells may obliterate thoracic duct and produce altered lymphatic flow with resultant chylothorax
- Lymphangioleiomyoma: Chyle-filled encapsulated mass

Microscopic Features

- Neoplastic smooth muscle (LAM) cells around bronchioles, alveolar walls, vessels, axial lymphatics, and cyst walls
 - LAM cell clusters: Central spindle-shaped cells and peripheral epithelioid cells
- Type II pneumocyte proliferation, elastin and collagen fiber destruction in cyst walls
- Immunoreactivity for a-smooth muscle cell actin, desmin, vimentin, and human melanin black (HMB-45)
- Micronodular pneumocyte hyperplasia; virtually pathognomonic for TSC
- Lymphangioleiomyomas: Lymphatics infiltrated by LAM cells with intrinsic slit-like vascular channels

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Progressive symptoms
 - Exertional dyspnea, chest pain, cough, wheezing, hemoptysis, chyloptysis, chylothorax
 - Pneumothorax
 - 40-70% at presentation; > 70% recurrence
 - Exacerbation of symptoms with menstruation, pregnancy, and exogenous estrogen
 - Pulmonary function tests
 - Obstructive lung disease, increased lung volume
 - → FEV1 &/or diffusing capacity for carbon monoxide (DLCO)
- Other signs/symptoms
 - o Flank pain from rapid growth of renal AMLs
 - Hypotension: Hemorrhage in renal AMLs
 - Abdominal, flank/pelvic pain, abdominal distention, incontinence, chyluria, hematuria, lower extremity lymphedema, and paresthesias from abdominal and pelvic lymphangioleiomyomas

Demographics

- Age
 - Women of childbearing age; mean: 34 years, median: 38 years; documented in postmenopausal women usually in association with exogenous estrogen
- Sex
 - Almost exclusively women; women and men in TSC-LAM
- Epidemiology: S-LAM prevalence: 1-7.5/1 million women
- Diagnosis
 - Vascular endothelial growth factor D (VEGF-D): Proven diagnostic biomarker in appropriate clinical setting; lung biopsy is not necessary to establish diagnosis of LAM

- Characteristic HRCT findings but no additional features of LAM: VEGF-D testing to establish diagnosis prior to proceeding to histologic diagnosis via transbronchial or surgical lung biopsy
- Characteristic HRCT findings (> 10 thin-walled, round, well-defined, air-filled cysts, preserved or increased lung volume, and no other significant pulmonary involvement) considered **diagnostic** in patients with TSC, renal AMLs, serum vascular endothelial growth factor D (*VEGF-D*) ≥ 800 pg/mL, chylous effusion, or CT evidence of lymphangioleiomyomas

Natural History & Prognosis

- Prognosis (poor long term)
 - Progressive airflow obstruction and respiratory failure
 - Poor prognosis; milder disease in TSC-LAM
 - Poorer outcome in patients diagnosed at younger age and those with extensive cystic lung disease
 - Lung function deterioration and ↑ pneumothoraces in pregnancy
- Overall 5-year survival ~ 60-70%

Treatment

- Pneumothorax
 - Drainage, pleurodesis, pleurectomy; may complicate lung transplantation
- Chylothorax
 - Thoracic duct ligation, pleurovenous shunt
- Avoidance of estrogen
- Sirolimus (mTOR inhibitor)
 - Patient with LAM with abnormal or declining lung function
 - Patient with LAM with problematic chylous effusions
- Lung transplantation
 - Advanced disease
 - Recurrent disease reported in transplanted lung

DIAGNOSTIC CHECKLIST

Consider

- LAM in women with unexplained progressive dyspnea and increased lung volume on radiography
- LAM in women with diffuse bilateral thin-walled lung cysts ± pneumothorax or pleural effusion

Image Interpretation Pearls

- Chest radiographs may appear normal or near normal
- Pulmonary manifestations of TSC-LAM are identical to those of S-LAM

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Lymphangioleiomyomatosis





(Left) Axial CECT of a 31-yearold woman with lymphangioleiomyomatosis who presented with several years of progressive dyspnea shows profuse bilateral thinwalled pulmonary cysts 🔁 with little intervening normal lung parenchyma. (Right) Coronal CECT of the same patient shows the uniform distribution of the pulmonary $cysts \longrightarrow throughout both$ lungs. The cyst walls are thin and uniform, and there are no pulmonary nodules. This case illustrates characteristic HRCT features of lymphangioleiomyomatosis.





(Left) Composite image with CECT in lung (left) and soft tissue (right) window of a 48year-old woman with lymphangioleiomyomatosis shows innumerable pulmonary cysts *⊡* and right paraesophageal lymphadenopathy 🔁. (Right) Axial CECT of a 46-year old woman with lymphangioleiomyomatosis shows a large heterogeneously enhancing left renal mass *→* with predominant fat attenuation, characteristic of a renal angiomyolipoma, found in 1/3 of affected patients.





(Left) Axial HRCT of a 57-yearold woman with lymphangioleiomyomatosis shows innumerable thinwalled pulmonary cysts with normal intervening lung parenchyma and small, left larger than right, bilateral pleural effusions 🔁 that represented bilateral chylothroraces. (Right) Coronal NECT of the same patient obtained 5 years later when she presented with acute left chest pain shows a left pneumothorax 🔁 Note left pleural effusion and a partially visualized left pleural catheter 🔁.

KEY FACTS

TERMINOLOGY

• Amyloidosis: Deposition of abnormal insoluble proteins within tissues throughout body

IMAGING

- Pulmonary nodular amyloidosis: Solitary or multiple pulmonary nodules, often with calcification
- Diffuse alveolar septal amyloidosis: Interlobular septal thickening, perilymphatic nodules, consolidation
- Airway amyloidosis: Focal or diffuse tracheobronchial wall thickening that may be circumferential, ± calcification
- Cardiac amyloidosis: Biventricular hypertrophy, diastolic dysfunction, circumferential subendocardial delayed enhancement

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary nodular amyloidosis: Granulomatous infection
- Alveolar septal amyloidosis: Lymphangitic carcinomatosis
- Cardiac amyloidosis: Hypertrophic cardiomyopathy

PATHOLOGY

- Protein deposition within tissues
- Proteins: Combination of serum amyloid P, glycosaminoglycans, and fibril proteins
- Proteins arranged in sheets that retain Congo red dye with characteristic apple-green birefringence

CLINICAL ISSUES

- Pulmonary amyloidosis
 - Nodular: Usually asymptomatic
 - Alveolar septal: Progressive dyspnea, respiratory failure, development of pulmonary hypertension
- Tracheobronchial amyloidosis: Symptoms depend on whether proximal, mid, or distal airway involvement
 - Dyspnea, cough, hemoptysis
 - Proximal: Stridor
 - Mid and distal: Wheezing
- Cardiac amyloidosis: Diastolic dysfunction; progressive biventricular failure

(Left) Axial NECT (soft tissue window) of a patient with diffuse alveolar septal amyloidosis shows a partially calcified middle lobe consolidation 🔁. The lingula *is also involved but to a* lesser extent. Note the small right pleural effusion 🔁. The patient experienced progressive respiratory failure and eventually underwent lung transplantation. (Right) Axial HRCT of the same patient shows beaded interlobular septal thickening \square and subpleural \square and centrilobular 🔁 micronodules.





(Left) Composite image with low-power photomicrographs of a specimen from the same patient with Congo red stain (top) and under polarized light (bottom) shows characteristic apple-green birefringence ₽. Amyloid appears as amorphous interstitial and perivascular eosinophilic deposits on H&E stain. (Right) Axial NECT of a patient with a solitary amyloidoma shows a partially calcified lobulated mass \supseteq in the subpleural left upper lobe and a small left pleural effusion 🔁. The diagnosis was confirmed on biopsy.





TERMINOLOGY

Abbreviations

- Amyloid light chain (AL)
- Serum amyloid A (AA)
- Transthyretin amyloid (ATTR)

Definitions

• Deposition of abnormal insoluble proteins within tissue

IMAGING

General Features

- Best diagnostic clue
 - Pulmonary parenchyma: Partially calcified nodules or consolidations, interlobular septal thickening
 - Airway: Partially calcified, focal or diffuse airway wall thickening
 - Cardiac: Circumferential, subendocardial, myocardial delayed enhancement

Radiographic Findings

- Pulmonary parenchymal amyloidosis
 - Nodular parenchymal type: Solitary or multiple pulmonary nodules ± calcification
 - Diffuse alveolar septal type: Reticulonodular opacities ± confluent opacities that may contain calcification
- Radiography insensitive for diagnosis of airway amyloidosis

CT Findings

- Pulmonary parenchymal amyloidosis
 - Nodular parenchymal type
 - Well-circumscribed, solitary or multiple lung nodules
 Calcification (common)
 - □ Cavitation (rare)
 - Lung cysts in patients with Sjögren syndrome and associated lymphoid interstitial pneumonia
 - Diffuse alveolar septal amyloidosis
 - Interlobular septal thickening
 - Micronodules 2-4 mm; centrilobular or perilymphatic
 - Confluent consolidation ± calcification (common)
 - Pleural thickening and pleural effusions (common)
 - Cavitation (rare)
- Airway amyloidosis
 - More often localized than systemic
 - Focal or diffuse submucosal airway deposition along any portion of tracheobronchial tree
 - Long segment wall thickening more common than focal endobronchial lesion
 - Areas of calcification (common)
 - Involvement of posterior tracheal membrane
- Cardiac amyloidosis: Myocardial hypertrophy
- Mediastinal amyloidosis: Asymptomatic lymphadenopathy in systemic disease

MR Findings

- Cardiac amyloidosis
 - Biventricular hypertrophy
 - o Diastolic dysfunction, decreased diastolic relaxation
 - Delayed gadolinium enhancement
 - Early cardiac involvement: Subendocardial circumferential myocardial enhancement

- Late cardiac involvement: Diffuse transmural myocardial enhancement
- Atrial walls and cardiac valves may enhance
- Early clearance of gadolinium from blood pool and retention in cardiac tissues
 - TI scout sequences: Blood pool nulls before myocardium, which is reverse of normal
- Small pericardial effusion (common)
- Emerging: Elevated precontrast T1 relaxation times (T1 maps), indicating infiltrating fibrotic process

Nuclear Medicine Findings

- Amyloid exhibits FDG avidity on FDG PET
- F-18 florbetapir emerging as imaging biomarker, binds specifically to AL and ATTR

Imaging Recommendations

- Best imaging tool
 - o Alveolar septal amyloidosis: HRCT
 - o Cardiac amyloidosis: MR

DIFFERENTIAL DIAGNOSIS

Pulmonary Parenchymal Amyloidosis

- Nodular: Granulomatous infection, vasculitis (granulomatosis with polyangiitis), primary lung cancer
- Diffuse alveolar septal: Lymphangitic carcinomatosis, pneumoconiosis, atypical granulomatous infection

Airway Amyloidosis

- Cartilaginous lesions: Tracheobronchopathia osteochondroplastica, relapsing polychondritis (spares posterior trachea; amyloid does not)
- Neoplasm: Squamous cell carcinoma, adenoid cystic carcinoma
- Inflammatory: Granulomatosis with polyangiitis, sarcoidosis

Cardiac Amyloidosis

• Sarcoidosis, hypertrophic cardiomyopathy, myocardial infarction

PATHOLOGY

General Features

- Abnormal insoluble protein deposition throughout body
- Protein deposits: Combination of serum amyloid P, glycosaminoglycans, and fibril proteins
 - Fibril proteins are abnormally folded and organized into sheets
 - o Amyloid proteins are insoluble, deposit in tissue

Staging, Grading, & Classification

- Anatomic classification based on location of abnormal protein deposition
 - Localized: Deposition within single organ
 - Systemic: Deposition within multiple organs
 - Primary systemic: Associated with plasma cell dyscrasias
 - Secondary systemic: Patients with chronic infection/inflammation
- Biochemical classification system based on type of fibril protein in deposit
 - o > 30 proteins identified

- o AL
 - Most common type of amyloid in industrialized countries
 - Abnormal breakdown of normal immunoglobulin light chains produced by plasma cells
 - Occurs in patients with underlying plasma cell dvscrasia
 - Patients with AL have deposition of abnormal protein
- AA: Acute phase reactant, produced by liver
 - Can be elevated without amyloidosis in setting of systemic infection/inflammation
 - Amyloidosis: Abnormally folded AA proteins deposit in tissues
 - Patients with AA and β -2M amyloid: Abnormal deposition of normal but over abundant protein
- ο β-2 microglobulin: Dialysis-related protein
- o ATTRwt: Senile systemic amyloidosis
- o Hereditary forms
 - Hereditary ATTR, ALys, AGel, hereditary β-2 microglobulin

Microscopic Features

- Amorphous eosinophilic deposits of amyloid along interstitium and vessels
- Calcification and ossification (common)
- Congo red stain: Pulmonary amyloid deposits exhibit applegreen birefringence under polarized light

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Diverse clinical symptoms and presentation as any organ can be affected
 - o Localized forms are often asymptomatic; systemic forms often symptomatic
 - AL: Macroglossia and periorbital purpura in ~ 1/3 patients
 - Cardiac deposition: Restrictive cardiomyopathy is leading cause of morbidity and mortality
 - 50% patients with AL amyloidosis; rare in AA amyloidosis
 - □ Usually manifests with diastolic dysfunction with right ventricle > left ventricle failure
 - o Pulmonary parenchymal or airway deposition
 - Localized nodular form, usually asymptomatic, incidental finding on chest radiography
 - Diffuse alveolar septal form often progresses to respiratory failure, development of pulmonary hypertension
 - Tracheobronchial amyloidosis
 - □ Symptoms dependent on whether proximal, mid, or distal airways involved
 - Dyspnea, cough, stridor, wheezing, hemoptysis, recurrent pneumonia
 - o Renal deposition: Most common in AA and AL amyloidosis
 - Proteinuria
 - Nephrotic syndrome
 - Neuropathy
 - AL: 1/5 of patients have peripheral neuropathy at presentation

• Soft tissues: Deposition in muscles and salivary glands; may produce macroglossia, carpal tunnel syndrome

Demographics

- Epidemiology
 - o Generalized (or systemic) amyloidosis: 80-90%
 - Localized amyloidosis: 10-20%
 - Respiratory system commonly involved (50%), often as part of generalized amyloidosis
- Age: 6th and 7th decades of life

Natural History & Prognosis

- Pulmonary parenchymal amyloidosis
 - Nodular: Benign course, slow growth, remains asymptomatic
 - o Diffuse alveolar septal: Progressive respiratory decline, median survival is 16 months
- Tracheobronchial amyloidosis: Slowly progressive, proximal airway involvement with worse prognosis than distal airway involvement
- Airway amyloidosis: Overall 5-year survival of 30-50%
- Cardiac amyloidosis: Progressive disease, poor prognosis

Treatment

- Type of amyloid fibril and location of deposition determines • therapy
- Goals of therapy
 - Reduction in precursor proteins: Most important
 - AL amyloidosis: Treat underlying plasma cell dyscrasia
 - AA amvloidosis: Treat underlving infectious/inflammatory disorder
 - Maintain function of affected amyloidotic organs
 - Airway amyloidosis □ Endobronchial treatment: Laser, stent

DIAGNOSTIC CHECKLIST

Consider

• Alveolar septal amyloidosis in patient with chronic respiratory symptoms and CT findings of partially calcified consolidations and interlobular septal thickening

Image Interpretation Pearls

- Pulmonary nodular amyloidosis: Solitary or multiple pulmonary nodules/masses, often partially calcified
- Alveolar septal amyloidosis: Diffuse interlobular septal thickening and partially calcified consolidations
- Tracheobronchial amyloidosis: Diffuse or focal airway wall • thickening involving posterior tracheal wall, ± calcification
- Cardiac amyloidosis: Subendocardial circumferential • delayed enhancement; myocardium nulls before blood pool on T1 scout sequence

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(Left) Axial NECT of a patient with tracheobronchial amyloidosis shows circumferential tracheal wall thickening \supseteq with intrinsic areas of calcification 🔁 and resultant tracheal stenosis. Note that this process also involves the posterior membranous trachea. (Right) Sagittal NECT of the same patient shows tracheal wall thickening \supseteq with intrinsic calcification 🖾. Tracheostomy was required due to subglottic stenosis. Tracheobronchial amyloidosis occurs more often as a localized disease than as systemic involvement.





(Left) Coronal NECT of a patient with Sjögren syndrome, lymphoid interstitial pneumonia, and nodular amyloidosis shows multiple bilateral calcified nodules \supseteq and bilateral lung cysts 🖾. The association of amyloidosis with lymphoid interstitial pneumonia is a rare but known entity in the setting of Sjögren syndrome. (Right) High-power photomicrograph (H&E stain) of a specimen from the same patient shows amorphous eosinophilic amyloid deposition *⊡* and foci of ossification \square





(Left) Axial SSFSE MR of a patient with amyloidosis shows biventricular hypertrophy 🔁 and biatrial wall thickening 🔁. Amyloid deposition in the cardiac chamber walls is a common finding in cardiac amyloidosis. (Right) Short-axis delayed enhancement MR shows diffuse delayed enhancement of the entire left ventricular myocardium 🔁 and enhancement of portions of the right ventricular wall 🖄 Amyloid deposition begins in the subendocardial region but eventually extends through the entire myocardial wall.

KEY FACTS

TERMINOLOGY

- Pulmonary alveolar proteinosis (PAP): Syndrome characterized by accumulation of surfactant in alveoli and terminal bronchioles
 - o Autoimmune (90%)
 - o Secondary
 - Hereditary
 - Congenital

IMAGING

- Ground-glass pattern
 - Geographic distribution in autoimmune PAP
 - Diffuse distribution in secondary PAP
- Crazy-paving pattern
 - Surfactant accumulation in periphery of air spaces adjacent to interlobular septa &/or interstitial fibrosis
 - o Autoimmune PAP (75%)
 - Secondary PAP (25%)
- Consolidation

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary edema
- Diffuse alveolar hemorrhage
- Acute respiratory distress syndrome
- Pneumocystis jirovecii pneumonia

PATHOLOGY

• Surfactant accumulation in alveoli and terminal bronchioles

CLINICAL ISSUES

- Subacute or chronic indolent course with delayed diagnosis
- Dyspnea, cough, fatigue, weight loss

DIAGNOSTIC CHECKLIST

- Consider PAP in patient with subacute or chronic respiratory symptoms and geographic crazy-paving pattern on CT
- Differential diagnosis of ground-glass opacities and crazypaving pattern is broad and should not be limited to PAP

(Left) PA chest radiograph of a patient with autoimmune pulmonary alveolar proteinosis shows diffuse bilateral airspace disease 🖂 and basilar reticular opacities *⊠*. The findings may mimic those of pulmonary edema or alveolar hemorrhage. (Right) Axial HRCT of the same patient shows patchy groundglass opacities on a background of thick interlobular septa and intralobular lines, the socalled crazy-paving pattern, and right paratracheal lymphadenopathy 🔁.





(Left) Composite image with gross photograph of the right lung (left) and bronchoalveolar lavage fluid (right) shows alveolar proteinosis manifesting with areas of yellowish parenchymal discoloration 🔁 and "milky" lipid- and proteinrich bronchoalveolar lavage fluid. (Right) Low-power photomicrograph (H&E stain) shows pulmonary alveolar proteinosis manifesting with intraalveolar proteinaceous material 🖂, preserved lung architecture, and intact alveolar walls 🔁. (From DP: Thoracic.)





Abbreviations

• Pulmonary alveolar proteinosis (PAP)

Synonyms

• Pulmonary alveolar lipoproteinosis

Definitions

- PAP: Syndrome of altered surfactant homeostasis characterized by accumulation of surfactant in alveoli and terminal bronchioles
 - Autoimmune (primary): 90% of cases
 - o Secondary
 - Hereditary
 - Congenital

IMAGING

General Features

- Best diagnostic clue
 - Crazy-paving pattern in autoimmune PAP, ground-glass opacities in secondary PAP

Radiographic Findings

- Radiography
 - Range: Ill-defined ground-glass opacities to ill-defined consolidations
 - Related to alveolar filling
 - o Variable distribution
 - Symmetric perihilar or basilar (22%)
 - Resemble pulmonary edema; no cardiomegaly or pleural effusion
 - Asymmetric, unilateral, peripheral, lobar
 - Spares lung apices
 - o Ill-defined nodules at margins of consolidations
 - Reticular or reticulonodular opacities
 - Pneumothorax; ruptured subpleural cyst
 - Superimposed infection
 - Common organisms: Nocardia species, mycobacteria (tuberculosis, nontuberculous), fungi (Aspergillus, Cryptococcus, Histoplasma, Zygomycetes)
 - Pleural effusion
 - Mass or cavitation
 - Lymphadenopathy

CT Findings

- HRCT
 - Ground-glass pattern
 - Geographic distribution in autoimmune PAP
 - Diffuse distribution in secondary PAP
 - Subpleural sparing in autoimmune PAP
 - Crazy-paving pattern
 - Ground-glass opacities with superimposed thick interlobular septa and intralobular lines
 - Accumulation of proteinaceous material in periphery of air spaces adjacent to interlobular septa &/or interstitial fibrosis
 - Autoimmune PAP (75%)
 - Secondary PAP (25%)
 - o Consolidation
 - Few air bronchograms

- Traction bronchiectasis
- Initial HRCT (9%)
- Follow-up HRCT (23%)
- Honeycombing
- Follow-up HRCT (5%)
- Lung cysts (20%)
- Alveolar wall destruction by fibrosis or cigarette smoking
- o Mediastinal lymphadenopathy
 - 1 or 2 enlarged lymph nodes
 - > 1 cm in short-axis diameter
- o Silicoproteinosis
 - Dependent consolidation with areas of calcification
- Crazy-paving pattern uncommon

Imaging Recommendations

- Best imaging tool
 - HRCT

DIFFERENTIAL DIAGNOSIS

Hydrostatic Pulmonary Edema

- Acute clinical presentation
- Ground-glass opacity/crazy-paving/consolidation
- Gravitational distribution
- Cardiomegaly, pleural effusion

Acute Respiratory Distress Syndrome

- Acute clinical presentation
- Ground-glass opacity/crazy-paving/consolidation
- Anteroposterior gradient of lung involvement
- Pulmonary &/or extrapulmonary disease

Diffuse Alveolar Hemorrhage

- Clinical setting: Autoimmunity, pulmonary-renal syndrome
- Ground-glass opacity/crazy-paving/consolidation
- Variable distribution
- Anemia, hemoptysis

Pneumocystis jirovecii Pneumonia

- Subacute clinical course
- Impaired immune system: Acquired immune deficiency syndrome (AIDS)
- Ground-glass opacity/crazy-paving
- Lung cysts (pneumatoceles)

Lung Cancer

- Constitutional symptoms
- May exhibit crazy-paving pattern
 Adenocarcinoma subtype
- Focal or multifocal distribution
- Lymphadenopathy, pulmonary nodules

Other Diseases That Exhibit Crazy-Paving Pattern

- Sarcoidosis
- Nonspecific interstitial pneumonia
- Organizing pneumonia
- Lipoid pneumonia
- Chronic eosinophilic pneumonia

PATHOLOGY

General Features

- Etiology
 - Disruption of granulocyte-macrophage colonystimulating factor (GM-CSF) signaling, required by pulmonary alveolar macrophages to clear surfactant
- Autoimmune PAP
 - Disruption of granulocyte-macrophage colonystimulating factor (GM-CSF) signaling caused by high levels of anti-GM-CSF autoantibody
- Secondary PAP
 - Diseases that impair alveolar macrophage numbers or function (including surfactant catabolism)
 - Hematologic diseases
 - Myeloid disorders: Myelodysplastic syndrome, acute myeloid leukemia, chronic myeloid leukemia
 - Lymphoid disorders: Acute lymphoid leukemia, lymphoma (Hodgkin, non-Hodgkin), adult T-cell leukemia/lymphoma
 - Nonhematologic malignancies
 Glioblastoma, lung cancer, mesothelioma
 - Autoimmune disorders
 - Psoriasis, amyloidosis, immunoglobulin G monoclonal gammopathy
 - Immunodeficiency
 - Thymic alymphoplasia, immunoglobulin A deficiency, severe combined immunodeficiency disorder, immunosuppression for organ transplantation
 - Toxic inhalation exposures
 - Silica, cotton, cement, titanium, aluminum, cellulose
- Surfactant production disorders
 - SFTPB mutations
 - SFTPC mutations
 - ABCA3 mutations
 - o TTF1 (NKX2-1) mutations
- GM-CSF autoantibody
 - GM-CSF autoantibodies are polyclonal (IgG1, IgG2, and small amounts of IgG3 and IgG4)
 - Risk of PAP increased when GM-CSF autoantibody threshold > 5 µg/mL
 - GM-CSF autoantibodies: Diagnostic sensitivity and specificity; 100% and 98%

Gross Pathologic & Surgical Features

- Bronchoalveolar lavage fluid
 - Milky and turbid with thick sediment
 - Contains phospholipids and surfactant proteins A, B, and D, with lower concentrations of phosphatidylcholine and phosphatidylglycerol

Microscopic Features

- Intraalveolar accumulation of eosinophilic proteinaceous granular material
- May also involve bronchioles and alveolar ducts
- Cholesterol clefts, macrophages, and globular clumps of eosinophilic material found in granular eosinophilic material
- Proteinaceous material is positive for periodic acid-Schiff
- Mild interstitial thickening without inflammation or fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Subacute or chronic indolent clinical course with resultant delayed diagnosis for months or years
 - Dyspnea
 - Cough
 - Fatigue
 - Weight loss
- Other signs/symptoms
 - o Fever
 - Sputum production
 - o Crackles, clubbing, cyanosis
- Smoking history (autoimmune PAP)
 - German cohort (79%), Italian cohort (64%), Japanese cohort (57%)
- Dust or fume exposure
 - German cohort (54%), Italian cohort (32%), Japanese cohort (26%)

Demographics

- Age
 - o Median age at diagnosis: 51-52 years
- Sex
 - M:F ratio: 2.1:1 to 2.7:1
- Epidemiology
 - 3.7-6.2 cases per million population

Natural History & Prognosis

- Variable course
 - o Spontaneous remission (5-7%)
 - Persistent, unceasing symptoms
 - Progressive course with respiratory failure
- Good prognosis
 - o 5-year survival
 - 85% without therapy
 - 94% with whole-lung lavage therapy

Treatment

- Whole-lung lavage
- Subcutaneous or inhaled GM-CSF, rituximab, plasmapheresis, lung transplantation

DIAGNOSTIC CHECKLIST

Consider

• PAP in patient with subacute or chronic respiratory symptoms and geographic crazy-paving pattern on CT

Image Interpretation Pearls

 Differential diagnosis of ground-glass opacities and crazypaving pattern is broad and should not be limited to PAP

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(Left) Axial HRCT of a patient with pulmonary alveolar proteinosis shows geographic areas of crazy paving. The crazy-paving pattern is common in autoimmune pulmonary alveolar proteinosis, but diffuse ground-glass opacities are more common in secondary pulmonary alveolar proteinosis. (Right) Coronal HRCT of the same patient shows geographic areas of crazy-paving opacities, characterized by ground-glass opacities on a background of interlobular septal thickening and intralobular lines.





(Left) Axial HRCT of a patient with autoimmune pulmonary alveolar proteinosis shows diffuse ground-glass opacities, peribronchovascular 🔁 and subpleural 🔁 reticulation, and traction bronchiectasis \square , consistent with pulmonary fibrosis, a distribution that is not typical of usual interstitial pneumonia pattern. (Right) Coronal HRCT of the same patient shows diffuse bilateral ground-glass opacities with peribronchovascular and subpleural reticulation and traction bronchiectasis \supseteq .





(Left) Axial CECT of a patient with pulmonary alveolar proteinosis shows pulmonary ground-glass opacities and superimposed nocardiosis that manifests as several left upper lobe cavitary nodules 🔁 (Right) Axial HRCT of a patient with leukemia and secondary pulmonary alveolar proteinosis shows diffuse bilateral ground-glass opacities without thick interlobular septa and mediastinal lymphadenopathy ➡. The crazy-paving pattern is uncommon in secondary pulmonary alveolar proteinosis.

Lipoid Pneumonia

KEY FACTS

TERMINOLOGY

- Lipoid pneumonia (LP)
- Exogenous LP: Airspace disease from aspiration of vegetable, animal, or mineral oils; scant or no acute inflammation
- Endogenous LP: Airspace disease from accumulation of secretions distal to bronchial obstruction

IMAGING

- Radiography
- Basilar predominant consolidation, nodule, mass
- CT
 - Consolidation or ground-glass opacities; pulmonary nodule or mass
 - Macroscopic fat attenuation
 - Crazy-paving pattern
- FDG PET/CT
 - FDG activity secondary to superimposed infection/inflammation

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary hamartoma
- Lipoma
- Liposarcoma
- Pulmonary alveolar proteinosis
- Lung cancer
- Pneumonia

PATHOLOGY

- Mineral oil and vegetable-based oils cause minimal to mild inflammation
- Abnormalities based on type, amount, frequency, and length of time of aspirated/inhaled oils/fats

CLINICAL ISSUES

- Acute LP: Cough, dyspnea, and low-grade fever
- Chronic LP: Often asymptomatic older adult patients
- Treatment: Discontinuation of exposure to inciting agent; supportive care

(Left) PA chest radiograph of a 43-year-old woman with exogenous lipoid pneumonia shows right upper and left mid lung ill-defined, spiculated, mass-like opacities 🔁 that were initially considered to be malignant. (Right) Coronal CECT of the same patient shows bilateral lung masses \supseteq with intrinsic fat attenuation. The presence of intrinsic macroscopic fat is the most specific imaging finding of lipoid pneumonia, although it can also be seen in other entities, such as pulmonary hamartoma and liposarcoma metastases.





(Left) Low-power photomicrograph (H&E stain) of a specimen from the same patient shows numerous fat droplets \supseteq separated by fibrous tissue, lymphocytes, and alveolar foamy histiocytes ➡ The presence of foamy histiocytes and extracellular fat droplets is characteristic of lipoid pneumonia. (Right) High-power photomicrograph (Sudan black stain) of the same specimen confirms the presence of microscopic intraalveolar fat, which manifests as brown-staining areas 🔁.





Lipoid Pneumonia

TERMINOLOGY

Abbreviations

• Lipoid pneumonia (LP)

Synonyms

- Lipid pneumonia
- Cholesterol pneumonia
- Golden pneumonia

Definitions

- LP classified as exogenous or endogenous types based on etiology
- Exogenous LP: Airspace disease resulting from aspiration of vegetable, animal, or mineral oils; scant or no acute inflammatory reaction
 - Acute LP: Uncommon, typically caused by aspiration of large quantity of petroleum-based product
 - Chronic LP: Repeated episodes of aspiration or inhalation of animal fat, mineral, or vegetable lipids over extended period of time
- Endogenous LP: Airspace disease resulting from accumulation of secretions distal to bronchial obstruction
 - Also called "cholesterol" or "golden pneumonia"
 - Often associated with non-small cell lung cancers; may occasionally be associated with pulmonary infection

IMAGING

General Features

- Best diagnostic clue
- Consolidation with macroscopic areas of fat attenuationLocation
 - Lower lobes and middle lobe

Radiographic Findings

- Radiography
 - Acute LP
 - Consolidation or ill-defined opacities
 - 🗆 Lobar or segmental, bilateral, or unilateral
 - Middle &/or lower lobes
 - Potential complications: Pneumothorax and pneumomediastinum
 - o Chronic LP
 - Consolidations involving lower lobes &/or middle lobe
 - Nodule or mass

CT Findings

- HRCT
 - Acute LP
 - Consolidation or ground-glass opacities
 - □ Lower lobes &/or middle lobe
 - Crazy-paving pattern: Ground-glass opacities on background of interlobular septal thickening and intralobular lines
 - Complications: Pneumatocele, pneumothorax, pneumomediastinum
 - o Chronic LP
 - Consolidation or ground-glass opacities in one or more pulmonary segments
 Lower lobe predominant involvement

- Consolidations may exhibit peribronchovascular distribution
- Crazy-paving pattern
- Intrinsic fat attenuation
 - Superimposed inflammatory changes may obscure fat components
- Nodule(s) mass(es) ± fat attenuation
- □ Between -40 HU and -150 HU
- Fibrosis
 - Architectural distortion associated with consolidation
 - Interlobular septal thickening or bronchiectasis
- PET/CT
 FDG avidity secondary to superimposed infection/inflammation

MR Findings

• T1WI

• High signal intensity consistent with lipid content

Imaging Recommendations

- Best imaging tool
 - Thin-section CT/HRCT + clinical history (i.e., use, aspiration, or inhalation of oil-based material)
- Protocol advice

attenuation

Identification of fat attenuation on soft tissue window
 Averaging of soft tissue and air may mimic fat

DIFFERENTIAL DIAGNOSIS

Pulmonary Hamartoma

- Benign neoplasm, common cause of solitary pulmonary nodule
- Circumscribed nodule or mass with smooth or lobulated margins
- Variable size, most < 4 cm
- Cartilage and fat are most prominent tissue components

Lipoma

- Uncommon mesenchymal neoplasm originating from adipose tissue
- Well-defined nodule or mass with homogeneous fat attenuation
 - Subpleural mass originating from chest wall adipose tissue (often erroneously referred to as pleural lipoma)
 - Endobronchial lipoma manifests as fatty or soft tissue intrabronchial nodule

Liposarcoma

- Well-differentiated liposarcoma represents most common type of soft tissue liposarcoma
- Primary intra- or extrathoracic liposarcomas may metastasize to lungs
 - Well-differentiated liposarcoma metastases may contain variable amounts of fat
 - Multiple well-defined nodules with intrinsic fat attenuation

Pulmonary Alveolar Proteinosis

• Rare lung disorder of unknown etiology characterized by alveolar accumulation of surfactant

- Strong association with tobacco use; men 3x more frequently affected than women
- Bilateral central and symmetric opacities with ground-glass attenuation and crazy-paving pattern
- Apices and lung bases relatively spared

Lung Cancer

- Smokers; men more frequently affected than women
- Mass, nodule, or mass-like consolidation
- Associated intrathoracic lymphadenopathy may be present

Pneumonia

- Acute onset; fever, cough, sputum production
- Dense consolidations or ground-glass opacities without specific distribution

PATHOLOGY

General Features

- Diagnosis of exogenous LP based on history of ingestion or inhalation of oils with consistent imaging findings
- Bronchoalveolar lavage (BAL) or biopsy necessary in cases in which LP manifests as mass or nodule without fat attenuation
- LP characterized by presence of intraalveolar foamy (lipidladen) macrophages
- Mineral oil and vegetable oils tend to cause minimal to mild inflammatory reaction
 - Mineral oil is inert and may inhibit cough reflex and ciliary motility, thus promoting aspiration
 - LP from vaping e-cigarettes has been associated with vegetable glycerin
- Parenchymal abnormalities in LP depend on type, amount, frequency, and length of time of aspirated or inhaled oils or fats

Microscopic Features

- Intraalveolar and interstitial foamy histiocytes
- Extracellular fat droplets
- Fat droplets may coalesce in alveoli and become encapsulated by fibrous tissue, producing nodule or mass (paraffinoma)
- Foreign body giant cell reaction may be present
- Animal fats hydrolyzed by lung lipases into free fatty acids that may cause severe inflammatory reaction manifesting as focal edema and intraalveolar hemorrhage; may progress to fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Symptoms often nonspecific
 - o Symptoms often nonspeci
 - Acute LP
 - Cough, dyspnea
 - Low-grade fever
 - Chronic LP
 - Frequently asymptomatic
 - Chronic cough or dyspnea
 - Fever
 - Weight loss
 - Chest pain
 - Hemoptysis

- Exposure often identified retrospectively after diagnosis
 Directed questioning to elicit history
- Other signs/symptoms
 - Superimposed infection may result in progression of pulmonary findings

Demographics

- Age
 - Acute LP: Accidental exposure to oily material
 Middle-aged patients
 - Chronic LP: Older adult patients; teenagers/adults from vaping e-cigarettes
- Epidemiology
 - Occupational exposure: Fire eaters, oil blasting industries, lubricants industry, cleaning oil-containing vats
 - Chronic use of oil-based traditional folk remedies in some cultures
 - Vaping e-cigarettes
 - Chronic use of laxatives by older adults
 - Predisposing factors: Mental retardation, cleft palate, anatomic or functional swallowing abnormality, Zenker diverticulum, hiatal hernia, gastroesophageal reflux, critically ill patients with nasoenteric feeding

Natural History & Prognosis

- Variable natural history based on amount, length of time, and type of aspirated or inhaled oil-based material
- Acute LP may manifest radiologically within 30 minutes of aspiration or inhalation
 - Pulmonary opacities visible within 24 hours in most affected patients
 - Clinical and radiologic manifestations improve or resolve within few weeks
- Chronic LP
 - Clinical symptoms improve with cessation of exposure to oil-based substances
 - Radiologic abnormalities may improve slowly over time but typically remain stable even if exposure discontinued

Treatment

- Discontinuation of exposure to inciting agent
- Supportive care

DIAGNOSTIC CHECKLIST

Consider

• LP in asymptomatic older adult patients with chronic lower lobe consolidations

Image Interpretation Pearls

• LP may initially manifest as pulmonary mass or nodule without areas of fat attenuation and may be indistinguishable from primary lung cancer

Reporting Tips

• Careful clinical history is important in order to identify possible source of aspirated or inhaled lipid material

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Lipoid Pneumonia





(Left) Axial CECT of a 41-yearold patient with lipoid pneumonia shows a left lower lobe consolidation with intrinsic low attenuation 🛃 due to macroscopic fat. The presence of fat attenuation on CT is the imaging hallmark of lipoid pneumonia. (Right) Axial HRCT of a 37-year-old fireeater shows exogenous lipoid pneumonia manifesting as multifocal ground-glass opacities with superimposed interlobular septal thickening and intralobular lines (crazypaving pattern), an uncommon but well-described pattern in cases of lipoid pneumonia.





(Left) Axial CECT of an asymptomatic 48-year-old man with lipoid pneumonia and a history of chronic use of oil-based nose drops shows ground-glass opacities 🔁 in the middle lobe. (Right) Coronal CECT of the same patient shows multifocal, bilateral, lower lobe groundglass opacities \supseteq Groundglass opacity is a nonspecific imaging finding, which has been identified in both acute and chronic exogenous lipoid pneumonia, and has been recently described in lipoid pneumonia from vaping ecigarettes.





(Left) Coronal CECT of a 83year-old patient with lipoid pneumonia shows lower lobe dense consolidations 🖾 and ground-glass opacities 🖂 (Right) Axial CECT of the same patient shows bilateral lower lobe consolidations with intrinsic fat attenuation, characteristic of lipoid pneumonia. It should be noted that associated inflammatory changes may obscure the fat attenuation of these lesions. Bronchoalveolar lavage or biopsy may be necessary if lipoid pneumonia manifests as a mass or nodule without fat attenuation.

KEY FACTS

TERMINOLOGY

• Dendriform pulmonary ossification (DPO)

IMAGING

- Idiopathic DPO
 - Small nodules and branching structures
 - Exhibit tiny associated calcifications
 - Peripheral and basilar predominance
- DPO associated with interstitial lung disease
- Small calcified nodules and branching structures
 - Reticulation and traction bronchiectasis/honeycombing related to underlying disease
- Image review in "osteoporosis window setting" (window width 818, level 273) to confirms parenchymal calcifications

TOP DIFFERENTIAL DIAGNOSES

- Nodular pulmonary ossification
- Metastatic pulmonary calcification
- Dystrophic pulmonary calcification

PATHOLOGY

- DPO: Idiopathic or associated with interstitial lung disease
- DPO without associated interstitial lung disease may be related to chronic low-level acid aspiration
- Tubular bone deposits in alveolar walls and interstitium
- Bony spicules form contiguous branching pattern

CLINICAL ISSUES

- Asymptomatic patients (idiopathic)
- Idiopathic DPO: Indolent process, chronic course, good prognosis
- Average age: 64 years
- M:F = 6:1
- Prognosis of DPO associated with interstitial lung disease is related to underlying condition

DIAGNOSTIC CHECKLIST

• Consider DPO in patients with lower lobe small calcified nodules and branching structures

(Left) Axial NECT of a patient with idiopathic dendriform pulmonary ossification shows right lower lobe predominant high-attenuation small nodules and branching structures 🔁. Note absence of associated changes of pulmonary fibrosis, which is a common associated finding. (Right) Axial NECT MIP reformatted image (bone window) of the same patient confirms the presence of micronodules \square and branching structures with high-attenuation coefficients.





(Left) PA chest radiograph of a patient with idiopathic pulmonary fibrosis shows bilateral peripheral subpleural and basilar predominant reticular opacities. (Right) Axial NECT (bone window) of the same patient shows tiny subpleural calcifications related to dendriform pulmonary ossification (). Note the presence of honeycombing and traction bronchiolectasis () related to idiopathic pulmonary fibrosis.





Abbreviations

• Dendriform pulmonary ossification (DPO)

Synonyms

• Disseminated pulmonary ossification

Definitions

• DPO: Process characterized by presence of metaplastic ectopic bone in lung

IMAGING

General Features

- Best diagnostic clue
- Small calcified nodules and branching structures
- Location
 - Lower lobe predominance (posterior and lateral basilar segments)

CT Findings

- Idiopathic DPO
 - Small nodules and branching opacities
 - Exhibit calcification
 - Peripheral and basilar predominance
- DPO associated with interstitial lung disease
 - Small calcified nodules and branching structures
 - Reticulation and traction bronchiectasis/honeycombing according to underlying disease

Imaging Recommendations

- Best imaging tool
 - CT with mediastinal window setting (window width 350, level 50); may show high-attenuation foci that do not correspond to pulmonary ossification
 - Image review with "osteoporosis window setting" (window width 818, level 273) to confirm parenchymal calcifications

DIFFERENTIAL DIAGNOSIS

Nodular Pulmonary Ossification

- Lamellar deposits of calcified osteoid material within alveolar spaces
- Associated with chronic pulmonary venous congestion (mitral stenosis)

Metastatic Pulmonary Calcification

- Deposition of calcium salts in previously normal lung
- Chronic renal regurgitation
- Primary hyperparathyroidism

Dystrophic Pulmonary Calcification

- Deposition of calcium salts in previously injured lung
- Granulomatous disorders (histoplasmosis, tuberculosis, and sarcoidosis)
- Viral infections (postvaricella pneumonia)

Granulomas

• Isolated or miliary; may be indistinguishable from DPO

PATHOLOGY

General Features

- Inflammation and secondary anoxia with abnormal pH
 Acidic environment may lead to fibroblastic proliferation
 → metaplastic ossification in pulmonary interstitium
- DPO: Idiopathic or associated with interstitial lung disease
- DPO without associated interstitial lung disease may be related to chronic low-level acid aspiration
- Pulmonary diseases associated with DPO
 Idiopathic pulmonary fibrosis
 - Chronic obstructive pulmonary diseases (chronic bronchitis or emphysema)
 - o Pneumoconiosis

Microscopic Features

- Tubular bone deposits in alveolar walls and peripheral interstitium
- Bony spicules form contiguous branching pattern
- Fat or marrow elements
- Background of interstitial fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic patients (idiopathic)
 - DPO associated with interstitial lung disease
 - Clinical manifestations of underlying disease
- Other signs/symptoms
 - Recurrent spontaneous pneumothorax

Demographics

- Age
- Average age: 64 years
- Sex
- o M:F = 6:1

Natural History & Prognosis

- Idiopathic DPO: Indolent process with chronic course and good prognosis
- Prognosis of DPO associated with interstitial lung disease is related to underlying condition

DIAGNOSTIC CHECKLIST

Consider

• DPO in patients with lower lobe small calcified nodules and branching structures

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SECTION 7 Connective Tissue Disorders, Immunological Diseases, and Vasculitis

Introduction and Overview

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Imaging Modalities

Imaging of patients with connective tissue disorders, immunological diseases, and vasculitis with symptoms referable to the thorax typically begins with chest radiography but often requires advanced imaging with CT or HRCT for accurate detection and characterization of pleuropulmonary abnormalities. In some cases, the pleuropulmonary imaging findings of these disorders are the initial manifestation of the disease, which may not become clinically apparent until months or years later.

Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD)

Connective tissue diseases (also called collagen vascular diseases) comprise a group of autoimmune disorders characterized by damage to connective tissue components at various anatomic locations in the body. These include rheumatoid arthritis, scleroderma, mixed connective tissue disorder, polymyositis and dermatomyositis, systemic lupus erythematosus, Sjögren syndrome, and ankylosing spondylitis. These diseases may be associated with focal or diffuse pulmonary abnormalities.

The majority of connective tissue diseases have the potential to produce a chronic diffuse fibrosing interstitial lung disease known as CTD-ILD, that is indistinguishable from idiopathic interstitial pneumonias on imaging. Such interstitial lung diseases include usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), lymphoid interstitial pneumonia (COP) among others. However, diagnosis of CTD-ILD is important, as it bears a better prognosis than idiopathic pulmonary fibrosis (IPF). Patients with CTD-ILD and pulmonary fibrosis are at risk for primary lung cancer. Thus, new lung nodules or masses in this setting are highly concerning for malignancy, and a definitive diagnosis should be aggressively pursued.

Idiopathic Interstitial Pneumonia With Autoimmune Features (IPAF)

IPAF is a relatively recently described entity that denotes the presence of interstitial lung disease either on imaging or pathologically in association with features of autoimmunity (either clinical or serological) but not meeting full criteria for a specific connective tissue disease. Correct diagnosis is important, as it entails a better prognosis compared with idiopathic interstitial pneumonia and particularly IPF. IPAF is a diagnosis of exclusion that requires that idiopathic interstitial pneumonias and other entities (e.g., asbestosis) be excluded before the diagnosis can be considered. IPAF is a progressive disease and should be diagnosed and treated early to avoid progression to end-stage pulmonary fibrosis.

Immunocompromised Patients

In recent decades, several factors have led to an increased number of immunocompromised patients, including the widespread use of ablative chemotherapy in the management of patients with cancer, an increase in the frequency of solid organ and bone marrow transplantation, and the epidemic of human immunodeficiency virus (HIV) infection. Identification of pleuropulmonary imaging abnormalities in immunocompromised patients should always prompt consideration of infection as an important differential diagnostic possibility. However, many other diseases that mimic infection must also be excluded, including cytotoxic and noncytotoxic drug reactions, interstitial lung diseases, lymphoproliferative disorders, and malignant neoplasms.

The chest radiograph is an important initial imaging modality in the evaluation of symptomatic immunocompromised patients, but may be normal in 10% of patients with pulmonary complications. CT and HRCT provide improved accuracy for demonstrating imaging abnormalities, their patterns, distribution, and the extent of pulmonary involvement. When combined with clinical and epidemiological information, imaging findings may help to narrow the differential diagnosis and determine the next best steps in the diagnostic process. Comparison with prior imaging is critical for recognizing new abnormalities and for determining the temporal sequence of their progression.

Presence or absence of lymphadenopathy &/or pleural effusion may help narrow the differential diagnostic possibilities. Specific clinical and imaging features may be important clues. For example, lung nodules, masses, and consolidations detected by CT or HRCT in association with neutropenia should suggest angioinvasive aspergillosis as the leading diagnosis. The finding of ground-glass attenuation on CT in patients with HIV/AIDS is highly suggestive of *Pneumocystis jirovecii* pneumonia (PCP). It should be noted that management decisions in the treatment of opportunistic infections in immunocompromised patients are frequently made based only on imaging abnormalities without microbiologic confirmation.

Pulmonary Hemorrhage and Vasculitis

Pulmonary vasculitis syndromes include several diseases, some of which frequently affect the lung (e.g., granulomatosis with polyangiitis, Churg-Strauss syndrome, and microscopic polyangiitis). Pulmonary vasculitis also occurs in miscellaneous systemic disorders, diffuse pulmonary hemorrhage syndromes, and other secondary localized processes. The pulmonary vasculitis syndromes are clinicopathologic entities; their diagnosis is based not solely on pathologic findings, but rather on a correlation between clinical, imaging, and pathologic features.

Clinical settings in which pulmonary vasculitis may occur are variable and include diffuse pulmonary hemorrhage, pulmonary renal syndromes, pulmonary nodular &/or cavitary disease, and upper airway lesions. When patients present with pulmonary hemorrhage, corroborated by imaging findings and clinical testing, pulmonary vasculitis should be considered as a differential diagnostic possibility, including the most common vasculitis syndrome, granulomatosis with polyangiitis. The diagnosis of idiopathic pulmonary hemorrhage is always a diagnosis of exclusion.

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Connective Tissue Disease-Associated Interstitial Lung Disease



Connective Tissue Disease-Associated Interstitial Lung Disease





Connective Tissue Disease-Associated Interstitial Lung Disease

(Left) HRCT of a patient with scleroderma shows esophageal dilatation P and posterior subpleural groundglass 🔁 and reticular opacities ∂. Ground-glass opacity is typically the predominant imaging abnormality in nonspecific interstitial pneumonia. (Right) HRCT of a patient with scleroderma shows pulmonary fibrosis and honeycombing \square . A focal middle lobe solid nodule 🔁 represents associated primary lung cancer. Lung cancer risk is increased in patients with interstitial lung disease.



Connective Tissue Disease-Associated Interstitial Lung Disease



(Left) CECT of a patient with lupus pneumonitis shows patchy ground-glass opacities that involved both lungs. The CT imaging differential diagnosis of ground-glass opacity in patients with lupus also includes pneumonia and pulmonary hemorrhage. (Right) CECT of a patient with systemic lupus erythematosus shows bibasilar subpleural reticular opacities, traction bronchiectasis, and early honeycombing 🔁. Affected patients may exhibit CT manifestations of usual interstitial pneumonia.



Pulmonary Hemorrhage



(Left) CECT of a patient with polymyositis shows findings of nonspecific interstitial pneumonia with subpleural reticular and ground-glass opacities. Note the relative sparing of the subpleural lung $\overline{\square}$, a CT finding that is very suggestive of nonspecific interstitial pneumonia. (Right) CECT of a patient with idiopathic diffuse alveolar hemorrhage shows bilateral multifocal ground-glass opacities. Approximately 25% of patients with diffuse alveolar hemorrhage subsequently develop an autoimmune disorder.

KEY FACTS

TERMINOLOGY

- Interstitial pneumonia based on histology or HRCT/CT without complete rheumatologic criteria for specific connective tissue disease (CTD) but with clinical, serological, and morphologic criteria that suggest autoimmunity
- Term proposed by European Respiratory Society and American Thoracic Society task force in 2015 in response to absence of consensus regarding terminology

IMAGING

- Nonspecific interstitial pneumonia: Reticular &/or groundglass opacities with apicobasal gradient
- Organizing pneumonia: Bilateral consolidations or groundglass opacities with subpleural and lower lung zone predominance
- Lymphoid interstitial pneumonia: Lower lobe predominant patchy ground-glass or reticular opacities; lung cysts
- Usual interstitial pneumonia: Subpleural honeycombing with apicobasal gradient

TOP DIFFERENTIAL DIAGNOSES

- Nonspecific interstitial pneumonia
- Cryptogenic organizing pneumonia
- Lymphoid interstitial pneumonia
- Idiopathic pulmonary fibrosis
- Connective tissue disease-associated interstitial lung disease

CLINICAL ISSUES

- Criteria
 - Presence of interstitial pneumonia by HRCT/CT or surgical lung biopsy and
 - Exclusion of alternative etiologies and
 - Failure to meet criteria of defined CTD and
 - At least 1 feature from at least 2 of 3 domains (clinical, serologic, morphologic)
- Task force does not recommend specific treatment and leaves it to the discretion of individual provider

(Left) Axial HRCT of a 55-yearold woman with interstitial pneumonia with autoimmune features shows multifocal bilateral ground-glass opacities (that exhibited an apicobasal gradient). The patient did not meet rheumatologic criteria for any specific autoimmune disease. However, antinuclear and anti-EJ antibodies were present. (Right) Axial HRCT of the same patient shows basilar predominant bilateral ground-glass opacities and subtle intrinsic traction bronchiectasis 🔁.





(Left) Axial prone HRCT of the same patient shows persistence of bilateral basilar predominant ground-glass opacities. (Right) Low-power photomicrograph (H&E stain) of a specimen from the same patient shows mild alveolar wall thickening 🔁, consistent with early cellular nonspecific interstitial pneumonia with interspersed areas of normal lung parenchyma 🔁. Note prominent nodular lymphoid hyperplasia \square , which is a morphologic criterion for the diagnosis of interstitial pneumonia with autoimmune features.





Abbreviations

• Interstitial pneumonia with autoimmune features (IPAF)

Synonyms

- Undifferentiated connective tissue disease-associated interstitial lung disease (CTD-ILD)
- Lung-dominant connective tissue disease (CTD)
- Autoimmune-featured interstitial lung disease (ILD)

Definitions

• Interstitial pneumonia demonstrated by histology or HRCT/CT without complete rheumatologic criteria for specific CTD diagnosis, but with clinical, serological, and morphologic criteria that suggest autoimmunity

Associated Syndromes

- Usual interstitial pneumonia (UIP)
- Nonspecific interstitial pneumonia (NSIP)
- Organizing pneumonia (OP)
- Lymphoid interstitial pneumonia (LIP)

Historic Perspective

- IPAF diagnosis proposed in 2015 by European Respiratory Society and American Thoracic Society task force in response to absence of consensus regarding terminology
 - Term considered work in progress that requires further scientific testing and validation
 - Revisions of criteria will likely occur as more data becomes available
 - Guidelines or recommendations for clinical care. diagnostic testing, or management not included in task force proposal

Diagnostic Criteria

- Presence of interstitial pneumonia by HRCT/CT or surgical lung biopsy **and**
- Exclusion of alternative etiologies and
- Failure to meet criteria of defined CTD and
- At least 1 feature from at least 2 of following 3 domains o Clinical domain
 - Distal digital fissuring (i.e., "mechanic hands")
 - Distal digital tip ulceration
 - Inflammatory arthritis or polyarticular morning joint stiffness ≥ 60 minutes
 - Palmar telangiectasia
 - Raynaud phenomenon
 - Unexplained digital edema
 - Unexplained fixed rash on digital extensor surfaces (Gottron sign)
 - o Serologic domain
 - Antinuclear antibodies (ANA) ≥ 1:320 titer, diffuse speckled homogeneous patterns or ANA nucleolar pattern (any titer), or ANA centromere pattern (any titer)
 - Rheumatoid factor $\geq 2x$ upper limit of normal
 - Anti-CCP (anticyclic citrullinated peptide)
 - Anti-dsDNA (antidouble stranded DNA)
 - Anti-Ro (SS-A): Anti-Sjögren-syndrome-related antigen A, also called anti-Ro

- Anti-La (SS-B): Anti-Sjögren-syndrome-related antigen B, also called anti-La
- Antiribonucleoprotein
- Anti-Smith
- Antitopoisomerase (Scl-70)
- Anti-tRSNA synthetase
- □ Jo-1 (antihistidyl)
- □ PL-7 (antithreonyl)
- □ PL-12 (antialanyl)
- □ Others: EJ (antiglycyl), OJ (antiisoleucyl), KS (antiasparaginyl), Zo (antiphenylalanyl), tRS
- Anti-PM-Scl (antiexosome)
- Anti-MDA-5 (melanoma-differentiation-associated gene 5)
- Morphologic domain
 - Suggestive patterns on HRCT/CT
 - □ NSIP
 - □ OP
 - □ LIP
 - □ NSIP with OP overlap
 - Histopathology patterns or features by surgical lung biopsy
 - □ NSIP
 - □ OP
 - □ LIP
 - □ NSIP with OP overlap
 - □ Interstitial lymphoid aggregates with germinal centers
 - □ Diffuse lymphoplasmacytic infiltration (± lymphoid follicles)
 - Multicompartmental involvement (in addition to interstitial pneumonia)
 - □ Unexplained pleural effusion or thickening
 - Unexplained pericardial effusion or thickening
 - □ Unexplained intrinsic airways disease (by pulmonary function tests, imaging, or pathology)
 - Unexplained pulmonary vasculopathy

IMAGING

CT Findings

- UIP
 - Most common pattern
 - Honeycombing and pulmonary hypertension □ Worse prognosis when these features present
 - Subpleural honeycombing
 - Apicobasal gradient
 - HRCT UIP pattern (i.e., subpleural reticular opacities and honeycombing with apicobasal gradient ± traction bronchiectasis) may be seen in IPAF; does not exclude diagnosis, but is not included in morphologic domain - Rationale
 - - □ Pattern alone does not increase likelihood of having CTD
 - Controversy
 - □ UIP is common pattern in patients with IPAF
 - □ Not including UIP in morphologic domain may not allow diagnosis of IPAF in patient with UIP pattern with positive serologies but no features in clinical domain; such patients may be classified as having idiopathic pulmonary fibrosis

- Diseases, and Vasculitis
- NSIP
 - o Reticular &/or ground-glass opacities with apicobasal aradient
 - Traction bronchiectasis
 - Peribronchovascular involvement
 - Subpleural sparing
- OP
 - Bilateral consolidations or ground-glass opacities with subpleural and lower lung zone predominance
 - Peribronchovascular consolidations, ground-glass opacities, or nodules
 - Reversed halo (atoll) sign
- LIP
 - o Lower lobe predominant patchy ground-glass or reticular opacities
- Scattered lung cysts
- NSIP with OP overlap
 - Feature in morphologic domain
 - Lower lobe predominant consolidation, often peridiaphragmatic, associated with features of fibrosis (e.g., traction bronchiectasis, reticular abnormality, or lower lobe volume loss)
 - Controversy: Term seldom used by radiologists; description fits imaging features of NSIP
- Unexplained intrinsic airways disease: Mosaic attenuation pattern, air-trapping (on expiration), bronchial wall thickening, and bronchiectasis
- Unexplained pulmonary vasculopathy: Dilated pulmonary trunk &/or pulmonary arteries
- Unexplained pleural or pericardial effusion/thickening

DIFFERENTIAL DIAGNOSIS

Nonspecific Interstitial Pneumonia

- Identical imaging features
- Idiopathic cases do not meet criteria for any autoimmune disease
- IPAF diagnosis requires 1 feature in at least 2 of 3 domains (i.e., clinical, serologic, and morphologic)

Cryptogenic Organizing Pneumonia

- Identical imaging features
- Does not meet criteria for any autoimmune disease

Lymphoid Interstitial Pneumonia

- Identical imaging features
- Common associated autoimmune diseases: Sjögren syndrome and rheumatoid arthritis

Idiopathic Pulmonary Fibrosis

- Identical imaging features
- Does not meet criteria for any autoimmune disease

Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD)

- Identical imaging features
- Fulfills specific CTD diagnostic criteria

PATHOLOGY

General Features

• Multiple pathologic patterns included within morphologic domain (e.g., NSIP, OP, NSIP with OP, or LIP)

• UIP not listed in morphologic domain, but its presence does not exclude diagnosis

Staging, Grading, & Classification

- Histopathology patterns or features by surgical lung biopsy o OP
 - NSIP with OP overlap
 - o LIP
 - Interstitial lymphoid aggregates with germinal centers
 - Diffuse lymphoplasmacytic infiltration (± lymphoid follicles)

CLINICAL ISSUES

Presentation

- Other signs/symptoms
 - o Unexplained intrinsic airways disease
 - Reduced forced expiratory volume in 1 second (FEV1) or low FEV1:forced vital capacity (FVC) ratio - Elevated airways resistance
 - Unexplained pulmonary vasculopathy - Pulmonary hypertension defined as mean pulmonary pressure of > 25 mm Hg
 - Pulmonary capillary wedge pressure < 15 mm Hg

Demographics

- Age
 - o 5th-6th decades of life
 - Sex
 - o F>M
- Ethnicity
 - More common in non-Hispanic White populations
- Epidemiology
 - Typically nonsmokers

Natural History & Prognosis

- Clinical findings still unclear; further investigation required
- IPAF survival is similar to that CTD-ILD when HRCT or surgical lung biopsy is different than UIP pattern
- IPAF survival is better than that of idiopathic pulmonary fibrosis

Treatment

• Task force does not recommend specific treatment and leaves it to discretion of individual provider

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<u>Connective Tissue Disorders, Immunological</u>





(Left) High-power

photomicrograph (H&E stain) shows interstitial pneumonia with autoimmune features manifesting with minimally thickened alveolar septa with interstitial lymphoid infiltrates → (Right) High-power photomicrograph (H&E stain) of the same specimen shows mild septal fibrosis 🔁 and interstitial lymphoid infiltrates. Histologic findings in interstitial pneumonia with autoimmune features include nonspecific interstitial pneumonia, organizing pneumonia, and lymphoid interstitial pneumonia.





(Left) Axial HRCT of a 68-yearold woman with interstitial pneumonia with autoimmune features shows a nonspecific interstitial pneumonia pattern on HRCT with subpleural lower lobe ground-glass and reticular opacities and traction bronchiolectasis 🔁. Despite the presence of antinuclear antibodies, there were insufficient criteria to diagnose a specific connective tissue disease. (Right) Sagittal HRCT of the same patient shows subpleural ground-glass and reticular opacities and traction bronchiolectasis 🖂





(Left) Axial HRCT of a 35-yearold woman with interstitial pneumonia with autoimmune features demonstrates subtle subpleural ground-glass opacities 🖻 suggestive of a nonspecific interstitial pneumonia pattern. Despite the presence of antinuclear antibodies, there were insufficient rheumatologic criteria for diagnosing connective tissue disease. (Right) Axial prone HRCT of the same patient shows persistent of subpleural ground-glass opacities that exhibit a nonspecific interstitial pneumonia pattern.
Rheumatoid Arthritis

KEY FACTS

TERMINOLOGY

- Rheumatoid arthritis (RA)
- Autoimmune, destructive, systemic disorder characterized by symmetric polyarthritis with chronic inflammation, erosion, and damage of cartilage

IMAGING

- Lungs
 - Several patterns of diffuse lung disease
 - Usual interstitial pneumonia
 - Nonspecific interstitial pneumonia
 - Organizing pneumonia
 - Necrobiotic rheumatoid nodule
 - Drug toxicity
 - Pulmonary infection
- Pleura: Effusion; thickening and enhancement
- Large airways: Bronchiectasis
- Small airways: Follicular bronchiolitis, bronchiolitis obliterans

• Cardiovascular: Pericardial effusion, pulmonary hypertension, myocarditis

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic interstitial pneumonia
- Interstitial pneumonia with autoimmune features
- Progressive systemic sclerosis

CLINICAL ISSUES

- Imaging abnormalities may precede respiratory symptoms
- Pleuritic chest pain is most common symptom
- Medical therapy is mainstay of treatment
 - Corticosteroids
 - Disease-modifying antirheumatic drugs: Gold, penicillamine, methotrexate
 - Biologic agents: Infliximab, rituximab

DIAGNOSTIC CHECKLIST

• Consider RA in patient with arthropathy and pleural effusion

(Left) Axial CECT of a 62-yearold asymptomatic woman with rheumatoid arthritis shows smooth left pleural thickening ⊇. Pleural &/or pericardial effusions or thickening are the most common thoracic manifestation a of rheumatoid arthritis. (Right) Axial CECT of a patient with rheumatoid arthritis shows bilateral pleural effusions \supseteq and a large pericardial effusion \square , consistent with serositis. Pleural disease is identified in up to 73% of affected patients at autopsy, but less than 3% are symptomatic.





(Left) PA chest radiograph of a 69-year-old woman with rheumatoid arthritis shows low lung volume and diffuse bilateral lower lung zone predominant reticular opacities. (Right) Axial NECT of the same patient shows bilateral basilar predominant subpleural honeycombing, consistent with usual interstitial pneumonia. Usual interstitial pneumonia is the most common interstitial lung disease in patients with rheumatoid arthritis followed by non-specific interstitial pneumonia.





Rheumatoid Arthritis

TERMINOLOGY

- Abbreviations
- Rheumatoid arthritis (RA)

Synonyms

• Rheumatoid lung

Definitions

- Autoimmune, destructive, systemic disorder characterized by symmetric polyarthritis with chronic inflammation, erosion, and cartilage damage
 - Most common connective tissue disease
- Pulmonary complications in 60-80% of patients
 Related to RA or to treatment

IMAGING

General Features

- Best diagnostic clue
 - Articular pain and swelling + serositis (i.e., pleural &/or pericardial effusion)
- Location
 - Pleural disease is most common intrathoracic abnormality
 - Pleural-pericardial inflammation
 - Lung and airways
 - Pulmonary vasculature
- Size
 - Necrobiotic (rheumatoid) nodules; few mm to several cm
- Patients with RA 9x more likely to develop interstitial lung disease than general population

Radiographic Findings

- Radiography
 - o Lung
 - Interstitial lung disease: Subpleural
 - reticular/reticulonodular opacities
 - Organizing pneumonia (OP): Patchy peripheral consolidations
 - Infection: Lobar, segmental, subsegmental opacities
 - Pleura: Small to moderate, usually unilateral pleural effusions
 - Heart and pericardium: Pericardial effusion

CT Findings

- CECT
 - Pleural disease in 38-73% of cases at autopsy; < 3% symptomatic
 - Effusion: Inflammation (sterile exudative effusion)
 - Small to moderate, unilateral
 - May appear pseudochylous due to cholesterol crystals, often + rheumatoid factor
 - Thickening and enhancement
 - May involve parietal and visceral pleura
 - □ Smooth or nodular thickening
 - Impaired lung expansion; "trapped lung"
- HRCT
 - Evidence of interstitial lung disease in up to 25%
 - Usual interstitial pneumonia (UIP)
 - Subpleural reticular opacities ± honeycombing with apicobasal gradient

- Subpleural ground-glass opacities with apicobasal gradient
- ± traction bronchiectasis
- Increased risk of lung cancer; pulmonary nodule or mass should be regarded with suspicion
- o Nonspecific interstitial pneumonia (NSIP)
 - Predominantly subpleural ground-glass opacities with apicobasal gradient
 - Reticular opacities, traction bronchiectasis, lower lobe volume loss
- o OP
 - Unilateral or bilateral patchy consolidations, peripheral and peribronchial distribution
 - Polygonal (perilobular) opacities, reversed halo sign (rounded area of ground-glass opacity surrounded by ring of consolidation)
- Necrobiotic nodules
 - Well-defined borders; variable size: 0.5-5 cm
 - Peripheral distribution, cavitation in 50% of cases, may cause pneumothorax
 - May exhibit instrinsic calcification
- o Infection
 - Tuberculosis, nocardiosis, aspergillosis, histoplasmosis, coccidioidomycosis, pneumocystis pneumonia, cytomegalovirus infection
- o Other
 - Reactive amyloidosis
 - Severe complication of RA, serious, life-threatening disorder caused by deposition of amyloid A (AA) fibrils in multiple organs
 - Drug-associated lung toxicity
- o Large airways
 - Bronchiectasis in 30% of patients with RA
 - Cricoarytenoid luxation
 - Dyspnea and stridor
- o Small airways
- Follicular bronchiolitis
 - □ Lymphoid hyperplasia of bronchus-associated lymphoid tissue (BALT)
 - Small centrilobular nodules, peribronchial nodules, ground-glass opacities, mosaic attenuation, airtrapping
 - Bronchiolitis obliterans
 - Progressive concentric narrowing of membranous bronchioles
 - Mosaic attenuation, bronchiectasis, bronchial wall thickening
- Bone CT
 - o Sternoclavicular, glenohumeral joints
 - Periarticular osteoporosis, joint space narrowing, subcortical cysts, erosions, subluxation
- CTA
 - o Cardiovascular
 - Pulmonary hypertension (obliterative vasculopathy)
 - Enlarged pulmonary arteries, dilated right heart chambers, contrast reflux into inferior vena cava and hepatic veins
 - Myocarditis
 - Cardiomegaly, heart failure

MR Findings

- T1WIFS
 - Enhancement of erosions or joint spaces suggests hypervascular synovitis

Ultrasonographic Findings

- Grayscale ultrasound
 - Evaluation of sternoclavicular and glenohumeral joints: Intraarticular fluid, joint space widening, synovial hypertrophy

Imaging Recommendations

- Best imaging tool
 - HRCT for evaluation of interstitial lung disease
- Protocol advice
 - HRCT with inspiratory and expiratory phases

DIFFERENTIAL DIAGNOSIS

Idiopathic Interstitial Pneumonia

- Indistinguishable from connective tissue disease-interstitial lung disease on imaging
- Differentiation relies on clinical and paraclinical criteria

Interstitial Pneumonia With Autoimmune Features

- Indistinguishable from connective tissue disease-associated interstitial lung disease on imaging
- Differentiation relies on clinical and paraclinical criteria

Progressive Systemic Sclerosis

- NSIP: Most common pattern of interstitial lung disease, up to 80% of patients with systemic disease
 - Bilateral, symmetric ground-glass opacities, subpleural distribution
 - Reticular pattern and traction bronchiectasis
 - Honeycombing in 10-30% of affected patients
- Pulmonary hypertension in up to 30% of affected patients
- Dilated esophagus

Polymyositis/Dermatomyositis

- Cutaneous disease
- OP: Patchy areas of consolidation, subpleural or peribronchial distribution
- NSIP

Systemic Lupus Erythematous

- Pleural disease is most common thoracic manifestation • Pleural and pericardial effusion
- Diffuse pulmonary hemorrhage
 Bilateral consolidations
- UIP
- Deep venous thrombosis and pulmonary thromboembolism

PATHOLOGY

General Features

- Etiology
 - Multifactorial
 - Genetic susceptibility (up to 70% of patients with RA express *HLA-DR4*)
 - Environmental factors (smoking), infectious agents

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - May be asymptomatic despite significant radiographic abnormalities
 - o Pleuritic pain, exertional dyspnea, cough, wheezing
 - Fatigue, generalized weakness
 - o Arthralgia, joint swelling, and stiffness
 - RA-associated lung disease occurs within 5 year of RA diagnosis
- Other signs/symptoms
 - Nonarticular manifestations: Vasculitis, episcleritis, keratoconjunctivitis sicca, subcutaneous nodules, and mononeuritis multiplex
 - o Felty syndrome: RA + splenomegaly + leukopenia

Demographics

• Age

- Peak: Between 45-65 years
- Sex
 - F:M ratio = 3:1
- Epidemiology
 - RA affects 1% of adult population
 - Higher incidence in Native Americans
 - Development of interstitial lung disease in RA is associated with older age, male sex, positive rheumatoid factor, and history of smoking

Natural History & Prognosis

 Imaging abnormalities may precede development of respiratory symptoms

Treatment

- Medical therapy is mainstay of treatment
 - Corticosteroids
 - Disease-modifying antirheumatic drugs
 - Gold, penicillamine, methotrexate
 - Biologic agents: Infliximab, rituximab
- Several drugs used to treat RA may induce lung toxicity
 Interstitial lung disease: Gold, penicillamine,
 - methotrexate
 - o Biologic agents: Sarcoidosis-like disease

DIAGNOSTIC CHECKLIST

Consider

• RA in patient with arthropathy and pulmonary disease

Image Interpretation Pearls

 Inspiratory and expiratory imaging to diagnose small airways disease

Reporting Tips

- Consider infection or drug toxicity in patients with RA, acute pulmonary symptoms, and new pulmonary opacities
- Exclude lung/pleural disease associated with RA in patients with chronic pulmonary symptoms

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Rheumatoid Arthritis





(Left) Axial CECT of a 60-yearold man with rheumatoid arthritis undergoing treatment with methotrexate shows bilateral ground-glass and reticular subpleural opacities. (Right) Axial CECT of the same patient shows bilateral basilar ground-glass opacities and traction bronchiectasis \supseteq . The findings are consistent with nonspecific interstitial pneumonia. Note absence of honeycombing, which is a feature characteristically seen in usual interstitial pneumonia.





(Left) Axial CECT of a patient with rheumatoid arthritis and follicular bronchiolitis shows scattered tree-in-bud opacities \square amid a background of mosaic attenuation. Follicular bronchiolitis should be suspected when pulmonary opacities do not improve after treatment for infection. (Right) Composite image with axial inspiratory (left) and expiratory (right) HRCT of a woman with rheumatoid arthritis complicated by constrictive bronchiolitis shows normal lung attenuation on inspiration and air-trapping on expiration.





(Left) Axial NECT of a 52-yearold woman with rheumatoid arthritis shows numerous bilateral subpleural nodular opacities 🖂 (Right) Axial NECT of the same patient obtained during a CT-guided biopsy shows the biopsy needle approaching one of the lung lesions, which exhibited chronic inflammation and focal organizing pneumonia. Organizing pneumonia may be secondary to rheumatoid arthritis or may be associated with treatment (drug-toxicity), and usually resolves completely after treatment with steroids.

Scleroderma

KEY FACTS

TERMINOLOGY

• Generalized connective tissue disorder that affects multiple organs, including skin, lungs, heart, and kidneys

IMAGING

- Radiography
 - Symmetric basilar reticular opacities
 - Decreased lung volume, sometimes out of proportion to lung disease
 - Dilated, air-filled esophagus best seen on lateral radiograph
- CT
 - Interstitial lung disease: Nonspecific interstitial pneumonia > > usual interstitial pneumonia
 - Thin-walled subpleural cysts: 10-30 mm
 - Esophageal dilatation (80%)
 - Pulmonary arterial hypertension
 - o Lymphadenopathy (60-70%)

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic pulmonary fibrosis
- Aspiration pneumonia
- Nonspecific interstitial pneumonia

PATHOLOGY

• Collagen overproduction and deposition in tissue

CLINICAL ISSUES

- Pulmonary disease usually follows skin manifestations
- Increased risk of lung cancer, usually in patients with pulmonary fibrosis
- Poor prognosis; death usually from aspiration pneumonia

DIAGNOSTIC CHECKLIST

- Consider scleroderma in patient with chronic interstitial lung disease and dilated esophagus
- Consider lung carcinoma in patient with scleroderma and dominant solid or sub-solid lung nodule

(Left) Axial HRCT of a patient with known scleroderma shows symmetric peripheral ground-glass and reticular opacities with subpleural sparing \boxtimes and a markedly dilated distal esophagus \supseteq . (Right) Coronal NECT minIP reformatted image of the same patient shows basilar predominant lung disease 🔁 and debris within a markedly dilated distal esophagus \implies , which is highly suggestive of esophageal dysmotility. Esophageal dysmotility is commonly present in patients with scleroderma.





(Left) Axial HRCT of a patient with scleroderma shows peripheral ground-glass and reticular opacities \supseteq , traction bronchiolectasis, and a dilated distal esophagus \boxtimes , consistent with esophageal dysmotility. (Right) Frontal hand radiograph of the same patient shows joint space narrowing, osteopenia \blacksquare , and soft tissue calcifications 🛃. Concomitant imaging findings of skeletal abnormalities and soft tissue calcifications in the setting of collagen vascular disease are helpful in suggesting the specific diagnosis.





TERMINOLOGY

Synonyms

• Systemic sclerosis

Definitions

- Generalized connective tissue disorder affecting multiple organs, including skin, lungs, heart, and kidneys
- Limited cutaneous systemic sclerosis (60%)
 Skin involvement: Hands, forearms, feet, face
 - Longstanding Raynaud phenomenon
 - CREST syndrome: Calcinosis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasias
- Diffuse cutaneous systemic sclerosis (40%)
 - Acute onset: Raynaud phenomenon, acral and truncal skin involvement
 - High frequency of interstitial lung disease
- Scleroderma sine scleroderma (rare)
 - Interstitial lung disease without skin manifestations

IMAGING

General Features

- Best diagnostic clue
 - Basilar interstitial fibrosis + dilated esophagus
- Location
 - Lower lung zones

Radiographic Findings

- Radiography
 - Abnormal in 20-65% of cases
 - o Lungs
 - Symmetric basilar reticular pattern
 - Progression of fine basilar reticulation (lace-like) to coarse fibrosis
 - **Decreased lung volume**, sometimes out of proportion to lung disease
 - Elevated diaphragm; may also be due to diaphragmatic muscle atrophy and fibrosis
 - Associated findings
 - Dilated, air-filled esophagus best seen on lateral chest radiography
 - Pleural thickening and effusions rare (< 15%)
 - Superior and posterolateral rib erosion (< 20%)
 - Resorption of distal phalanges, tuft calcification
 - Secondary lung cancer, often adenocarcinoma or adenocarcinoma in situ
 - Cardiomegaly
 - Pericardial effusion
 - Pulmonary arterial hypertension
 - Myocardial ischemia due to small vessel disease
 - Infiltrative cardiomyopathy

CT Findings

- CECT
 - Esophageal dilatation (80%)
 - Lymphadenopathy (60-70%)
 - Rarely identified on chest radiography
 - Most often reactive
 - Usually seen associated with interstitial lung disease

- Pulmonary artery enlargement from pulmonary hypertension; may occur without interstitial lung disease
- o Pleural thickening (pseudoplaques, 33%)
 - Subpleural micronodules
 - Pseudoplaques (90%): Confluence of subpleural micronodules < 7 mm in width
 - Diffuse pleural thickening (33%)
- Discrete pulmonary nodules; solid or sub-solid
 - Must be regarded as concerning for malignancy
 Consider PET/CT &/or biopsy: Nodules > 1 cm with concerning features (e.g., spiculation, lobulation, partsolid attenuation with significant solid component)
- HRCT
 - Abnormal in 60-90% of cases
 - Interstitial lung disease
 - Most often nonspecific interstitial pneumonia (NSIP)
 - □ Basilar predominant ground-glass opacities
 - Posterior and subpleural reticulation
 - Traction bronchiectasis and bronchiolectasis; degree of bronchiectasis often "out proportion" to amount of fibrosis, compared to other interstitial lung diseases
 - Bronchovascular distribution with subpleural sparing; highly suggestive of NSIP
 - Often peripheral predominant
 - Absent to mild honeycomb lung
 - Usual interstitial pneumonia (UIP) pattern less common
 - Subpleural and basilar distribution
 - □ Honeycomb lung should suggest diagnosis
 - Minimal ground-glass opacity: Significant groundglass opacity in acute exacerbation or superimposed atypical infection
 - o Cysts
 - Thin-walled subpleural cysts; 10-30 mm in size
 - Predominantly in mid and upper lungs

Other Modality Findings

- Esophagram
 - o Dilated, aperistaltic esophagus (50-90%)
 - o Gastroesophageal reflux
 - Patulous gastroesophageal junction

Imaging Recommendations

- Best imaging tool
 - HRCT more sensitive than radiography for identification of pulmonary involvement
 - Esophagram to assess esophageal motility

DIFFERENTIAL DIAGNOSIS

Idiopathic Pulmonary Fibrosis

- No esophageal dilatation or musculoskeletal changes
- Interstitial lung disease more coarse, honeycomb lung more common
- Ground-glass opacities less common
- Subpleural distribution

Aspiration Pneumonia

• Recurrent dependent opacities and chronic fibrosis

• Known esophageal motility disorder

Nonspecific Interstitial Pneumonia

- Identical HRCT pattern
- Esophagus not dilated

Asbestosis

- Pleural plaques (80%)
- UIP pattern of pulmonary fibrosis
- No esophageal dilatation

Rheumatoid Arthritis

- No esophageal dilatation
- May exhibit identical HRCT pattern (UIP > NSIP)
- Symmetric articular erosive changes

Drug Reaction

- No esophageal dilatation
- May exhibit identical HRCT pattern

Sarcoidosis

- No esophageal dilatation
- Perilymphatic micronodules predominantly in mid and upper lungs

PATHOLOGY

General Features

- Etiology
 - Reduced circulating T-suppressor cells and natural killer cells, which suppress fibroblast proliferation
 - Antitopoisomerase I (30%), anti-RNA polymerase III, and antihistone antibodies associated with interstitial lung disease
 - Anticentromere antibodies in CREST variant associated with absence of interstitial lung disease
- Genetics
- Suspect genetic susceptibility &/or environmental factors (silica, industrial solvents)
- Overproduction and tissue deposition of collagen
- Lung is 4th most commonly affected organ after skin, arteries, esophagus

Staging, Grading, & Classification

- American College of Rheumatology criteria: Scleroderma requires 1 major or 2 minor criteria
 - **Major criterion**: Involvement of skin proximal to metacarpophalangeal joints
 - Minor criteria
 - Sclerodactyly
 - Pitting scars
 - Loss of finger tip tufts
 - Bilateral pulmonary basilar fibrosis

Microscopic Features

- Pulmonary hypertension
 - Most distinctive finding: Concentric laminar fibrosis with few plexiform lesions
- NSIP: Cellular or fibrotic (80%)
- UIP: Fibroblast proliferation, fibrosis, and architectural distortion (10-20%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Pulmonary disease usually follows skin manifestations
 - Most common presentation is Raynaud phenomenon (up to 90%), tendonitis, arthralgia, arthritis
 - Dyspnea (60%), cough, pleuritic chest pain, fever, hemoptysis, dysphagia
- Other signs/symptoms
 - Skin tightening, induration, and thickening
 - Vascular abnormalities
 - o Musculoskeletal manifestations
 - o Visceral involvement of lungs, heart, and kidneys
 - Esophageal dysmotility, gastroesophageal reflux, esophageal candidiasis, esophageal stricture, weight loss
 - Renal disease: Hypertension, renal failure
 - Antinuclear antibodies (100%)
 - Pulmonary function tests
 - Restrictive or obstructive
 - Decreased diffusion capacity
 - Bronchoalveolar lavage varies from lymphocytic to neutrophilic alveolitis (50%)

Demographics

- Age
 - o Usual onset: 30-50 years
- Sex
- o M:F = 1:3
- Epidemiology
 - o 1.2 cases/100,000 persons
 - Pulmonary disease in > 80% at autopsy

Natural History & Prognosis

- Lung disease is indolent and progressive
- Increased risk for lung cancer; associated with pulmonary fibrosis
 - Often adenocarcinoma or adenocarcinoma in situ
- Poor prognosis: 70% 5-year survival rate
- Cause of death usually aspiration pneumonia

Treatment

- Directed toward affected organs
- Interstitial lung disease: Cyclophosphamide, corticosteroids
- Aggressive blood pressure control important for prevention of renal failure

DIAGNOSTIC CHECKLIST

Consider

- Scleroderma in patient with chronic interstitial lung disease and dilated esophagus
- Lung carcinoma in patient with scleroderma and dominant solid or sub-solid lung nodule

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Scleroderma





(Left) Axial HRCT of a patient with scleroderma shows peripheral ground-glass opacities and reticulation \blacksquare with mild traction bronchiolectasis. Pericardial effusion \boxtimes in the setting of scleroderma without an alternative explanation suggests pulmonary hypertension. (Right) Coronal NECT of a patient with nonspecific interstitial pneumonia related to scleroderma shows basilar predominant ground-glass opacities and reticulation and a small left upper lobe subpleural air cyst 🛃.





(Left) PA chest radiograph of a patient with scleroderma shows low lung volume and basilar reticular opacities $\overline{\rightarrow}$. In affected patients with suspected interstitial lung disease, further evaluation with HRCT is mandatory. (Right) Axial CECT of a patient with scleroderma shows basilar lower lobe bronchiectasis 之, mild ground-glass opacities, and reticulations with associated crowding of vessels and airways, consistent with volume loss. Note dilated distal esophagus 乏 with intrinsic air-fluid level.





(Left) Axial HRCT of a patient with scleroderma shows nonspecific interstitial pneumonia that manifests with peripheral predominant ground-glass and reticular opacities 🛃 and subpleural sparing 🖂. (Right) Axial HRCT of the same patient shows , basilar and peribronchovascular distribution of fibrosing interstitial lung disease, traction bronchiectasis \supseteq , and subpleural sparing 🖂, suggestive of nonspecific interstitial pneumonia.

KEY FACTS

TERMINOLOGY

 Mixed connective tissue disease (MCTD): Distinct clinical entity with features of systemic lupus erythematosus, systemic sclerosis, rheumatoid arthritis, or polymyositis/dermatomyositis, and high-titer antibodies to ribonucleoprotein

IMAGING

- Radiography
 - Low lung volume, basilar reticulation
 - Pleural &/or pericardial effusion
 - Enlarged pulmonary arteries
- CT
 - Nonspecific interstitial pneumonia (35%)
 - Pulmonary hypertension: Enlarged pulmonary arteries, mosaic attenuation, right ventricular hypertrophy
 - o Pleural thickening, effusion (10%)
 - o Dilated, patulous esophagus
 - Pulmonary thromboembolism

TOP DIFFERENTIAL DIAGNOSES

- Other connective tissue diseases
- Primary pulmonary hypertension

PATHOLOGY

 Serology showing antibodies directed against U1 ribonucleoprotein

CLINICAL ISSUES

- Female > male (9:1 ratio)
- No presenting symptoms unique to MCTD
 - Raynaud phenomenon (99% of affected patients)
 - Symptoms of pulmonary hypertension
- Possibly responsive to corticosteroids but no randomized controlled trials of treatment for MDCT

DIAGNOSTIC CHECKLIST

 Consider MCTD in young women with pulmonary hypertension, interstitial lung disease, &/or patulous dilated esophagus

(Left) Coronal NECT of a patient with mixed connective tissue disease shows right upper lobe honeycombing 🔁 and bronchiectasis 🔁 and lower lobe ground-glass opacities 🖾. Open lung biopsy showed nonspecific interstitial pneumonia. (Right) Axial NECT of a patient with mixed connective tissue disease shows peribronchovascular consolidations 🔁 bronchiectasis 🔁, trace pleural effusions 🖾, and a patulous esophagus 🖾. Biopsy showed organizing pneumonia and nonspecific interstitial pneumonia.

(Left) Axial NECT of a patient with mixed connective tissue disease shows basilar reticulation, bronchiolectasis *▶*, and ground-glass opacities with subpleural sparing \square , consistent with fibrotic nonspecific interstitial pneumonia. Note the patulous esophagus 🖾. (Right) Axial NECT of a patient with mixed connective tissue disease shows an enlarged pulmonary trunk *→* suggestive of pulmonary hypertension. Cardiac catheterization showed a pulmonary artery pressure of 30 mm Hg.









TERMINOLOGY

Abbreviations

- Mixed connective tissue disease (MCTD)
- Systemic lupus erythematosus (SLE)
- Systemic sclerosis (SSc)
- Rheumatoid arthritis (RA)
- Polymyositis/dermatomyositis (P/D)
- Sjögren syndrome (SS)

Definitions

• MCTD: Overlap syndrome and distinct clinical entity with features of SLE, SSc, RA, P/D, and high-titer antibodies to ribonucleoprotein

IMAGING

Radiographic Findings

- Nonspecific findings determined by predominance of SLE, SSc, RA, or P/D
- Low lung volume, basilar reticulation (interstitial lung disease)
- Pleural effusion &/or pericardial effusion (serositis)
- Enlarged pulmonary arteries (pulmonary hypertension)

CT Findings

- No unique features: Manifestations of SLE, SSc, RA, or P/D
- Nonspecific interstitial pneumonia (NSIP) (35%)
 - Cellular: Basilar ground-glass (most common) and reticular opacities
 - Fibrotic: Reticular opacities, architectural distortion, traction bronchiectasis, ± subpleural sparing
- Pulmonary hypertension (10-45%): Enlarged pulmonary arteries, mosaic attenuation/perfusion, right ventricular hypertrophy
- Pleural thickening, effusion (10%)
- Dilated, patulous esophagus
- Pulmonary thromboembolism
- Rare manifestations
 - Usual interstitial pneumonia pattern: Basilar subpleural honeycombing
 - Organizing pneumonia: Subpleural or peribronchial consolidation, perilobular distribution, ± reversed halo sign
 - o Diffuse alveolar hemorrhage

Imaging Recommendations

- Protocol advice
 - HRCT for assessment of interstitial lung disease
 - CTA for diagnosis of thromboembolic disease

DIFFERENTIAL DIAGNOSIS

Other Connective Tissue Diseases

- SSc or SLE: Pulmonary hypertension
- SSc: NSIP pattern, esophageal dilatation
- RA or SLE: Pleural/pericardial effusion
- SLE: Diffuse alveolar hemorrhage
- RA: Usual interstitial pneumonia pattern

Primary Pulmonary Hypertension

• May be indistinguishable from pulmonary hypertension associated with MCTD

PATHOLOGY

General Features

- No specific pathologic feature other than serology showing antibodies directed against U1 ribonucleoprotein
- Pulmonary hypertension: Secondary to proliferative vasculopathy rather than underlying interstitial lung disease

Staging, Grading, & Classification

- Alarcon-Segovia criteria most commonly used
 - Required criterion: High titer of antibodies directed against U1 ribonucleoprotein
 - 1 of 5 clinical criteria: Raynaud phenomenon; swollen "puffy" hands; synovitis; myositis; acrosclerosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - No symptoms unique to MCTD; any symptoms may also be seen in SLE, SSc, RA, P/D
 - Raynaud phenomenon (99%)
 - Pulmonary hypertension: Exercise intolerance, dyspnea, peripheral edema, ascites
 - o Inflammatory arthritis
 - Serositis (pleuritis, pericarditis)
 - o Myositis
 - Esophageal dysfunction
- Other signs/symptoms
 - Chest pain or dyspnea from thromboembolism
 - Hemoptysis from alveolar hemorrhage (rare)

Demographics

- Female > male (9:1 ratio)
- Peak incidence: Age 40 years; 7-23% with disease onset in childhood

Natural History & Prognosis

- Thoracic manifestations in 20-80% patients: Thoracic diseases seen in SLE, SSc, RA, P/D
- Pulmonary hypertension is most common cause of death in patients with MCTD
- Pulmonary hypertension carries poor prognosis
 - Faster progression and shorter survival compared to pulmonary hypertension associated with other connective tissue diseases

Treatment

- Thought to respond to corticosteroids, but no randomized control trials of treatment for MDCT have been performed
- Therapy based on experience from treatment of other related connective tissue disorders

DIAGNOSTIC CHECKLIST

Consider

• MCTD in young women with pulmonary hypertension, interstitial lung disease, &/or patulous dilated esophagus

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- 2. Sapkota B et al: Mixed Connective Tissue Disease 2021

KEY FACTS

TERMINOLOGY

- Polymyositis/dermatomyositis (P/D): Autoimmune myopathy manifesting with inflammation and weakness
 - o Polymyositis: Proximal muscle involvement over weeks or months
 - Dermatomyositis: Variety of cutaneous manifestations

IMAGING

- Radiography
 - Connective tissue disease-associated interstitial lung disease (CTD-ILD): Volume loss, basilar reticulation
 - Organizing pneumonia (OP): Consolidation
- CT
 - CTD-ILD: Nonspecific interstitial pneumonia (NSIP) or usual interstitial pneumonia (less common)
 - Basal subpleural ground-glass opacities (85%)
 - Interlobular septal thickening and reticulation (45%)
 - Traction bronchiectasis (50%)
 - Honeycombing (15%)

- OP: Subpleural &/or peribronchovascular consolidations
- Diaphragmatic &/or chest wall muscle weakness ± shrinking lung syndrome
- Antisynthetase syndrome: Ground-glass opacities (in NSIP) and peribronchovascular consolidations (in OP)

TOP DIFFERENTIAL DIAGNOSES

- Idiopathic interstitial pneumonias
- Interstitial pneumonia with autoimmune features
- Systemic lupus erythematosus
- Other autoimmune diseases

CLINICAL ISSUES

- Initial treatment: Systemic corticosteroids
- Recurrent or refractory P/D: Rituximab, cyclophosphamide, azathioprine, methotrexate

DIAGNOSTIC CHECKLIST

 Consider CTD-ILD in patients with bilateral subpleural pulmonary opacities and idiopathic inflammatory myopathy

(Left) Axial CECT of a 49-yearold man with polymyositis shows multifocal bilateral ground-glass opacities \square and mild subpleural reticulation Note sparing of subpleural lung 🖾 (Right) Coronal CECT of the same patient shows bibasilar ground-glass \supseteq and mild reticular opacities with sparing of the mid and upper lung zones. Open lung biopsy showed findings consistent with nonspecific interstitial pneumonia, the most common pattern of interstitial lung disease identified in the setting of

polymyositis/dermatomyositis.











Polymyositis/Dermatomyositis

TERMINOLOGY

Abbreviations

• Polymyositis/dermatomyositis (P/D)

Synonyms

- P/D interstitial lung disease (ILD)
- Idiopathic inflammatory myopathy ILD

Definitions

- Autoimmune myopathy
 - Manifests with inflammation and weakness
 - Dermatomyositis exhibits variety of cutaneous manifestations
 - Polymyositis involves proximal muscles over weeks or months
- May be complicated by connective tissue diseaseassociated ILD (CTD-ILD), aspiration bronchiolitis, &/or hypoventilation from affected respiratory muscles
 - CTD-ILD: Diffuse interstitial pneumonia secondary to P/D
 - Aspiration bronchiolitis: Typically diffuse

IMAGING

General Features

- Best diagnostic clue
 - Diffuse bilateral pulmonary abnormalities in patient with known idiopathic inflammatory myopathy should suggest CTD-ILD
- Location
 - Lower lobe predominance
- Morphology
 - CTD-ILD: Subpleural reticular opacities ± honeycombing

Radiographic Findings

- Radiography
- CTD-ILD
 - Volume loss
 - Lower lobe predominant reticular opacities
- Organizing pneumonia (OP)
 - Subsegmental consolidations; may be migratory on serial imaging
- Diaphragmatic &/or chest wall muscle weakness ± shrinking lung syndrome
- Soft tissue calcifications common

CT Findings

- HRCT/CT
 - CTD-ILD
 - May exhibit features of nonspecific interstitial pneumonia (NSIP) or usual interstitial pneumonia (UIP)
 - Basilar subpleural ground-glass opacities (85%)
 - Interlobular septal thickening and reticulation (45%)
 - Traction bronchiectasis (50%)
 - Honeycombing (15%)
 - Less common than in idiopathic pulmonary fibrosis
 Consolidation (55%); usually associated with OP
 - o OP
 - Subpleural &/or peribronchovascular subsegmental consolidations
 - Reversed halo (or atoll) sign
 - Migratory opacities on serial imaging

- Antisynthetase syndrome
 - Ground-glass opacities (in NSIP) and peribronchovascular consolidations (in OP); often occur synchronously
- Aspiration
 - Diffuse aspiration bronchiolitis &/or aspiration pneumonia
 - Tree-in-bud opacities ± bronchiectasis
 Consolidations
- Mediastinal, hilar, and axillary lymphadenopathy (often reactive)
- Chest wall
 - Diaphragmatic &/or chest wall muscle weakness ± shrinking lung syndrome
 - Low lung volume without discrete findings of CTD-ILD
 - Muscular atrophy and fatty replacement
 - Subcutaneous calcifications

Imaging Recommendations

- Best imaging tool
- HRCT/CT

DIFFERENTIAL DIAGNOSIS

Idiopathic Interstitial Pneumonias

- Idiopathic pulmonary fibrosis (IPF), NSIP, OP
 Indistinguishable from ILD associated with P/D
 - Diagnosis and differentiation rely on absence of clinical or serologic evidence of autoimmunity

Interstitial Pneumonia With Autoimmune Features

- ILD on biopsy or based on HRCT that does not meet full criteria for CTD-ILD but exhibits clinical or serological features that suggest autoimmunity
- HRCT and pathologic features include UIP, NSIP, lymphoid interstitial pneumonia (LIP), and OP

Systemic Lupus Erythematosus

- May manifest with CTD-ILD and OP with identical features
- May manifest as shrinking lung syndrome (i.e., restrictive physiology without CTD-ILD)

Other Autoimmune Diseases

- Rheumatoid arthritis
- Progressive systemic sclerosis
- Mixed connective tissue disease
- Sjögren syndrome
- May manifest with CTD-ILD, LIP, and OP with identical features

Drug-Induced Lung Disease

- May manifest with imaging and pathologic features of UIP, NSIP, or OP
- History (often current or recent) of administered medication known to cause pulmonary reaction

Diffuse Aspiration Bronchiolitis

- May be due to P/D and progressive systemic sclerosis
- Common etiologies
 - Esophageal disorders ± neurologic conditions involving deglutition and esophageal peristalsis
 - Achalasia, hiatus hernia

- Gastroesophageal reflux
- Parkinson disease, cerebrovascular accident
- Imaging features identical to those of other causes of diffuse aspiration bronchiolitis

Asbestosis

- Manifests as UIP in patients occupationally exposed to asbestos
- Discontinuous bilateral pleural thickening or pleural plaques indicative of asbestos-related pleural disease (hallmark of asbestos exposure)

PATHOLOGY

Microscopic Features

- Various histologic and morphologic patterns described in CTD-ILD due to P/D
 - NSIP, UIP, OP, LIP; diffuse alveolar damage (DAD), i.e., acute interstitial pneumonia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Polymyositis and dermatomyositis: Systemic and autoimmune diseases characterized by chronic inflammation of striated muscle; predominantly manifest with proximal muscle weakness (upper or lower extremity and trunk)
 - In addition to skin involvement, polymyositis and dermatomyositis are similar enough that term P/D is often used
 - Polymyositis: Absence of skin manifestations
 - o Dermatomyositis: At least 1 skin manifestation
 - Heliotrope rash: Erythematous to violaceous rash of upper eyelids ± edema
 - Gottron papules: Symmetric erythematous to violaceous papules over dorsal aspects of interphalangeal and metacarpophalangeal joints
 - Gottron sign: Erythematous to violaceous macules or papules on extensor surfaces of elbows, knees, and ankles
 - Calcinosis cutis: Dermal calcium deposits
 - Other: Facial erythema, poikiloderma in areas exposed to light, generalized erythroderma, psoriasiform changes of scalp, etc.
- Other signs/symptoms
 - Muscle pain, abnormal electromyogram, nondestructive arthritis or arthralgia, systemic inflammatory signs
 - Laboratory abnormalities
 - Elevated serum creatine kinase
 - Abnormal electromyogram
 - Positive anti-Jo-1 (histadyl tRNA synthetase) antibody
 - Pathologic findings compatible with inflammatory myositis
 - Myocardial involvement
 - Frequently subclinical
 - Conduction abnormalities and arrhythmias
 - o Antisynthetase syndrome
 - Subset of patients with P/D
 - □ Antisynthetase (anti-ARS) antibodies

- □ ILD
- Fever
- Arthralgias
- Raynaud phenomenon
- Hand exanthema

Demographics

- Higher prevalence in women (F:M = 2:1)
- Adults > 20 years; peak incidence: 45-60 years
- 20-40% of patients with idiopathic inflammatory myopathy develop ILD
- 5-7x increased risk of cancer (70% adenocarcinomas) compared to general population; particularly high in patients with dermatomyositis
 - Lung cancer, ovarian cancer, adenocarcinomas of cervix, pancreas, bladder, and stomach

Natural History & Prognosis

- Patients with CTD-ILD associated with P/D have worse prognosis than those without pulmonary involvement
- 40% mortality from pulmonary complications
- Respiratory muscle weakness leads to hypoventilation, atelectasis, and pneumonia
- Pharyngeal muscle dysfunction may result in diffuse aspiration bronchiolitis &/or aspiration pneumonia
- Poor prognostic indicators include: ILD, UIP pattern, pulmonary hypertension, advanced age, and associated malignancy

Treatment

- Initial treatment: Systemic corticosteroids
- Recurrent or refractory P/D: Rituximab, cyclophosphamide, azathioprine, methotrexate

DIAGNOSTIC CHECKLIST

Consider

• CTD-ILD in patients with bilateral subpleural pulmonary opacities associated with idiopathic inflammatory myopathy (P/D)

Image Interpretation Pearls

• Discrete and dominant nodules in affected patients should be regarded as suspicious for primary lung cancer

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Polymyositis/Dermatomyositis





(Left) Axial HRCT of a 48-yearold man with polymyositis and connective tissue diseaseassociated interstitial lung disease shows bilateral ground-glass opacities 🖂 peribronchovascular reticulation and honeycombing , and subpleural sparing. (Right) Sagittal HRCT of the same patient shows ground-glass opacities, peribronchovascular honeycombing \square , and traction bronchiectasis 🖂 with subpleural sparing, a common feature of nonspecific interstitial pneumonia.





(Left) Axial CECT of a 50-yearold woman with antisynthetase syndrome who presented with shortness of breath shows organizing pneumonia that manifests as multifocal bilateral groundglass opacities and consolidations 🖂. (Right) Coronal CECT of the same patient shows bilateral peribronchovascular nodular opacities and consolidations Biopsy showed organizing pneumonia, which may be seen as an isolated abnormality or in association with nonspecific interstitial pneumonia.





(Left) Coronal NECT (bone window) of a 41-year-old woman with dermatomyositis demonstrates patchy subpleural opacities \supseteq in the lower lobes and extensive calcifications 🔁 in the adjacent chest wall soft tissues. (Right) Axial NECT of a patient with polymyositis demonstrates extensive muscle atrophy and fatty replacement with almost no recognizable chest wall musculature, with the exception of small paravertebral muscles \supseteq . . Note reactive mediastinal lymphadenopathy 🔁.

KEY FACTS

TERMINOLOGY

• Systemic lupus erythematosus (SLE): Autoimmune disease with multiorgan system involvement

IMAGING

- Radiography
 - o Multifocal opacities: Alveolar, reticular
 - Pleural effusions, cardiomegaly, enlarged pulmonary arteries
- CT
 - Consolidation, ground-glass opacity: Pneumonia, hemorrhage, acute lupus pneumonitis
 - SLE-related interstitial lung disease: Reticulation, groundglass opacities, traction bronchiectasis
 - Pleuritis: Pleural thickening ± enhancement; bilateral pleural effusions
 - o Cardiovascular: Pericardial effusion &/or calcification
 - Complications: Pulmonary thromboembolism, pulmonary hypertension (PH)

TOP DIFFERENTIAL DIAGNOSES

- Rheumatoid arthritis and other collagen vascular diseases
- Pneumonia
- Acute respiratory distress syndrome
- Idiopathic pulmonary artery hypertension

CLINICAL ISSUES

- Relapsing and remitting course; females > males
- Multiorgan involvement, including lungs, bones, brain, kidneys, skin
- Risk of death from SLE highest in first 3 years after diagnosis
- Mortality in SLE
 - Active SLE (~ 30%); infection (~ 20%); cardiovascular disease (~ 10%); cerebrovascular disease (~ 10%)

DIAGNOSTIC CHECKLIST

• Consider SLE in women of childbearing age with pulmonary thromboembolism or PH, pleural &/or pericardial effusions

(Left) Axial HRCT of a woman with systemic lupus erythematosus and severe dyspnea shows multifocal ground-glass opacities 🖂 and consolidations 🔁 Streptococcal pneumonia was diagnosed on bronchoscopy. (Right) Axial NECT of a patient with systemic lupus erythematosus shows bilateral ground-glass opacities on a background of thick interlobular septa and intralobular lines (crazypaving pattern) 🔁 due to alveolar hemorrhage and small bilateral pleural effusions 🔁.











TERMINOLOGY

Abbreviations

• Systemic lupus erythematosus (SLE)

Definitions

- SLE: Autoimmune systemic disease of unknown etiology
 Production of various autoantibodies
 - Antidouble stranded DNA (dsDNA) and anti-Smith antibodies specific for SLE

IMAGING

General Features

- Best diagnostic clue
 - Pleural &/or pericardial effusions in woman of childbearing age
 - Unexplained thromboembolic disease or pulmonary hypertension (PH) in woman of childbearing age
- Location
 - Pleuritis is most common thoracic manifestation
 - o May also involve lung, airways, cardiovascular system

Radiographic Findings

- Multifocal opacities: Pneumonia, alveolar hemorrhage, acute lupus pneumonitis
- Reticular opacities related to interstitial lung disease (ILD)
- Small lung volume with shrinking lung syndrome (SLS)
 o Elevated hemidiaphragms without lung opacities
- Pleural effusions: Small, bilateral
- Enlarged central pulmonary arteries from PH
- Enlarged cardiopericardial silhouette from pericardial effusion or (less likely) myocarditis
- Pericardial calcification

CT Findings

- Pneumonia: Most common pulmonary complication, often related to immunosuppressive therapy
 - Focal or diffuse ground-glass opacities &/or consolidations
- Diffuse alveolar hemorrhage: Multifocal ground-glass opacities ± septal thickening (crazy-paving pattern)
- Acute lupus pneumonitis: Ground-glass opacities &/or consolidations, traction bronchiectasis, architectural distortion
- SLE-related ILD: Fine reticulation, ground-glass opacities, architectural distortion, traction bronchiectasis
 - Usual interstitial pneumonia (UIP) pattern (rare); possible
 UIP pattern [nonspecific interstitial pneumonia (NSIP)]
- Airway involvement
 - Tracheal wall thickening; rarely significant luminal narrowing
 - Bronchiectasis
- Pleuritis: Pleural thickening ± enhancement; small to moderate bilateral pleural effusions
- Cardiovascular involvement
 - Pulmonary thromboembolic disease
 - Acute: Arterial filling defects and luminal distention
 - Old/chronic: Webs, eccentric filling defects, diminutive pulmonary arteries, mosaic perfusion/attenuation; often associated with PH

- SLE-PH (primary or secondary): Enlarged pulmonary arteries (pulmonary trunk:aorta ratio > 1), right heart enlargement, reflux of contrast into inferior vena cava and hepatic veins
- Pericardial effusion: Small to moderate
- Pericardial calcification from recurrent inflammatory pericarditis
- Coronary artery atherosclerosis: 5x increased risk of premature atherosclerosis
 - Likely multifactorial, including SLE-related inflammation and corticosteroids
- Libman-Sacks and bacterial endocarditis: Gated CTA
 Small valvular vegetations; valvular regurgitation

MR Findings

- Pericardial effusion and pericardial thickening
 - Effusion usually follows water signal intensity; ± pericardial enhancement
- Libman-Sacks and bacterial endocarditis: Valve thickening, small valve vegetations, valve regurgitation
 Mitral valve most often involved
- SLE myocarditis
 - Delayed enhancement; primarily mid myocardial (nonischemic pattern)
 - High myocardial signal intensity on T2WI, correlates with disease activity

Imaging Recommendations

- Best imaging tool
 - HRCT for evaluation of ILD
 - CTA for exclusion of pulmonary thromboembolism and assessment of PH
- Protocol advice
 CECT to identify pleural/pericardial enhancement

DIFFERENTIAL DIAGNOSIS

Rheumatoid Arthritis and Other Collagen Vascular Diseases

- SLE and rheumatoid arthritis (RA) may cause serositis
- RA: Higher incidence of ILD; may exhibit cavitary nodules
- Common clinical overlap of SLE and other collagen vascular disorders

Pneumonia

- Focal or multifocal ground-glass opacities &/or consolidations
- Atypical infection may mimic acute lupus pneumonitis on imaging

Acute Respiratory Distress Syndrome (ARDS)

- Acute lupus pneumonitis may mimic ARDS
- Pleural effusions more common in SLE than in ARDS

Idiopathic Pulmonary Artery Hypertension

• Pleural effusions favor SLE

PATHOLOGY

General Features

- Serositis
 - Pleural involvement more common than in any other collagen vascular disease (60% of patients)

- Nonspecific pleural abnormalities: Lymphocytic and plasma cell infiltration, fibrinous pleuritis
- Pericarditis: Most common cardiovascular manifestation (60% patients; only 25% symptomatic)
- Acute lupus pneumonitis: Diffuse alveolar damage ± diffuse alveolar hemorrhage
- SLS: Postulated diaphragmatic myopathy vs. phrenic neuropathy
- Diffuse alveolar hemorrhage
 - Most frequently bland hemorrhage
 - Hemorrhage from capillaritis with immune complex deposition
- SLE-associated ILD: Typically NSIP
 - UIP and lymphoid interstitial pneumonia rarely associated with SLE
- SLE-PH: Pathology similar to that of idiopathic PH
 - Plexiform angiomatous lesions, thickening of pulmonary artery muscular walls, intimal fibrosis
 - Secondary to chronic thromboembolic disease or ILD
- Upper airway involvement (uncommon): Laryngeal mucosal inflammation, mucosal ulcerations, cricoarytenoiditis, vocal cord neuropathy, (rarely) necrotizing vasculitis
- Libman-Sacks endocarditis: 50% patients on echocardiography
 - Immune complex deposition with resultant inflammatory reaction
 - May progress to valvular stenosis or regurgitation
- Myocarditis (uncommon)
 - Immune-mediated inflammatory process directed against striated muscle

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Involvement: Lungs, bones, brain, kidneys, skin
 - o Photosensitive rash, glomerulonephritis, arthritis
 - o Pleural and lung involvement (50-60% of patients)
- Other signs/symptoms
 - Thoracic manifestations usually late in disease
 - Pneumonia common; immunosuppression
 - \uparrow incidence of tuberculosis in patients with SLE
 - Most common chest symptom: Pleurisy (~ 60%)
 ± exudative pleural effusions
 - SLS, pulmonary vascular disease: Chronic dyspnea, chest pain, fatigue
 - Acute lupus pneumonitis: Rare (1-10% patients); high morbidity and mortality
 - Fever, cough, dyspnea, hypoxia, ± hemoptysis
 - Diffuse alveolar hemorrhage: Hemoptysis, dyspnea, cough, ± fever
 - SLE-related ILD: Nonproductive cough, progressive dyspnea
 - SLE-PH: Dyspnea, chest pain, nonproductive cough, fatigue
 - Thromboembolic disease: Chest pain, dyspnea, hypoxia
 - Upper airway involvement: Hoarseness, stridor, dyspnea, (rarely) life-threatening airway obstruction
 - Cardiac involvement
 Chest pain: Pericarditis, myocarditis, infarction

- Libman-Sacks and subacute bacterial endocarditis: Stroke, myocardial infarction, pulmonary embolism
- Clinical profile
 - Serum antibodies associated with SLE
 - Anti-dsDNA, anti-Smith antibodies (specific)
 - Antinuclear antibody (ANA), antiphospholipid antibody (APA), Anti-SSA (less specific)
 - Pleuritis: Exudative effusions
 - SLE-related ILD: Decreased diffusing capacity, restrictive pulmonary function
 - SLS: Normal diffusing capacity, restrictive pulmonary function
 - Diffuse alveolar hemorrhage: Usually with active lupus nephritis (pulmonary-renal syndrome)
 - SLE-PH: High prevalence in patients with lupus anticoagulant &/or APA

Demographics

- F > M; women of childbearing age most frequently affected
- 3x increased incidence in African Americans
- Genetic component: SLE in 5-10% of 1st-degree relatives of patients with SLE

Natural History & Prognosis

- Relapsing and remitting course
- Risk of death from SLE highest in first 3 years post diagnosis
- Mortality in SLE
 - Active SLE (~ 30%)
 - o Infection (~ 20%)
 - o Cardiovascular disease (~ 10%)
 - Cerebrovascular disease (~ 10%)

Treatment

- Nonsteroidal antiinflammatory drugs or low-dose corticosteroids for pleuritis or pericarditis
- Acute lupus pneumonitis: Plasmapheresis, mechanical ventilation, high-dose corticosteroids, immunosuppressants (i.e., cyclophosphamide)
- SLS: Corticosteroids and immunosuppressants; generally good response
- Diffuse alveolar hemorrhage: Plasmapheresis, immunosuppressants
- SLE-related ILD: Corticosteroids and immunosuppressants (i.e., cyclophosphamide, azathioprine)

DIAGNOSTIC CHECKLIST

Consider

- SLE in women of childbearing age with pulmonary thromboembolism or PH
- SLE in patients with unexplained pleural &/or pericardial effusions
- SLE in patients with hemoptysis and multifocal groundglass opacities on CT/HRCT

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(Left) AP chest radiograph of a patient with systemic lupus erythematosus and shrinking lung syndrome shows bilateral low lung volume and basilar subsegmental atelectasis 🖂 The resultant restrictive lung disease is postulated to result , from diaphragmatic dysfunction. (Right) Axial NECT of a patient with systemic lupus erythematosus shows subtle right upper lobe ground-glass nodules \supseteq and several discrete thin-walled pulmonary cysts 🔁. Biopsy revealed lymphoid interstitial pneumonia.





(Left) Axial NECT of a patient with systemic lupus erythematosus and progressive dyspnea shows extensive bilateral groundglass opacities with minimal reticulation \supseteq . Lung biopsy revealed histologic features of cellular nonspecific interstitial pneumonia. (Right) Axial HRCT of a patient with systemic lupus erythematosus shows bilateral nodular subpleural and peribronchovascular ground-glass opacities and consolidations that exhibit the reversed halo sign 🔁 characteristic of organizing pneumonia.





(Left) Four-chamber SSFP MR of a patient with systemic lupus erythematosus shows a large pericardial effusion 🖂 Note high-signal subepicardial fat deep to the serous visceral pericardium 🖾. The parietal pericardium is of normal thickness with no nodularity. (Right) Axial CECT of a patient with systemic lupus erythematosus shows multiple central pulmonary artery filling defects \supseteq , consistent with acute pulmonary thromboembolism. Thromboembolic disease is a common manifestation of systemic lupus erythematosus.

Sjögren Syndrome

KEY FACTS

TERMINOLOGY

- Sjögren (SS) is caused by chronic lymphocytic infiltration of exocrine glands and other extraglandular sites
- SS is characterized by dryness of eyes and mouth
- SS may be primary or associated with other connective tissue diseases, most commonly rheumatoid arthritis

IMAGING

- Pulmonary manifestations: Interstitial lung disease (ILD), airways disease, and lymphoproliferative disorders
 - Nonspecific interstitial pneumonia (NSIP): Most common ILD pattern in patients with SS
 - Subpleural lower lobe reticular and ground-glass opacities
 - o Small airways disease: Follicular bronchiolitis
 - Small centrilobular and peribronchial micronodules
 - Lymphoproliferative disorders: Non-Hodgkin Lymphoma
 Pulmonary nodules, consolidations, masses &/or lymphadenopathy

TOP DIFFERENTIAL DIAGNOSES

- Cystic lung diseases
- Idiopathic pulmonary fibrosis
- Organizing pneumonia
- Mucosa-associated lymphoid tissue lymphoma
- Rheumatoid arthritis

CLINICAL ISSUES

- Middle-aged women (peak: 56 years)
- Much more common in women; F:M ratio = 10:1
- Diagnostic criteria: Keratoconjunctivitis sicca + xerostomia + extensive lymphocytic infiltrate of minor salivary glands + laboratory evidence of autoimmune disease [rheumatoid factor (+) or antinuclear antibody (+) or SS-A or SS-B (+)]

DIAGNOSTIC CHECKLIST

• Consider lymphoma in patients with SS with persistent nodules, consolidations, masses &/or lymphadenopathy

(Left) Axial CECT of a 68-yearold woman with Sjögren syndrome shows bilateral ground-glass opacities and subpleural reticulations 🖂, consistent with nonspecific interstitial pneumonia. (Right) Coronal CECT of the same patient confirms bilateral lower lobe subpleural opacities, consistent with nonspecific interstitial pneumonia and absence of honeycombing. Nonspecific interstitial pneumonia is the most common interstitial lung disease in patients with Sjögren syndrome.





(Left) Axial CECT of a 51-yearold woman with Sjögren syndrome and follicular bronchiolitis shows tiny right upper lobe micronodules 🔁 and a small subpleural nodular opacity in the left upper lobe Image: Coronal CECT of the same patient shows subtle bilateral diffuse ground-glass centrilobular micronodules. Follicular bronchiolitis shares the imaging features of other causes of cellular bronchiolitis, but the presence of Sjögren syndrome should suggest the diagnosis.





TERMINOLOGY

AbbreviationsSjögren syndrome (SS)

Synonyms

- Sicca syndrome
- Gougerot-Sjögren disease

Definitions

- Autoimmune disease characterized by dryness of eyes and mouth
 - Caused by chronic lymphocytic infiltration of exocrine glands and other extraglandular sites
- Second most common autoimmune disorder after rheumatoid arthritis
 - SS can be primary or associated with other connective tissue diseases, most commonly rheumatoid arthritis
 - Clinically significant pulmonary involvement in 9-24% of affected patients and more common in secondary than in primary SS
- Pulmonary manifestations: Interstitial lung disease (ILD), airways disease, and lymphoproliferative disorders
- ILD
 - Nonspecific interstitial pneumonia (NSIP) is most common ILD pattern in patients with SS (~ 45%)
- Airways disease
 - o Small airways disease
 - Chronic bronchiolitis
 - Follicular bronchiolitis,
 - Constrictive bronchiolitis
 - Upper airway inflammation and dryness
- Lymphoproliferative disorders
 - Increased risk of non-Hodgkin lymphoma (NHL)
 - Marginal zone B cell lymphoma and mucosa-associated lymphoid tissue (MALT) lymphoma or MALToma: Most common subtypes in SS

IMAGING

Radiographic Findings

- Radiography
 - o NSIP
 - Bilateral, reticular, or heterogeneous opacities; lower lung zone predominant
 - o Usual interstitial pneumonia (UIP)
 - Subpleural reticular opacities; lower lung zone predominant
 - Lymphoid interstitial pneumonia (LIP)
 - Reticulonodular opacities; lower lung zone predominant
 - o NHL
 - Multicompartmental mediastinal and hilar lymphadenopathy
 - Primary pulmonary lymphoma
 Single nodule/mass (65% of cases)
 - o Airways disease
 - Ill-defined small or clustered nodules
 - Air-trapping
 - □ Hyperlucency &/or oligemia

CT Findings

- Associated findings
 - Mediastinal abnormalities
 - Thymic hyperplasia, multilocular thymic cysts, thymic epithelial neoplasms
 - Persistent and extensive lymphadenopathy, in NHL
 - Pulmonary hypertension
 - Pleural effusion: Uncommon
 - Almost exclusively in secondary SS, associated with rheumatoid arthritis and systemic lupus erythematosus
 - Increased incidence of pulmonary embolism associated with antiphospholipid antibodies
- HRCT
- o ILD
 - NSIP pattern
 - Subpleural lower lobe reticular and ground-glass opacities; peribronchovascular distribution with subpleural sparing
 - □ Traction bronchiectasis
 - UIP pattern
 - Subpleural reticular opacities &/or honeycombingTraction bronchiectasis
 - LIP
 - □ Ground-glass opacities, centrilobular and subpleural nodules
 - Round, thin-walled cysts, randomly distributed (common)
 - Diffuse lymphoid hyperplasia (DLH)
 - May rarely progress to fibrosis in late stages (i.e., honeycombing)
 - Interlobular septal thickening, intralobular lines, and thick peribronchovascular interstitium should suggest DLH
 - Organizing pneumonia (OP)
 - Bilateral, patchy, nonsegmental consolidations or ground-glass opacities with subpleural &/or peribronchovascular predominance
 - Reversed halo sign
- Follicular bronchiolitis
 - Small centrilobular and peribronchial micronodules
 - Tree-in-bud and ground-glass opacities; rarely bronchial dilatation and interlobular septal thickening
- Constrictive bronchiolitis
 - Mosaic attenuation
 - Air-trapping on expiration
- Other pulmonary manifestations
 - Cylindrical bronchiectasis: Bronchial dilatation, expiratory air-trapping
- o MALT lymphoma or MALToma
 - Solitary or multiple nodule(s) or mass(es)
 - Areas of airspace consolidation or ground-glass opacity with air bronchograms
 - Lymphadenopathy is uncommon unless there is progression to diffuse large B-cell NHL

Imaging Recommendations

- Best imaging tool
 - HRCT is optimal imaging modality for demonstrating pattern of disease and extent of pulmonary involvement

DIFFERENTIAL DIAGNOSIS

Cystic Lung Diseases

- Langerhans cell histiocytosis: Mid and upper lung zone predominant cysts with nodular walls and bizarre shapes; smoking-related disease
- Lymphangioleiomyomatosis: Thin-walled, spherical cysts; sporadic or associated with tuberous sclerosis complex
- Birt-Hogg-Dubé syndrome: Lung cysts; autosomal dominant inheritance, associated with facial papules (fibrofolliculomas) and malignant renal neoplasms
- Light-chain deposition disease: Systemic deposition of immunoglobulin light chains in lymphoproliferative disorders and autoimmune conditions

Idiopathic Pulmonary Fibrosis

- No imaging or pathologic differences between idiopathic and connective tissue disease-associated ILD
- Differentiation based on clinical parameters

Organizing Pneumonia

 No imaging or pathologic differences between OP associated with connective tissue disease or that associated with other diseases

Mucosa-Associated Lymphoid Tissue Lymphoma

• May mimic lung cancer and other malignancies on imaging; differentiation relies on histologic features

Rheumatoid Arthritis

- Women
- Rheumatoid factor (+)
- Arthralgia, joint swelling and stiffness
- Pleural effusion, pleural thickening
- UIP > NSIP
- Bronchiectasis
- Rheumatoid nodules
- Skeletal changes: Erosive changes of clavicles, glenohumeral joints, and superior rib notching

PATHOLOGY

General Features

- Etiology
 - Precise etiology is unclear
 - Combination of genetic and environmental triggers
 - Several conditions may play role
 - Infection: Viruses [hepatitis C virus, cytomegalovirus, human immunodeficiency virus (HIV), human T-cell leukemia virus]
 - Genetic predisposition
 - Hormonal deregulation
- Genetics
 - Genetic predisposition
 - HLA-DRB1 and HLA-DQB1 may increase predisposition
- Associated abnormalities
 - Other autoimmune diseases (e.g., Hashimoto thyroiditis, primary biliary cirrhosis, and autoimmune hepatitis)
- Diagnosis of lymphoproliferative disorders requires histopathologic confirmation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dry cough and dyspnea
- Other signs/symptoms
 - Dry skin, dry eyes, skin rashes, joint and muscle pain, swollen salivary glands, prolonged fatigue, cystitis, reflux esophagitis, peptic ulcer, pancreatitis
- Clinical profile
 - Positive serum anti-SS-A/Ro &/or anti-SS-B/La (or positive rheumatoid factor and antinuclear antibodies)
- Criteria for diagnosis of SS
 - Keratoconjunctivitis sicca + xerostomia + extensive lymphocytic infiltrate of minor salivary glands + laboratory evidence of autoimmune disease
 - Rheumatoid factor (+) or antinuclear antibody (+) or SS-A or SS-B (+)

Demographics

- Age
 - Middle-aged women (peak: 56 years)
 - Most men affected after 65 years
- Sex
 - Much more common in women; F:M = 10:1
- Epidemiology
 - 2nd most common multisystem autoimmune disease after rheumatoid arthritis
 - o Lymphoma
 - NHL most common
 - Incidence 44x higher than in normal population
 - Develops in 10% of patients with SS
 - 50% have extranodal disease

Natural History & Prognosis

- Pulmonary manifestations typically develop late in disease
- Pulmonary involvement is associated with 4x increase in mortality risk after 10 years of disease

Treatment

- Most patients do not require drug therapy
 Symptom-specific therapy for dry eyes and skin
- Low-dose corticosteroids and immunosuppressive therapy may be necessary with exacerbation or progression of ILD

DIAGNOSTIC CHECKLIST

Consider

 Malignant lymphoma in patients with SS if persistent nodule(s), consolidation(s), or mass(es) &/or hilar/mediastinal lymphadenopathy

Image Interpretation Pearls

- Consider infection or drug toxicity in patients with SS, acute pulmonary symptoms, and radiographic abnormalities
- NSIP is most common ILD in patients with SS

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Sjögren Syndrome





(Left) PA chest radiograph of an 82-year-old woman with Sjögren syndrome shows low lung volume and bilateral subpleural reticular opacities *⊠*. (Right) Axial CECT of the same patient shows bilateral subpleural reticulation 🖂, focal honeycombing 🔁, and traction bronchiectasis, consistent with usual interstitial pneumonia (UIP). After nonspecific interstitial pneumonia, UIP is the most common interstitial pneumonia in patients with Sjögren syndrome.





(Left) Axial CECT of a 76-yearold woman with chronic Sjögren syndrome and pulmonary mucosa-associated lymphoid tissue (MALT) lymphoma shows dense bilateral upper lobe consolidations present for months. (Right) Whole-body FDG-PET shows metabolic activity within the bilateral upper lobe consolidations. Biopsy demonstrated pulmonary MALT lymphoma. Pulmonary lymphoma should be considered in patients with Sjögren syndrome and persistent nodules, consolidations, or masses.





(Left) Whole-body FDG PET of a patient with Sjögren syndrome and B-cell lymphoma shows multiple FDG-avid lymph nodes \supseteq and FDG avidity in the bilateral parotid glands, consistent with sialoadenitis 🔁. (Right) Axial FDG PET/CT of the same patient shows FDG-avid . intrathoracic lymph nodes ➡, consistent with lymphoma. Marginal zone B-cell lymphoma and MALT lymphoma are the most common types of non-Hodgkin lymphoma in patients with Sjögren syndrome.

(Left) Axial HRCT of a 47-yearold man with Sjögren syndrome and nonspecific interstitial pneumonia shows bilateral subpleural groundglass and reticular opacities \square and traction bronchiolectasis 🔁. (Right) Axial HRCT of the same patient shows ground-glass opacities, subpleural reticulations, and focal honeycombing 🔁. The predominance of ground-glass opacity is more consistent with nonspecific interstitial pneumonia than with UIP.





(Left) Axial inspiratory HRCT of a 65-year-old woman with Sjögren syndrome and constrictive bronchiolitis shows no abnormality. (Right) Axial expiratory HRCT of the same patient shows scattered areas of air-trapping 🖂, consistent with small airways disease. Air-trapping is common in patients with Sjögren syndrome and indicates small airways disease, such as follicular bronchiolitis, bronchiectasis, or, rarely, constrictive bronchiolitis.





(Left) Axial CECT of a 46-yearold woman with Sjögren syndrome and organizing pneumonia shows bilateral, patchy ground-glass opacities and mild reticulation. Organizing pneumonia may be a manifestation of pulmonary involvement but may also be associated with drug toxicity. (Right) Axial CECT of a 42year-old man with Sjögren syndrome undergoing chronic corticosteroid therapy shows a right lower lobe cavitary nodule 🔁 secondary to nocardiosis. Cavitary nodules in affected patients should suggest infection.





Sjögren Syndrome





(Left) Axial CECT of a 58-yearold woman with Sjögren syndrome and MALT lymphoma shows bilateral peribronchovascular nodular opacities 🔁, some with air bronchograms 2. (Right) High-power photomicrograph (H&E stain) of a biopsy specimen from the same patient shows an extensive diffuse lymphoid proliferation surrounding a bronchiole ᠫ with vague nodularity. MALT lymphoma is a low-grade lymphoma commonly seen in the setting of Sjögren syndrome.





(Left) Axial CECT of a 47-yearold man with Sjögren syndrome and MALT lymphoma shows a left upper lobe consolidation that did not resolve with medical therapy. MALT lymphoma may manifest as solitary or multiple pulmonary nodules, masses, or consolidations. (Right) Coronal FDG PET of the same patient shows mildly increased FDG uptake within the left upper lobe consolidation 🖾. Note the absence of FDG-avid lymphadenopathy.





(Left) Composite image with coronal FDG PET/CT of a 53year-old woman with Sjögren syndrome and diffuse large Bcell lymphoma shows extensive FDG-avid lymphadenopathy in the neck ➡, mediastinum ➡, and abdomen 🖾. (Right) Axial NECT of a patient with Sjögren syndrome shows a heterogeneous prevascular mediastinal mass \supseteq with intrinsic water attenuation and thin soft tissue components that represented a thymic cyst. Thymic lesions are described in patients with Sjögren syndrome.

Ankylosing Spondylitis

KEY FACTS

TERMINOLOGY

• Chronic seronegative inflammatory arthropathy with predilection for axial skeleton

IMAGING

- Spinal disease nearly always precedes lung involvement
- Radiography
 - o Bilateral symmetric apical pleural thickening
 - Upper lobe fibrosis and superior hilar retraction
- CT
 - Upper lobe fibrobullous disease
 - o Airways disease
 - Mosaic attenuation and air-trapping
 - Bronchial wall thickening
 - Traction bronchiectasis
 - Interstitial lung disease
 - Parenchymal bands
 - Intralobular lines, subpleural lines, and honeycombing
 - Mycetomas may be found in cysts or cavities

TOP DIFFERENTIAL DIAGNOSES

- Tuberculosis
- Sarcoidosis
- Silicosis and coal worker's pneumoconiosis
- Pleuroparenchymal fibroelastosis

CLINICAL ISSUES

- Most common signs/symptoms
 - Inflammation of sacroiliac joints (early manifestation)
 - Most serious complication: Spinal fracture, typically of cervical spine
 - Pulmonary involvement
 - Cough, dyspnea, fatigue, occasional hemoptysis
 - Upper lobe fibrobullous disease
 - Similar to pulmonary tuberculosis
- Other signs/symptoms
 - Pulmonary function tests: Restrictive > obstructive physiology
 - Presence of HLA-B27 not necessary for diagnosis

(Left) Graphic shows typical pulmonary involvement by ankylosing spondylitis, consisting of apical fibrosis, interstitial thickening, mild traction bronchiectasis \square and cyst or bulla formation Axial NECT of a patient with ankylosing spondylitis shows classic CT findings of pulmonary involvement, which include bilateral symmetric peripheral subpleural reticular opacities 🔁, mild traction bronchiolectasis 🔁, and honeycombing 🔁. Note bilateral subpleural upper lobe bullae 🖾.





(Left) Axial CECT of a patient with ankylosing spondylitis shows biapical subpleural fibrosis and apical caps related to pulmonary involvement. (Right) Coronal NECT of a patient with ankylosing spondylitis shows flowing spinal syndesmophytes . Note left apical consolidation with intrinsic traction bronchiectasis and volume loss.





Ankylosing Spondylitis

TERMINOLOGY

- Abbreviations
- Ankylosing spondylitis (AS)

Synonyms

- Bechterew disease
- Radiographic axial spondyloarthritis (r-axSpA)

Definitions

- Chronic multisystem inflammatory disorder with articular and extraarticular manifestations
 - Predilection for axial skeleton
 - Extraarticular thoracic manifestations
 - Pleuropulmonary disease
 - Cardiovascular involvement
- г-axSpA (AS)
- Definite sacroiliitis on radiographs
- Nonradiographic axial spondyloarthritis
 - Clinical diagnosis, absence of radiographic manifestations, possible sacroiliitis on MR
 - May eventually evolve to AS

IMAGING

General Features

- Best diagnostic clue
 - o Upper lobe fibrobullous disease + spinal ankylosis

Radiographic Findings

- Radiography
 - Flowing thoracic spine syndesmophytes typical of AS – "Bamboo spine"
 - Lung parenchymal lesions not visible in early stages
 - Bilateral symmetric apical pleural thickening
 - Upper lobe fibrosis and superior hilar retraction
 - Upper lung zone cyst/bulla formation (fibrobullous disease)
 - Difficult distinction of AS lung lesions from prior tuberculosis
 - Secondary heart failure: Aortic regurgitation

CT Findings

- Spinal disease nearly always precedes lung involvement
 Thoracic spine ankylosis (with syndesmophytes)
 - Vertebral body squaring and shiny corners (Romanus lesion)
- Lung
 - o Airways disease
 - Mosaic attenuation and air-trapping
 - Bronchial wall thickening
 - Traction bronchiectasis
 - Emphysema
 - Irregular (cicatricial) emphysema from scarring and bullous disease
 - May affect non-smokers
 - Interstitial lung disease
 - Parenchymal bands most common
 - Subpleural nodules, intralobular lines, subpleural lines, and honeycombing may be present
 - o Apical disease
 - Severe traction bronchiectasis with volume loss

- Tracheal dilatation (equivalent to traction bronchiectasis)
- Bilateral, symmetric, apical pleural thickening
- Apical fibrobullous areas prone to *Aspergillus* colonization
 - Mycetomas may be found in cysts or bullae
 - Chronic *Aspergillus* colonization (50-65%)
 - Hemoptysis common in patients with mycetoma
- Lymphadenopathy uncommon

MR Findings

- Romanus lesion: High T2 signal due inflammation at vertebral body corners
- Anderson lesion: High T2 signal in central discovertebral junction

Echocardiographic Findings

- Aortic root dilatation, thickening, stiffness
- Aortic regurgitation, mitral regurgitation

Nuclear Medicine Findings

- PET/CT
 - FDG uptake in spine and SI joints

Imaging Recommendations

- Best imaging tool
 - CT may reveal subtle apical abnormalities undetected on chest radiography
 - CTA or MRA for evaluation of aorta

DIFFERENTIAL DIAGNOSIS

Tuberculosis

- Apical fibrocavitary disease: Cavitation (50%)
- ↑ volume loss leads to ↑ signs of fibrosis
- Upper lobe apical and posterior segments, lower lobe superior segments
- Chronic nonspecific symptoms: Cough, low-grade fever, malaise, weight loss
- Diagnosis: Recovery of *Mycobacterium tuberculosis* organisms

Sarcoidosis

- Upper lung zone and peribronchovascular involvement
- Small perilymphatic nodules (1-5 mm)
- Nodular consolidations; ground-glass opacities
- Symmetric hilar and mediastinal lymphadenopathy
- Noncaseating epithelioid granulomas on histology

Silicosis and Coal Worker's Pneumoconiosis

- Upper lung zone centrilobular and subpleural nodules
- Silicotic nodules more sharply defined than those of coal worker's pneumoconiosis
- Symmetric hilar/mediastinal lymphadenopathy
 "Eggshell" lymph node calcification

Pleuroparenchymal Fibroelastosis

- Rare idiopathic interstitial pneumonia (IIP)
- Upper lobe subpleural and interstitial proliferation of predominantly elastic fibers
 - Fibrous interstitial pneumonia with > 80% fibroelastic changes in noncollapsed lung

- Upper lung zone pleuroparenchymal thickening, reticular opacities, honeycombing, bronchiectasis, consolidation
- Associated conditions: Infection, bone marrow transplantation, chemotherapy, autoimmunity, possible genetic predisposition

PATHOLOGY

General Features

- Etiology
 - o Unclear
 - Inflammatory or immunologic processes
 - Environmental causes
- Genetics
 - Strong association with histocompatibility antigen HLA-B27, but not necessary for diagnosis
 - Race-related differences in prevalence
 - > 90% of White patients with AS are HLA-B27(+)
 - ~ 50% of Black African American patients with AS are HLA-B27(+)
 - Nearly absent (prevalence of HLA-B27 < 1%) in Black Africans and Japanese
 - Strong familial pattern
 - 10% ↑ likelihood of AS among HLA-B27(+) 1st-degree relatives of HLA-B27(+) patients with AS
 - Antigen present in 6-10% of healthy individuals
 1-6% of HLA-B27(+) patients have AS
- Epidemiology
 - o Incidence of AS ~ 6.6/100,000 persons
 - Incidence of lung disease on chest radiography: 1-3%
 - Incidence of lung disease on HRCT: 60-88%
 - Worldwide prevalence: 0.1 to 1.4%

Staging, Grading, & Classification

- No universally accepted diagnostic criteria for AS or axSpA
- Many classifications used mainly for clinical research
 Modified New York classification
 - Assessment of SpondyloArthritis international Society (ASAS)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Inflammatory back pain (IBP) is key clinical symptom
 - Insidious-onset dull lower back pain or morning stiffness; improved with exercise, but not rest
 - Peripheral joints and extraarticular structures may also be affected
 - Anterior uveitis is most common extraarticular manifestation
 - Pulmonary disease
 - Rare and late manifestation of AS
 - □ On average, 2 decades after onset of symptoms
 - Slowly progressive fibrocystic changes in upper lobes
 - Respiratory signs/symptoms
 - Cough, dyspnea, fatigue, and occasional hemoptysis
 - Super-infection with fungi (Aspergillus) or nontuberculous mycobacteria (NTMB)

- Hemoptysis; usually indicates presence of mycetoma
- Spontaneous pneumothorax
 - Incidence 0.29% (higher than in general population)
- Anterior chest wall pain
 - Pain on inspiration and with arm movements; secondary to rib cage enthesitis, and sternoclavicular/manubriosternal joint inflammation
- o Sleep apnea mechanisms
 - Restrictive pulmonary disease, obstruction of oropharyngeal airway (temporomandibular joint involvement), and compression of medullary respiratory centers (cervical spinal disease)
- Other signs/symptoms
 - Pulmonary function tests
 - Restriction related to osseous ankylosis
 - Obstruction secondary to small airways disease

Demographics

- Age
 - Disease onset: Age < 45
- Sex
- M:F = 10-16:1

Natural History & Prognosis

- Initial involvement of sacroiliac joints with progression to spinal involvement
- Mortality: Aortitis, inflammatory bowel disease, nephritis (amyloid)
- Most serious complication: Spinal fracture, most commonly of cervical spine
- Progressive fibrobullous changes with advanced AS
 Correlate with disease duration

Treatment

- No effective treatment to stop progression of pulmonary involvement
- NSAIDs recommended as 1st-line drug treatment for patients with AS with chest pain and stiffness
- Symptomatic mycetoma may be treated with antifungal agents
 - Thoracic surgery for insufficient medical treatment
 - Bronchial artery embolization for life-threatening hemoptysis
- Sleep apnea
 - CPAP, smoking cessation, and weight loss
 - Adalimumab and golimumab improve sleep and sleep quality

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evalence: 0.1 to 1.4% , & Classification

Ankylosing Spondylitis





(Left) Axial HRCT of a patient with ankylosing spondylitis shows right upper lobe subpleural reticulation \supseteq and a left upper lobe mycetoma 🔁 within a preexistent bulla. (Courtesy N. L. Müller, MD, PhD.) (Right) Coronal CECT of a patient with ankylosing spondylitis who presented with a left spontaneous $pneumothorax \ge shows$ biapical subpleural opacities with intrinsic bronchiectasis and right upper lobe volume loss with architectural distortion and traction bronchiectasis \boxtimes that may mimic tuberculosis.





(Left) PA chest radiograph of a patient with ankylosing spondylitis shows right apical fibrobullous disease 🔁. An ovoid left upper lobe mycetoma 🖻 was confirmed after surgical resection. Note a moderate left spontaneous pneumothorax 🖂. (Right) Axial expiratory NECT of a patient with ankylosing spondylitis shows bilateral areas of basilar air-trapping ➡. Given the frequency of small airways disease, expiratory imaging should be included in the assessment of affected patients.





(Left) AP lumbar spine radiograph of a patient with ankylosing spondylitis shows bilateral sacroiliac joint ankylosis 🖾, ossification of the interspinous ligament (dagger sign) \supseteq , and ankylosis of the facet joints (tram-track sign) 🔁. (Right) Sagittal NECT of a patient with ankylosing spondylitis who sustained chest trauma shows a vertebral column fracture 🔁. Note the bamboo spine appearance characteristic of ankylosing spondylitis. Such a fracture though a rigid spine may have catastrophic consequences.

KEY FACTS

TERMINOLOGY

- Inflammatory bowel disease (IBD) likely results from inappropriate immune response to physiologic gut flora in host with genetic susceptibility
- Ulcerative colitis: Limited to colon
- Crohn disease: Any segment of gastrointestinal tract
- May affect lung, airways, pleura, or vasculature

IMAGING

- Bronchiectasis: Most common manifestation
- Tracheal wall thickening, tracheal stenosis
- Bronchiolectasis
- Organizing pneumonia, nonspecific interstitial pneumonia, eosinophilic pneumonia
- Pulmonary thromboembolism
- Pleural effusion, pleural thickening
- Drug toxicity
- Opportunistic infections

TOP DIFFERENTIAL DIAGNOSES

- Rheumatoid arthritis
- Pulmonary infections causing bronchiectasis (*Mycobacterium avium* complex)
- Asthma

PATHOLOGY

- Postulated etiology of pulmonary involvement
 - Common embryonic origin of respiratory and intestinal tracts
 - Exposure of epithelium to common antigens

CLINICAL ISSUES

• Pulmonary involvement in 75-85% of patients after IBD symptom onset, 5-10% at same time as IBD symptom onset, and 10-15% before IBD symptom onset

DIAGNOSTIC CHECKLIST

• Consider pulmonary involvement in patient with thoracic abnormalities or complaints and history of IBD

(Left) Axial NECT of a 47-yearold man with ulcerative colitis with new productive cough and dyspnea shows upper lobe bronchiectasis \supseteq and bronchial wall thickening. Airway inflammation in patients with inflammatory bowel disease may affect both large and small airways. (Right) Coronal NECT of the same patient shows bilateral cylindrical bronchiectasis 🔁 and bronchial wall thickening. Bronchiectasis is the most common large airway abnormality in patients with inflammatory bowel disease.





(Left) Axial CECT of a 43-yearold patient with ulcerative colitis and wheezing shows circumferential tracheal wall thickening \square , consistent with tracheitis. Upper airway disease in inflammatory bowel disease may involve the pharynx, larynx, trachea, and mainstem bronchi. (Right) Coronal CECT of a 37-year-old man with Crohn disease shows a right lower lobe pulmonary artery thromboembolus 🖂 and a lung infarct 🔁. Patients with inflammatory bowel disease are at greater risk for thromboembolism than the general population.





Inflammatory Bowel Disease

TERMINOLOGY

Abbreviations

• Inflammatory bowel disease (IBD)

Synonyms

• IBD-associated lung disease

Definitions

- Likely secondary to inappropriate immune response to physiologic gut flora in host with genetic susceptibility
- Ulcerative colitis (UC) and Crohn disease (CD)
- UC: Limited to colon
 CD: Any segment of gastrointestinal tract
- Extraintestinal manifestations of IBD in 16-40% of affected patients; more common in CD
 - Pulmonary manifestations rare but often overlooked
 - Secondary to disease itself or complication of drug therapy (e.g., drug toxicity, opportunistic infection)

IMAGING

General Features

- Best diagnostic clue
 - Pulmonary abnormalities in patient with IBD
- Location
 - Lung, small and large airways, pleura, vasculature

Radiographic Findings

- Radiography
 - May be normal
 - Nonspecific abnormalities
 - Patchy airspace opacities/consolidations
 - Bronchiectasis
 - Pleural effusion

CT Findings

- CECT
 - o Pleural disease
 - Effusion: Usually unilateral, may be hemorrhagic
 - Pleural thickening
 - Pericardial effusion
 - Pulmonary thromboembolic disease
 - Risk of embolism 3x higher compared to normal population
 - Filling defects in pulmonary arteries
 - Additional sites involved by thrombus: Cerebral, portal, mesenteric, retinal vessels
- HRCT
 - Large airway abnormalities strongly associated with UC
 - Tracheal inflammation
 - Ulceration of tracheal epithelium: Circumferential tracheal wall thickening
 - □ Glottic/subglottic stenosis
 - Bronchiectasis
 - Most common manifestation of IBD (66% of cases of airway involvement)
 - Bronchial wall thickening, bronchial dilatation, mucoid impaction
 - Small airways abnormalities
 - Bronchiolectasis
 - Bronchiolar wall thickening

- Mucoid impaction
- Centrilobular ground-glass nodules
- Mosaic attenuation
- Air-trapping
- Parenchymal disease
 - Organizing pneumonia
 - Scattered opacities/consolidations: Nonsegmental, unilateral or bilateral, subpleural, &/or peribronchovascular distribution
 - Ground-glass opacities
 - Reversed halo sign: Central ground-glass opacity surrounded by peripheral consolidation
 - Eosinophilic pneumonia (mesalazine therapy and peripheral eosinophilia)
 - Unilateral or bilateral peripheral consolidations
 - Upper lobe predominant involvement
 - Nonspecific interstitial pneumonia
 - Lower lobe predominant ground-glass opacities and reticulation
 - Interlobular septal thickening and intralobular lines
 - Subpleural sparing and peribronchovascular opacities common
 - □ Traction bronchiectasis, bronchiolectasis
- Opportunistic infections (anti-TNF-α monoclonal antibody treatment)
 - Tuberculosis
 - Screening for tuberculosis prior to treatment, prophylactic tuberculostatic treatment for latent infection
 - □ Tree-in-bud opacities, patchy consolidations, cavitation
 - Pneumocystis jirovecii pneumonia
 - Upper lobe predominant involvement
 - □ Ground-glass opacity, relative sparing of lung periphery
 - □ Septal lines ± intralobular lines superimposed on ground-glass opacity (i.e., crazy-paving pattern)
 - Nocardiosis
 - Consolidations, nodules, masses
 - Cavitation may occur
 - □ Chest wall involvement (uncommon)
 - Aspergillosis
 - Mass-like consolidation, nodules, halo sign, reversed halo sign, cavitation
 - Other: Actinomycosis, coccidiomycosis, histoplasmosis
- Additional abnormalities
 - Colobronchial, ileobronchial, esophagobronchial fistulae
 - Splenic flexure-left lower lobe colobronchial or colopleural fistula may cause recurrent pneumonia, empyema, fecopneumothorax
 - Necrobiotic nodules
 - □ Single or multiple (0.5-7.0 cm); peripheral mid and upper lung zone predominant involvement
 - Sarcoidosis
 - Incidental finding vs. possibly linked to IBD
 - Imaging findings: Hilar and mediastinal lymphadenopathy, perilymphatic pulmonary nodules

Imaging Recommendations

Best imaging tool
 HRCT or thin-section CT

DIFFERENTIAL DIAGNOSIS

Rheumatoid Arthritis

- Arthropathy involving small joints
- Bronchiectasis, pleural effusion, necrobiotic nodules, organizing pneumonia

Pulmonary Infections Causing Bronchiectasis (e.g., *Mycobacterium avium* Complex)

- Bronchiectasis, tree-in-bud opacities, and mosaic attenuation
- Middle lobe and lingula more severely involved

Asthma

- Bronchiectasis, bronchial wall thickening, airway narrowing and dilatation
- Mosaic perfusion/attenuation
- Eosinophilia

PATHOLOGY

General Features

- Etiology
 - Likely multifactorial
 - Genetic predisposition
 - Environmental factors
 - Immunologic dysfunction
 - Intestinal microbiota
 - Postulated pathogenesis of pulmonary involvement in patients with IBD
 - Common embryonic origin of respiratory and intestinal tracts
 - Exposure of epithelium to common antigens by inhalation and ingestion, causing sensitization of lymphoid tissue and inflammation
- Genetics
 - 10-20% of affected individuals have family history of IBD; highest risk among first-degree relatives
 - *NOD2* gene recently identified as first gene associated with CD
- Associated abnormalities
 - Most common extraintestinal manifestations of IBD involve musculoskeletal system and skin
 - Peripheral and axial arthropathies (sacroiliitis)
 - Pyoderma gangrenosum
 - Erythema nodosum
 - Other manifestations
 - Anterior uveitis, episcleritis, pericholangitis, fatty liver, nephrolithiasis, obstructive uropathy, fistulization of urinary tract
 - Coexistent autoimmune diseases may be present regardless of IBD activity
 - e.g., hemolytic anemia, primary sclerosing cholangitis, Hashimoto disease

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonspecific respiratory symptoms
 - Shortness of breath, dyspnea, stridor, hoarseness, dysphonia, chronic productive cough, asthma
- Other signs/symptoms
 - Pulmonary disease may be secondary to drug toxicity (e.g., methotrexate, azathioprine, sulfasalazine, mesalazine) or opportunistic infections related to immunosuppression
 - Respiratory symptoms may be present before or after diagnosis of IBD; may develop after colectomy
 - Pulmonary function abnormalities are frequently present, even in asymptomatic patients
 - Up to 50% in patients with UC
 - Obstructive or restrictive patterns on pulmonary function tests; bronchial hyperresponsiveness

Demographics

- Age
 - May occur at any age; typically diagnosed between 15-35 years of age
- Sex
- \circ M = F
- Ethnicity
 - Caucasians and people of Ashkenazi Jewish origin affected more frequently than other racial or ethnic subgroups

Natural History & Prognosis

- Pulmonary manifestations
 - o 75-85%: After IBD symptom onset
 - o 5-10%: At same time as IBD symptom onset
 - o 10-15%: Before IBD symptom onset
- Exacerbation of respiratory symptoms corresponds with periods of active IBD
 - Serositis usually associated with active IBD
 - Parenchymal abnormalities often develop in patients with inactive IBD

Treatment

- IBD-related pulmonary disease usually treated with steroids
- Drug-related pulmonary disease responds to drug withdrawal, steroids, and supportive measures
- Opportunistic infections secondary to anti-TNF drugs treated with antibiotics or antifungals

DIAGNOSTIC CHECKLIST

Consider

• Pulmonary involvement in patient with thoracic complaints or abnormalities and history of IBD

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Inflammatory Bowel Disease





(Left) Axial NECT of a 62-yearold man with ulcerative colitis shows a left upper lobe mass \implies suspicious for primary lung cancer. (Right) Coronal FDG PET/CT of the same patient shows FDG avidity within the $mass \implies without evidence of$ metastatic disease. Biopsy showed nocardiosis. The patient had received treatment with anti-TNF-a inhibitors. Opportunistic infections are common complications of drug-related suppression of T-cell-mediated immunity in patients undergoing biologic therapies.





(Left) PA chest radiograph of a 67-year-old woman with Crohn disease and eosinophilic pneumonia shows right greater than left bilateral heterogeneous consolidations Eosinophilic pneumonia usually occurs as drug-induced lung disease in patients with inflammatory bowel disease, but may be secondary to the disease itself. (Right) Coronal CECT of the same patient shows right greater than left bilateral peripheral $consolidations \supseteq secondary$ to eosinophilic pneumonia with typical peripheral distribution.





(Left) PA chest radiograph of a 52-year-old man with ulcerative colitis who presented with fever and pleuritic pain shows ill-defined bilateral lower lung zone opacities 🔁. (Right) Axial NECT of the same patient shows bilateral peripheral consolidations 🔁, consistent with organizing pneumonia, one of the most common lung manifestations of inflammatory bowel disease that may result from the disease or its therapy. Treatment consists of corticosteroids and cessation of drug therapy.

Erdheim-Chester Disease

KEY FACTS

TERMINOLOGY

- Erdheim-Chester disease (ECD)
- Non-Langerhans cell histiocytosis of unknown origin
- IMAGING

• Radiography

- Pulmonary involvement very common (90%)
- Interlobular septal thickening
- Mild to moderate pleural thickening
- Bilateral symmetric long bone osteosclerosis (95%)
- CT
 - Smooth pleural thickening ± effusions
 - Ground-glass opacity and smooth septal thickening (69%)
 - Subpleural lung nodules (36%)
 - Pericardial soft tissue thickening or effusion
 - Right atrial and atrioventricular groove involvement
 Soft tissue encasement of aorta and right coronary
 - artery (34-62%)

• Renal encasement by soft tissue (65%)

TOP DIFFERENTIAL DIAGNOSES

- Paget disease of bone
- Lymphoma
- Lysosomal storage diseases
 - Gaucher disease
 - Fabry disease
- Other histiocytic disorders
 Rosai-Dorfman disease
 - Adult xanthogranuloma
- IgG4-related disease

CLINICAL ISSUES

• Pleuropulmonary involvement: 3-year survival 66%

DIAGNOSTIC CHECKLIST

• Combination of pleural or diffuse septal thickening, perirenal soft tissue, aortic wall thickening, and bone sclerosis considered pathognomonic for ECD

(Left) Graphic shows thoracic features of Erdheim-Chester disease, including interlobular septal thickening \supseteq , pleural thickening 🖂, and soft tissue encasement of the aorta earrowand kidneys 🖂. (Right) Axial HRCT of a patient with Erdheim-Chester disease shows diffuse bilateral interlobular septal thickening ➡, patchy ground-glass opacities, and mild thickening of the left major fissure 🔁 The findings may mimic interstitial edema, but other findings (skeletal, periaortic, perirenal) usually suggest the correct diagnosis.





(Left) Axial NECT of a patient with Erdheim-Chester disease shows bilateral pleural thickening \triangleright and small bilateral pleural effusions \blacksquare . Long bone osteosclerosis should always be surveilled on radiographs of the extremities. (Right) Axial CECT of a patient with Erdheim-Chester disease shows diffuse hyperdense soft tissue encasement of the aorta \triangleright and the bilateral kidneys 🔁. This constellation of findings combined with interlobular septal thickening and ground-glass opacity in the lung is highly suggestive of Erdheim-Chester disease.





Erdheim-Chester Disease

TERMINOLOGY

Abbreviations

• Erdheim-Chester disease (ECD)

Definitions

• Non-Langerhans cell histiocytosis of unknown origin

IMAGING

General Features

- Best diagnostic clue
 - Triad of osteosclerotic bone lesions, perirenal soft tissue, and pleural &/or diffuse septal thickening

Radiographic Findings

- Pulmonary involvement very common (90%)
- Interlobular septal thickening
- Mild to moderate pleural thickening
- Generalized cardiac enlargement
- Bilateral symmetric long bone osteosclerosis

CT Findings

- CECT
 - **Smooth pleural thickening** extending into fissures, ± pleural effusions
 - Ground-glass opacities and **smooth, uniform** interlobular septal thickening (69%)
 - o Subpleural lung nodules (36%)
 - Smooth, long-segment encasement of aorta and great vessels by thick soft tissue (30%)
 - Renal encasement by soft tissue
 - Bilateral symmetric osteosclerosis of lower extremity long bone metaphyses and diaphyses: Considered pathognomonic
 - o Heart
 - Soft tissue-attenuation encasement of right coronary artery (34%)

Imaging Recommendations

- Best imaging tool
 - CECT and HRCT: Lung, pleural, aortic, and skeletal abnormalities

DIFFERENTIAL DIAGNOSIS

Paget Disease of Bone

• Not associated with extraosseous abnormalities

Lymphoma

• May exhibit multiorgan involvement and mimic ECD

Lysosomal Storage Diseases

- Gaucher disease
- Fabry disease

Other Histiocytic Disorders

- Rosai-Dorfman disease
- Adult xanthogranuloma

IgG4-Related Disease

• Infiltration by IgG4-positive plasma cells and associated fibrosis leads to multiple organ dysfunction; often associated with autoimmune pancreatitis

- Solid bronchovascular parenchymal nodules or mass-like lesions
- Bronchiectasis and honeycombing, similar to nonspecific interstitial pneumonia, air-space consolidation
- Hilar and mediastinal lymphadenopathy

PATHOLOGY

Gross Pathologic & Surgical Features

• Symmetric involvement: Long bones, pleura, perirenal areas, and lung; never unilateral

Microscopic Features

- Lymphangitic expansion by inflammatory cells and fibrosis
 Inflammatory cells: Large foamy histiocytes, lymphocytes, plasma cells, and Touton giant cells
 - Fibrosis: Fine fibrillary mature collagen without fibroblast proliferation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Slow onset of cough and dyspnea
 - Pulmonary function: Moderate restriction, decreased DLCO
- Other signs/symptoms
 - Diabetes insipidus (20%), exophthalmos (15%), renal failure (15%), xanthomas (10%)

Demographics

- Age
 - o > 40 years
- Sex
- No sex predilection

Natural History & Prognosis

- Slowly progressive disease; prognosis depends on extent of extraosseous disease
- Pleuropulmonary involvement: Significant morbidity and mortality; 3-year survival 66%

Treatment

- Corticosteroids
- Vincristine and related chemotherapeutic agents
- Radiotherapy for focal masses

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Combination of pleural or diffuse septal thickening, perirenal soft tissue, aortic wall thickening, and bone sclerosis considered pathognomonic for ECD

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KEY FACTS

TERMINOLOGY

- Hematopoietic stem cell transplantation (HSCT)
 - Bone marrow, peripheral blood stem cell, and cord blood stem cell transplantation
- Graft-vs.-host disease (GVHD): Donor T-cells attack recipient's organs as foreign bodies

IMAGING

- Imaging abnormalities vary with time elapsed after HSCT
- Neutropenic phase: 0-30 days after HSCT
 - Bacterial pneumonia: Consolidation
 - Fungal infection: Nodules ± cavitation
 - Pulmonary edema: Bilateral perihilar opacities
 - Alveolar hemorrhage: Patchy bilateral opacities
- Early phase: > 30-100 days after HSCT
 Viral pneumonia: Ground-glass opacities
- Late phase: >100 days after HSCT, GVHD
 - Constrictive bronchiolitis: Mosaic attenuation, airtrapping

• Organizing pneumonia: Peribronchovascular, perilobular, subpleural opacities

TOP DIFFERENTIAL DIAGNOSES

- Ground-glass opacities
 - Pulmonary edema
 - o DIffuse alveolar hemorrhage
 - o Viral pneumonia
- Nodules or masses
 - Septic emboli
 - Fungal infection
 - Organizing pneumonia

CLINICAL ISSUES

- Pulmonary complications in 40-60% of all recipients
- HVGD: 20-70% of allogeneic HSCT

DIAGNOSTIC CHECKLIST

• Consider time elapsed since HSCT and host immunity to suggest specific infections &/or complications

(Left) PA chest radiograph of a 45-year-old man who developed fever 25-days after bone marrow transplant for acute myeloid leukemia shows a well-defined right upper lobe mass 🛃. (Right) Axial CECT of the same patient shows a well-defined right upper lobe mass 🔁 with intrinsic low $attenuation \supseteq$, consistent with developing cavitation. Biopsy confirmed angioinvasive aspergillosis. Patients are susceptible to fungal and bacterial infection within the first 30-days after hematopoietic stem cell transplant.











TERMINOLOGY

Abbreviations

• Hematopoietic stem cell transplantation (HSCT)

Definitions

- HSCT
 - o Types
 - Bone marrow transplantation, peripheral blood stem cell transplantation, cord blood stem cell transplantation
 - Autologous transplantation uses patient's own stem cells
 - Allogeneic transplantation uses cells from human leukocyte antigen-consistent donor
 - o Procedure
 - High-dose chemotherapy &/or total body irradiation (TBI) followed by infusion of donor hematopoietic stem cells
 - Complications
 - Infectious and noninfectious
 - Noninfectious: Graft-vs.-host disease (GVHD); donor T-lymphocytes attack recipient's organs as foreign bodies, occurs with allogeneic transplantation

IMAGING

General Features

- Imaging abnormalities vary depending on time elapsed after HSCT
 - Complications classified as early or late
 - Early phase: First 100 days after transplant
 - Neutropenic or pre-engraftment period: Up to 30 days after transplant
 - Early post transplant period: 30-100 days after transplant
 - Late phase: > 100 days or 3 months

Early Phase: Neutropenic (Pre-Engraftment) 0-30 Days

- Transplanted bone marrow not yet functional
- Profound neutropenia: High risk for bacterial and fungal infection
- Infectious complications
 - Bacterial pneumonia
 - Consolidation
 - Pleural effusion
 - Fungal infection
 - Invasive pulmonary aspergillosis (IPA)
 - Pulmonary nodules
 - □ Air crescent sign: Cavitary nodule with soft tissue content surrounded by air
 - □ Airway IPA: Bronchial and bronchiolar wall thickening, tree-in-bud opacities
 - CT halo sign: Nodule surrounded by ground-glass opacity
 - Zygomyces: Mucor and Rhizopus
 - □ Nodules ± cavitation
 - □ CT halo sign
 - Reversed halo sign: Central ground-glass surrounded by consolidation

- Candida infection
 - Ill-defined nodules
 - Patchy opacities
 - Miliary nodules
- Non infectious complications
 - o Pulmonary edema
 - Bilateral ground-glass opacities
 - Interlobular septal thickening
 - Perihilar consolidations
 - Pleural effusions
 - Idiopathic pneumonia syndrome (IPS): Idiopathic pneumopathy after HSCT in absence of infection, fluid overload, cardiac, or renal dysfunction
 - Peri-engraftment respiratory distress syndrome
 - □ Diffuse capillary leak, cutaneous rash and fever
 - □ Ground-glass opacities, perihilar or peribronchial consolidation
 - Thick interlobular septa
 - Diffuse alveolar hemorrhage
 - Hemoptysis in 60% of cases, > 20% hemosiderinladen macrophages in bronchoalveolar lavage fluid
 - Bilateral ground-glass opacities
 - □ Interlobular septal thickening and intralobular lines
 - Cryptogenic organizing pneumonia
 - Peripheral ground-glass opacities, patchy consolidations
 - Peribronchial nodules and opacities
 - Reversed halo sign

Early Phase: Early Posttransplant (30-100 Days)

- Normal neutrophil count but impaired humoral and cellular immunity
 - Incidence of infection begins to decrease
 - High risk for viral and Pneumocystis jirovecii infection
- Infectious complications
 - Cytomegalovirus pneumonia
 - Small centrilobular and random nodules (1-5 mm)
 - Patchy or diffuse ground-glass opacities
 - Pleural effusions
 - *Pneumocystis jirovecii* pneumonia (PCP) now rare with effective prophylaxis
 - Diffuse ground-glass opacities
 - Pneumatoceles, cysts
 - Nodule/mass, pleural effusion, lymphadenopathy (uncommon)
 - Other viral pneumonias (respiratory syncytial virus, influenza, adenovirus)
 - Bilateral ground-glass opacities
 - Centrilobular nodules
 - Bronchial wall thickening
 - Tree-in-bud opacities

Non-infectious complications

- Acute radiation pneumonitis
 - Previous radiation for mediastinal lymphoma
 - Paramediastinal ground-glass opacities and dense consolidations
- Acute GVHD
 - Bilateral diffuse ground-glass opacities and dense consolidations
Late Phase (> 100 Days)

- Recovery of host immunity
- Pulmonary complications are primarily non-infectious
- GVHD is most common complication
- o GVHD
 - May manifest as bronchiolitis obliterans or organizing pneumonia
 - Bronchiolitis obliterans
 - □ Hyperinflation
 - Bronchiectasis, bronchial wall thickening
 - □ Mosaic attenuation
 - Organizing pneumonia
 - Deripheral, perilobular, peribronchial distribution
 - Patchy consolidation with air bronchogram
 Reversed halo sign
- Interstitial lung disease (nonspecific interstitial
 - pneumonia)
 - Ground-glass opacities
 - Reticular opacities and traction bronchiectasis
- o Pleuroparenchymal fibroelastosis
 - Pleural thickening, subpleural opacities
 - Traction bronchiectasis
- o Air-leak syndrome
 - Spontaneous interstitial emphysema, pneumothorax, pneumomediastinum, subcutaneous gas
 - Associated with GVHD
- Post transplant lymphoproliferative disorder
 - Epstein-Barr virus stimulation of B-lymphocytes in Tcell compromised host
 - Usually 6 months after allogeneic HSCT
 - Mediastinal and hilar lymphadenopathy
 - Pulmonary nodule(s), mass(es), consolidation

Imaging Recommendations

- Best imaging tool
 - Chest radiography for evaluation of suspected or documented pulmonary infection
 - CT more sensitive and specific than radiography for diagnosis of acute and late complications
 - HRCT: Air-trapping in bronchiolitis obliterans

DIFFERENTIAL DIAGNOSIS

Ground-Glass Opacities

- Pulmonary edema
- Diffuse alveolar hemorrhage
- Viral pneumonia
- Drug toxicity
- Peri-engraftment respiratory distress syndrome

Nodules or Masses

- Septic emboli
- Fungal infection
- Organizing pneumonia

PATHOLOGY

Microscopic Features

- Idiopathic pneumonia syndrome
- Diffuse alveolar damage in absence of lower respiratory tract infection

- Constrictive bronchiolitis
 - Chronic inflammatory and fibroproliferative process centered on terminal and respiratory bronchiole
 - Bronchiolar stenosis and scarring
- Organizing pneumonia
 - Granulation tissue, polyps in lumina of alveolar ducts and bronchioles
 - Interstitial inflammation and fibrosis

CLINICAL ISSUES

Demographics

- Epidemiology
 - Pulmonary complications in 40-60% of HSCT recipients
 - Infectious complications more common in allogeneic HSCT
 - GVHD reported in 20-70% of allogeneic HSCT
- Indications for HSCT
 - Acute and chronic leukemia
 - Lymphoma, multiple myeloma, myelodysplastic syndrome
 - o Thalassemia, sickle cell anemia, aplastic anemia

Graft-vs.-Host Disease

- Most common long-term complication after HSCT
- Exclusive with allogeneic HSCT
 - Immune-mediated reaction of donor lymphocytes against host tissue
- Acute or chronic
 - Acute GVHD: Uncommon lung involvement
- Chronic GVHD: Develops > 100 days after HSC, most common between 7-15 months after transplantation
 - Multiple organs affected
 - Skin: Rash
 - Gastrointestinal tract: Diarrhea
 - Liver: Jaundice
 - Pulmonary symptoms are nonspecific
 - Nonproductive cough, dyspnea, asymptomatic decline in pulmonary function
 - Obstructive pattern on pulmonary function tests
 - Treatment: Immunosuppressive therapy for bronchiolitis obliterans and organizing pneumonia
 Draanizing pneumonia is reversible
 - □ Organizing pneumonia is reversible
 - Bronchiolitis obliterans is severe and irreversible

DIAGNOSTIC CHECKLIST

Consider

- Opportunistic infection in patients who develop fever post HSCT
- Time elapsed since HSCT and host immunity to suggest specific infections and other complications

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- Shroff GS et al: Imaging of pneumonias and other thoracic complications after hematopoietic stem cell transplantation. Curr Probl Diagn Radiol. 48(4):393-401, 2019





(Left) Axial NECT of a 40-yearold man with dyspnea and fever 50 days after hematopoietic stem cell transplantation shows groundglass opacities 🖂 (Right) Axial NECT of the same patient shows bilateral . ground-glass opacities, a characteristic finding of Pneumocystis jirovecii pneumonia. In the early posttransplant phase, the predominant infection is viral, most commonly cytomegalovirus. Pneumocystis jirovecii also occurs but is less frequent due to effective prophylaxis.





(Left) Axial NECT of a 37-yearold man with acute lymphocytic leukemia, 1 year after hematopoietic stem cell transplantation shows multifocal subpleural consolidations
. (Right) Axial NECT of the same patient shows peribronchial 🔁 and subpleural nodular consolidations and ground-with organizing pneumonia due to chronic graft-vs.-host disease, the most common and relevant complication in longterm survivors after hematopoietic stem cell transplant.





(Left) Axial NECT of 34-yearold woman with T-cell lymphoma who developed dyspnea on exertion 2 years after allogeneic hematopoietic stem cell transplant shows no abnormality. (Right) Axial NECT of the same patient performed during expiration shows mosaic attenuation secondary to expiratory airtrapping \supseteq , consistent with constrictive bronchiolitis, a well-known manifestation of chronic graft-vs.-host disease in allogeneic hematopoietic stem cell transplant recipients.

Solid Organ Transplantation

KEY FACTS

TERMINOLOGY

- Solid organ transplant (SOT)
 Heart, lung, liver, kidney, small bowel, pancreas
- IMAGING
- Infection
 - Dense consolidation: Bacterial pneumonia
 - Viral: Diffuse or focal ground-glass opacities
 - Fungal: Nodules ± cavitation
- Bronchiolitis obliterans
 - Air-trapping, bronchiectasis
- Post-transplant lymphoproliferative disorder (PTLD)
 Pulmonary nodules, lymphadenopathy
- Kaposi sarcoma
 - Peribronchovascular nodular opacities
- Enhancing lymphadenopathy
- Lung cancer
 - Lung nodule/mass ± lymphadenopathy

- Role of Imaging
 - **Radiography** and **CT**: Detection of complications, monitoring treatment response
 - **PET/CT**: Staging/monitoring of PTLD and other malignancies

TOP DIFFERENTIAL DIAGNOSES

- Consolidation
- Infection
 - o Pulmonary edema
- Ground-glass opacities
 - o Pulmonary edema, acute respiratory distress syndrome
 - Viral infection
 - Drug toxicity
- Pulmonary nodules
 - Fungal or mycobacterial infection
 - Lung cancer
 - o Kaposi sarcoma
 - o PTLD

(Left) Axial CECT of a 50-yearold man obtained 7 days after liver transplantation shows Legionella pneumonia manifesting as bilateral consolidations \supseteq and groundglass opacities. Nosocomial pneumonias are most common in the first month after solid organ transplant. (Right) Axial NECT of a 62-year-old liver transplant recipient shows bilateral irregular nodules 🖂, consistent with angioinvasive aspergillosis, an opportunistic infection that is typically seen 1 to 6 months after solid organ transplantation.





(Left) Coronal CECT of a 73year-old man status post liver transplant shows a right lung pneumonia 🔁. The right hemidiaphragm elevation 🖾 was due to phrenic nerve injury during surgery. Phrenic nerve paralysis increases the risk of aspiration and pneumonia. (Right) Axial NECT of an 18-year-old patient status post liver transplant shows calcified pulmonary nodules 🖂, consistent with metastatic calcification. Metastatic pulmonary calcification is usually silent and occurs in renal and liver transplant recipients.





- Abbreviations
- Solid organ transplant (SOT)

Definitions

- Transplantation of heart, lung, liver, kidney, pancreas, small bowel, etc. (unlike hematopoietic stem cell transplant)
- Requires lifelong immunosuppressive therapy to prevent rejection of allografts

IMAGING

General Features

Imaging frequently used for evaluation of complications
 Complications: Infectious and noninfectious

Imaging Findings

- Infectious complications
 - Bacterial pneumonia
 - Consolidations, cavitation, lung nodules
 - **Viral infection**: Cytomegalovirus (CMV), severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2)
 - CMV: Diffuse or focal ground-glass opacities, consolidations, nodules
 - SARS-CoV-2: Bilateral subpleural ground-glass opacities, lower lobe predominant
 - Fungal infection: Aspergillus fumigatus
 - Nodules ± cavitation; consolidation
 - Mycobacterial infection
 - Nodules and masses ± cavitation
 - Tree-in-bud opacities
 - Lymphadenopathy
- Non-infectious complications
 - Pulmonary edema
 - Thick interlobular septa, ground-glass opacities
 - Pleural effusions, cardiomegaly
 - Acute respiratory distress syndrome (ARDS)
 - Gravitational grounds-glass opacities and consolidations
 - Drug toxicity
 - Sirolimus: Immunosuppressive agent
 - Organizing pneumonia: Patchy peribronchovascular or subpleural opacities
 - Interstitial pneumonia: Subpleural reticular opacities with basilar predominance
 - Venous thromboembolism: Vascular filling defects
 - **Other**: Pleural effusions, atelectasis
 - Neoplasm

Post-transplant lymphoproliferative disorder (PTLD)

- Thoracic involvement less common than abdominal involvement, most common in heart transplant recipients
- Pulmonary masses and nodules ± CT halo sign or central necrosis
- □ Lymphadenopathy
- Pleural or pericardial effusion
- Kaposi sarcoma (KS)
 - □ Peribronchovascular flame-shaped nodules
 - Enhancing lymphadenopathy

- Cancer recurrence in transplant recipient
 - □ Pulmonary nodules &/or lymphadenopathy
- Organ-specific complications

 Lung transplant
 - Dehiscence of bronchial anastomosis
 - Pneumonia, pneumothorax, empyema
 - □ Long-term complication: Stricture or
 - bronchomalacia Diaphragmatic durfunction
 - Diaphragmatic dysfunction
 - □ Traction on phrenic nerve during surgery
 - □ Increases incidence of pneumonia and aspiration
 - Bronchiolitis obliterans (obliterative bronchiolitis)
 - Chronic lung rejection: Defined by clinical criteria based on pulmonary function abnormalities of airflow obstruction rather than on histologic diagnosis
 - Bronchial wall thickening, bronchial dilatation, mosaic attenuation
 - Air-trapping on expiratory HRCT: Most sensitive predictor of bronchiolitis obliterans in lung transplant recipients
 - Lung cancer (highest risk of lung cancer among lung transplant recipients)
 - Imaging features similar to those of lung cancer in general population
 - □ Lung nodule/mass ± lymphadenopathy

Cardiac transplant

- Rejection
 - Increased heart size
 - □ Pulmonary edema
 - Pericardial and pleural effusions
 - □ Accelerated atherosclerosis in graft
- Diaphragmatic hernia
 - Failure of repair of left hemidiaphragm defects from pretransplantation indwelling left ventricular assist device
 - □ Intrathoracic herniation of fat, stomach, bowel

Lung cancer

- Renal transplant
 - Pulmonary metastatic calcification
 - Clinically silent, may occur even with normally functioning renal allograft
 - □ Upper lung zone predominance
 - Calcification in parenchymal opacities or nodules, calcification of chest wall vessels

• Liver transplant

- Hepatopulmonary syndrome
 - Precedes transplantation
 - Persistent hypoxemia + abnormal pulmonary vascular dilatation
- Diaphragmatic dysfunction
 - Right phrenic nerve injury by suprahepatic vena cava clamp
 - Increased incidence of pneumonia and aspiration
- Pulmonary metastatic calcification
- Less frequent than in renal transplantation

Imaging Recommendations

- Best imaging tool
 - CT: Useful in symptomatic patients with negative or nonspecific radiographic findings

- <u>Connective Tissue Disorders, Immunological</u> Diseases, and Vasculitis
- PET/CT: Staging and monitoring treatment response of PTLD and other malignancies

DIFFERENTIAL DIAGNOSIS

Consolidation

Infection

Ground-Glass Opacities

- Viral infection CMV, SARS-CoV-2
- Pneumocystis jirovecii pneumonia
- Pulmonary edema

Pulmonary Nodules

- Fungal infection
- Mycobacterial infection
- Lung cancer
- PTLD
- KS
- Recurrent malignancy

CLINICAL ISSUES

Presentation

- Clinical profile
 - First week (most common): Pulmonary edema, ARDS, pneumonia, pleural effusion, atelectasis
 - Infectious complications common during first year, especially first 6 months
 - 0-1 months: Nosocomial infection; 1-6 months opportunistic infection risk associated with immunosuppression; > 6 months improved immunosuppression (community-acquired pathogens)
 - > 6 months: Neoplasms, bronchiolitis obliterans

Infection

- Bacterial pneumonia
 - o First month: Nosocomial bacterial infection
 - Gram-negative rods, gram-positive cocci
 - > 6 months: Community-acquired pathogens
- CMV infection: 8-50% of SOT recipients
- First 6 months post transplant
 - o Flu-like symptoms
- Highest risk for CMV in recipients of CMV(+) organs
- Treatment and prophylaxis
 - IV ganciclovir or oral valganciclovir
- Fungal infection: Aspergillus, Zygomycetes; and Scedosporium and Blastoschizomyces with increasing frequency
 - Aspergillus
 - Invasive pulmonary aspergillosis (IPA): 2-4% of SOT recipients
 - Aspergillus isolated in 33% of lung transplant recipients in one study, colonization to IPA
 - First 6 months post transplant
 - o Treatment
 - Appropriate antibiotics
 - Surgical resection
- Mycobacterial infection
 - Mycobacterium tuberculosis
 - Up to 15% of SOT recipients in endemic regions

- Most commonly reactivation of latent tuberculosis in previously exposed patients
- Nontuberculous mycobacterial infection uncommon
- SARS-CoV-2
 - o Most reported cases: Community-acquired
 - Unclear if SOT recipients have higher risk of severe disease compared with nontransplant patients

Neoplasm

- Nonmelanoma skin cancer in up to 82% of transplant recipients
 - Squamous cell cancer most common
- PTLD
 - o 1-11% of SOT patients
 - Incidence highest in 1st year post transplant
 - Incidence highest in small bowel transplant (20%)
 - Usually B-cell proliferation related to Ebstein-Barr virus (EBV)
 - Wide disease range: Lymphoid hyperplasia to frank lvmphoma
 - Most likely to occur in anatomic location of allograft
 - Treatment
 - Reduction of immunosuppression
 - Rituximab: Anti-CD20 monoclonal antibody
- KS
 - 6% of SOT recipients
 - Incidence 500x higher in SOT recipients than in general population
 - Median time from transplant to KS diagnosis: 1.5 years
 - Associated with HHV-8 infection
 - Risk factors: Male, older age at transplantation
 - Treatment
 - Immunosuppression reduction, chemotherapy
- Lung cancer
 - Incidence 20-25x higher in SOT recipients than in general population
 - Highest risk of lung cancer among lung and heart transplant recipients
- Cancer recurrence related to malignancy in recipient • Manifests as early as 6 months after transplantation

Bronchiolitis Obliterans (Obliterative Bronchiolitis)

- Most important cause of morbidity and mortality in heartlung and lung transplant recipients after 1 year
 - o ~ 50% of transplant recipients by 5 years post transplant
 - ~ 30% of deaths > 1 year post transplant
- Risk factors
 - Acute rejection
 - o Lymphocytic bronchitis, bronchiolitis
 - o CMV pneumonia
 - Medication noncompliance
- Treatment
 - Increased immunosuppressive therapy

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(Left) Axial NECT of a 55-yearold patient obtained 6 years post liver transplantation who developed acute lung injury in the setting of SARS-CoV-2 shows consolidations and ground-glass opacities 🔁 in the right upper lobe. (Right) Axial NECT of the same patient shows additional , peripheral ground-glass opacities \supseteq . Treatment and adjustment of immunosuppressive regimens in patients with solid organ transplantation and COVID-19 infection are individualized based on disease severity.





(Left) Axial CECT of a 19-yearold liver transplant recipient with a history of hepatoblastoma shows multifocal small bilateral solid nodules 🖾. (Right) Coronal CECT of the same patient shows bilateral solid nodules 🖂 which represented biopsyproven metastases. The lung is the most common site of recurrence among liver transplant recipients with history of hepatic malignancy. Additional neoplastic disorders include posttransplant lymphoproliferative disorders, lung cancer, and Kaposi sarcoma.





(Left) Axial CECT of a 77-yearold woman with lung adenocarcinoma that developed after right lung transplantation for pulmonary fibrosis 7 years earlier shows a lobulated right upper lobe solid nodule 🖂. (Right) Coronal FDG PET of the same patient shows metabolic activity \supseteq in the right upper lobe nodule. The prevalence of lung cancer is higher in lung and heart transplant recipients compared to liver and renal transplant recipients. Lung cancer develops 1 year after transplantation.

KEY FACTS

TERMINOLOGY

- HIV: Retrovirus infection of helper T-cells, macrophages, dendritic cells → decreased cell-mediated immunity
- AIDS: HIV(+) patients with CD4 < 200 cells/µL
- Anti-retroviral therapy (ART)

IMAGING

- *Pneumocystis jirovecii* pneumonia (PCP): CD4 < 200
 Bilateral ground-glass opacities
- Tuberculosis (TB)
 - o CD4 > 200: Post-primary pattern
 - o CD4 < 200: Primary pattern
 - Very low CD4: Normal chest radiograph
- Kaposi sarcoma: CD4 < 200
 - Peribronchovascular flame-shaped lesions
- Enhancing lymphadenopathy
- Lymphoid interstitial pneumonia: Any CD4
 Centrilobular, peribronchovascular nodules
 - o Ground-glass opacities, cysts

- Multicentric Castleman disease: Any CD4
 Lymphadenopathy ± enhancement
- Immune reconstitution inflammatory syndrome: Paradoxical deterioration from recovery of immune function after ART

CLINICAL ISSUES

- Symptoms/signs
- o Cough, fever
- o Weight loss, weakness, malaise
- Lymphadenopathy
- Prognosis
 - Marked mortality reduction with ART
 - Poor prognosis for patients without access to or noncompliant with ART
- Treatment
 - o ART
 - Antibiotic prophylaxis for PCP, toxoplasmosis, TB, nontuberculous mycobacterial infection

(Left) Axial NECT of an HIV(+) 42-year-old man shows bilateral ground-glass Pneumocystis jirovecii pneumonia (PCP). The patient had dry cough and low-grade fever for 2 weeks. (Right) Coronal NECT of the same patient confirms the presence of diffuse bilateral groundglass opacities 🔁. Subsequent bronchoalveolar lavage was consistent with PCP. Bilateral ground-glass opacities in an HIV(+) patient with CD4 count < 200 and subacute onset of symptoms should be highly suggestive of PCP.





(Left) Axial NECT of an HIV(+) patient with S. pneumoniae pneumonia shows middle lobe consolidation with intrinsic air bronchograms and tiny cavities 🖾. Bacterial bronchitis and pneumonia are the most common causes of respiratory infection in HIV(+) patients with any CD4 count. (Right) Axial CECT of a 49year-old HIV(+) patient with cryptococcosis shows a right upper lobe cavitary mass 🖂 Cryptococcosis typically occurs with CD4 < 100, and cryptococcal pneumonia is the most common fungal infection in HIV(+) patients.





TERMINOLOGY

Abbreviations

- Human immunodeficiency virus (HIV)
- Acquired immunodeficiency syndrome (AIDS)
- Anti-retroviral therapy (ART)

Definitions

- HIV: Retrovirus infection of helper T-cells, macrophages, dendritic cells → decreased cell-mediated immunity
- CD4 count: Helper T-cell level
 - Widely accepted measure of immunosuppression in HIV(+) patients
- AIDS: HIV(+) patients with CD4 < 200 cells/µL at risk for opportunistic infections and malignant neoplasms

IMAGING

General Features

- Best diagnostic clue
 - *Pneumocystis jirovecii* pneumonia (PCP): Bilateral, symmetric ground-glass opacities, CD4 < 200
 - Kaposi sarcoma (KS): Flame-shaped lesions, enhancing lymphadenopathy, male patient, CD4 < 200

Complications of HIV/AIDS

- ART has changed spectrum of infectious and noninfectious pulmonary complications
 - ↓ incidence of opportunistic infection (e.g., PCP) but incidence of community acquired pneumonia has not ↓ proportionately
 - ↑ frequency of noninfectious complications (e.g., lung cancer, pulmonary hypertension [PH], chronic obstructive pulmonary disease, asthma)

• Infection

- **Bacterial pneumonia**: Most common respiratory infection, any CD4 count, encapsulated bacteria (e.g. *Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus*)
 - Segmental or lobar consolidation (50%)
 - Diffuse opacities, nodules, cavities (50%)
- **PCP**: ↓ prevalence but still most common opportunistic infection, presenting illness in patients with previously undiagnosed HIV infection; CD4 < 200
 - Normal chest radiograph: > 40% of cases
 - Bilateral, perihilar or diffuse, symmetric fine granular, reticular, or ground-glass opacities
 - Cysts or pneumatoceles: 10-40%
 Spontaneous pneumothorax
 - Aerosolized pentamidine prophylaxis ↑ atypical manifestations: Cysts, cavitation
- Tuberculosis (TB)
 - Imaging findings depend on CD4 count, 2nd most common opportunistic infection
 - CD4 > 200: Post-primary pattern
 - Upper lobe apical or posterior segments, lower lobe superior segments
 - $\hfill\square$ Cavitary lesions, tree-in-bud opacities
 - CD4 < 200: Primary pattern
 - Consolidation
 - □ Lymphadenopathy (peripheral enhancement, central necrosis)

Pleural effusion, empyema

□ Miliary nodules

- Very low CD4: Lack of immune response, minimal findings
 - Normal chest radiograph
 - □ Consolidation, ground-glass opacities, few tiny miliary nodules
- Nontuberculous mycobacterial infection:
 - Mycobacterium avium complex (MAC), Mycobacterium kansasii, CD4 < 50
 - Radiographic mimic of TB; miliary nodules uncommon
- Cryptococcus and other disseminated fungal infections (histoplasmosis, coccidioidomycosis), CD4 < 100
 - Nodules ± cavitation
 - Miliary nodules, lymphadenopathy
 - Cryptococcosis most common fungal pneumonia in HIV(+) patients
- Neoplasm
 - KS: ↓ incidence, mostly affects men, human herpes virus (HSV)-8, CD4 < 200,
 - Flame-shaped lesions: Ill-defined nodules surrounded by ground-glass opacity; along bronchovascular bundles
 - Interlobular septal thickening
 - Enhancing lymphadenopathy (mediastinal, hilar, axillary)
 - Hodgkin lymphoma: ↓ incidence, associated with Epstein-Barr virus, CD4 < 100, fever, night sweats, weight loss
 - Mediastinal and hilar lymphadenopathy
 - Solitary or multiple nodules
 - Consolidation
 - Lung cancer: ↑ risk due to altered immune function, any CD4 count
 - Pulmonary nodule or mass, adenocarcinoma is most common subtype
 - Lymphadenopathy
- Noninfectious, nonneoplastic conditions
- Lymphoid interstitial pneumonia (LIP):

Lymphoproliferative disorder, children > adults, any CD4 count

- Centrilobular, peribronchovascular nodules
- Ground-glass opacities, cysts
- Chronic lung disease
 - Bronchiectasis: More extensive and severe than expected with brief or no history of infection
 - Emphysema: Abnormal activity of cytotoxic T-cells, 15% of HIV(+) patients
 - Associated with smoking, inhalational and injected drugs
- Multicentric Castleman disease: Lymphoproliferative disorder associated with HSV-8, any CD4 count, more prevalent in ART era
 - Mediastinal, hilar, axillary lymphadenopathy ± enhancement
 - Peribronchovascular and interlobular septal thickening, nodules
 - Hepatosplenomegaly
- **Sarcoidosis**: ↑ incidence in era of ART, may relate to drug reaction or altered immune regulation
 - Perilymphatic micronodules, lymphadenopathy

- Cardiovascular complications
 - PH > 25 mm Hg with normal pulmonary wedge pressure;
 ≤ 15 mm Hg at right heart catheterization, any CD4 count: Enlarged pulmonary trunk, dilated right heart chambers
 - Cardiomyopathy: Cardiomegaly, pulmonary edema, pleural effusions
 - Premature atherosclerosis: Vascular calcification
- Immune reconstitution inflammatory syndrome (IRIS)
 Paradoxical clinical and imaging deterioration due to
 - recovery of immune function after initiation of ART
 - Risk factor: Low CD4 (< 50) and high viral load prior to ART initiation
 - Progression of underlying infections (common with mycobacterial infection) or neoplasm (KS, lymphoma) on imaging

Imaging Recommendations

- Best imaging tool
 - Radiography: Detection of complications and follow-up
 - CT: More sensitive and specific than radiography
 - Assessment of radiographically occult infection (PCP, TB)
 - Characterization of nonspecific radiographic findings
 - Planning or guidance of biopsy or drainage procedures
 - Staging of HIV-related neoplasms

DIFFERENTIAL DIAGNOSIS

Lymphadenopathy

- Diffusely enhancing
 - o KS
 - Castleman disease
- Peripherally enhancing with necrotic center
 - o TB
 - Nontuberculous mycobacterial infection
 - Fungal infection
- Soft tissue density
 - o Lymphoma
 - Lung cancer
 - o Generalized HIV lymphadenopathy
 - o Sarcoidosis

Lung Nodules

- Miliary nodules
- o TB
- Disseminated fungal infection
- Peribronchovascular nodules
 - o KS
 - o Lymphoma
 - o Sarcoidosis
- Macronodules > 1 cm
 - Lung cancer
 - Pulmonary lymphoma
 - Mycobacterial infection
 - Fungal infection
 - Septic emboli

Cysts

• PCP

• Lymphoid interstitial pneumonia

Consolidation

- Bacterial pneumonia
- TB
- Nontuberculous mycobacterial infection
- Fungal infection
- Lymphoma

Ground-Glass Opacities

- PCP
- Viral pneumonia
- Lymphoid interstitial pneumonia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Cough, fever
 - Abrupt onset (< 1 week): Bacterial pneumonia
 - Gradual onset (> 1 week): PCP, mycobacterial infection, neoplasm
 - o Weight loss
 - o Lymphadenopathy, weakness, malaise

Demographics

- Epidemiology
 - Spread through close contact with bodily fluids
 - Unsafe sex
 - Contaminated needles, IV drug use
 - Perinatal transmission from infected mother to child
 - Blood transfusion no longer common cause in developed countries
 - o 38 million people living with HIV worldwide in 2019

Natural History & Prognosis

- Marked reduction in morbidity and mortality with ART in developed countries
 - o Life expectancy: 20-50 years after HIV diagnosis
- Poor prognosis for patients without access to or noncompliant with ART
 Survival: 6-19 months after developing AIDS
 - Survival. 6-19 monuns arter developing

TreatmentART

 Prophylactic antibiotics (based on CD4 level) for PCP, toxoplasmosis, TB, nontuberculous mycobacterial infection

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Integrated management approach combines: Imaging pattern recognition, chronicity of symptoms, immune status, compliance with ART, and prophylactic antibiotics

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Diseases, and Vasculitis





(Left) PA chest radiograph of an HIV(+) 54-year-old woman with CD4 count < 200 shows a right upper lobe consolidation \blacksquare and mediastinal lymphadenopathy 🔁. (Right) Axial CECT of the same patient shows prevascular 😒 and right paratracheal lymphadenopathy with central necrosis 🖂. The imaging features of tuberculosis vary with CD4 count. HIV(+) adults with CD4 counts < 200 exhibit a primary pattern of infection that includes consolidation, necrotic lymphadenopathy, pleural effusion, and milliary nodules.





(Left) PA chest radiograph of a 30-year-old man with AIDS and Kaposi sarcoma shows bilateral irregular nodular opacities throughout both lungs. (Right) Axial CECT of the same patient shows bilateral irregular peribronchovascular nodules \square some of which exhibit ground-glass halos 🔁 and produce the so-called flameshaped lesions of Kaposi sarcoma, which typically occurs with CD4 counts < 200. Antiretroviral therapy has drastically reduced the incidence of Kaposi sarcoma, but mortality remains high.





(Left) Axial NECT of a 58-yearold-man with a longstanding history of HIV infection who presented with cough shows bilateral upper lobe bronchiectasis 🔁. (Right) Coronal NECT of the same patient confirms bilateral bronchiectasis 🔁. HIV(+) patients have a higher prevalence of bronchiectasis, and emphysema compared with the general population. This may relate to the increased rate of smoking and use of injected or inhalational drugs among HIV(+) patients, repetitive infection, &/or the virus itself.

Neutropenia

KEY FACTS

TERMINOLOGY

- Neutropenia: Absolute neutrophil count (ANC) of < 1,500/µL of blood
- Neutropenic fever (temperature > 38 °C) is common complication in cancer patients receiving chemotherapy

IMAGING

- Radiography
 - Often negative or nonspecific
- CT
 - Invasive pulmonary aspergillosis (IPA): Nodules with halo or air crescent sign
 - Mucormycosis: Solitary or multiple nodules, reversed halo sign
 - *Pneumocystis jirovecii* pneumonia (PCP): Bilateral ground-glass opacities
 - Viral pneumonia: Ground-glass opacities, consolidations, tree-in-bud opacities

PATHOLOGY

- Etiology
 - Neutropenia + nodular opacities
 - IPA
 - Mucormycosis
 - Septic emboli
 - Organizing pneumonia
 - Neutropenia + ground-glass opacities
 - PCP
 - Viral infection
 - Pulmonary hemorrhage
 - Pulmonary alveolar proteinosis (hematologic malignancy)

DIAGNOSTIC CHECKLIST

• Early imaging diagnosis of infection in febrile neutropenia is crucial for prompt and appropriate therapy

(Left) Axial CT of a 43-year-old patient with acute lymphoblastic leukemia and febrile neutropenia shows a mass-like consolidation 🔁 in the right upper lobe with a ground-glass opacity halo 🔁 that is highly suspicious for angioinvasive fungal infection. Biopsy confirmed invasive pulmonary aspergillosis. (Right) Axial CECT of the same patient obtained 12 weeks later shows extensive parenchymal cavitation 🖂 and intracavitary necrotic tissue 🔁. The presence of cavitation coincides with neutrophil recovery.





(Left) PA chest radiograph of 36-year-old patient 3 weeks after stem cell transplantation shows a right upper lobe masslike consolidation 🛃. Given the mass-like appearance of this lesion, fungal infection was suspected. (Right) Axial NECT of the same patient shows a right upper lobe mass \square that exhibits the reversed halo sign 🔁. Biopsy demonstrated mucormycosis. The reversed halo sign is an early sign of lung infarction, but is also seen in angioinvasive fungal infection in immunocompromised neutropenic patients.





Synonyms

• Granulocytopenia

Definitions

- Neutropenia
 - Neutropenia: Abnormally low level of neutrophils in blood
 - Neutrophils defend body against bacterial and fungal infection
 - Can be hereditary or acquired
 - Absolute neutrophil count (ANC) of < 1,500/µL of blood
 Severe neutropenia < 500/µL
 - Profound: < 100/µL
 - Neutropenic fever (temperature > 38°C): Common complication in cancer patients receiving chemotherapy
 - Neutropenia
 - After chemotherapy in solid organ cancer usually lasts
 5 days
 - After chemotherapy in hematologic malignancies usually lasts > 14 days
 - After high-dose chemotherapy and radiation prehematopoietic stem cell transplantation: 0-100 days after transplantation

IMAGING

General Concepts

- Chest radiography in febrile neutropenic patients
 - Low sensitivity even with respiratory symptoms
 Significant number of studies show nonspecific abnormalities
- Patients who received chemotherapy and present with fever are presumed neutropenic
- Lung infection may have polymicrobial etiology

Radiographic Findings

- Radiography
 - Ground-glass opacity
 - Consolidation
 - Lung nodule/mass: May exhibit cavitation
 - Reticular opacities
 - o Pleural effusion

CT Findings

- Invasive pulmonary aspergillosis (IPA)
 - **CT halo sign**: Central nodule or mass surrounded by ground-glass attenuation rim
 - Highly sensitive finding in early stage
 - Ground-glass opacity relates to angioinvasive nature of disease that produces perilesional hemorrhage
 - Empiric initiation of targeted antibiotic treatment for IPA at detection of CT halo sign in neutropenic patients improves survival
 - Reversed halo sign
 - Early sign of pulmonary infarct
 - Visualization of central ground-glass opacity surrounded by rim of consolidation
 - Air crescent sign: Cavity with intracavitary mass
 - Occurs later in course of IPA

- Coincident with resolution of neutropenia; favorable sign
- Central "mass" is due to necrotic lung, usually adherent to cavity wall, not gravity-dependent
- CTA of IPA
 - Interruption of pulmonary artery branch at border of focal lesion, nonvisualization of vessel within or peripheral to lesion
- o Airway-invasive aspergillosis
 - Centrilobular nodules
 - Bronchial wall thickening
 - Peribronchiolar ground-glass opacity or consolidation
 - Tracheobronchitis
- Pulmonary opacities may remain stable 1-2 weeks after initiation of appropriate treatment
 - Postulated immunological phenomenon due to recovery of neutrophil count
- Mucormycosis
 - Solitary or multiple nodules ± ground-glass halo
 - Reversed halo sign is more frequent in mucormycosis than in IPA
- Bacterial infection: Staphylococcus aureus, Streptococcus pneumoniae, Legionella pneumophila, Pseudomonas aeruginosa
 - o Pneumonia
 - Consolidations (segmental or lobar)
 - Pleural effusions
 - Small airway plugging and tree-in bud opacities
- Septic emboli
 - Multiple nodules ± cavitation
 - Peripheral and lower lobe distribution
- Pneumocystis jirovecii pneumonia (PCP)
 - o Bilateral ground-glass opacities
 - Interlobular septal thickening
 - Currently less frequent due to routine prophylaxis
 - o Pulmonary cysts
- Viral pneumonia: Cytomegalovirus, Respiratory syncytial virus, Adenovirus
- o Bilateral ground-glass opacities
- Consolidations
- Tree-in-bud opacities
- o Ill-defined centrilobular nodules
- Bronchial wall thickening
- Drug toxicity
 - General concepts
 - Many chemotherapeutic agents may induce neutropenia
 - Drug toxicity may produce variety of imaging abnormalities
 - Diffuse alveolar damage
 - Bilateral consolidations or ground-glass opacities
 - Organizing pneumonia
 - Patchy opacities with peribronchial and subpleural distribution and lower lobe predominance
 - Atoll or reversed halo sign
 - Central ground-glass opacity with rim of consolidation
 - Interstitial fibrosis: Usual interstitial pneumonia (UIP) or nonspecific interstitial pneumonia (NSIP) patterns
 - Subpleural reticular opacities

- Traction bronchiectasis
- Ground-glass opacities (NSIP)
- Honeycomb lung (UIP)

• Radiation pneumonitis

- Radiation &/or concurrent chemotherapy may cause neutropenia
- Geographic consolidations or ground-glass opacities in radiation port distribution

• Pulmonary hemorrhage

- Neutropenic patients may exhibit concurrent thrombocytopenia or coagulopathy
- o Hemoptysis
- Patchy or diffuse ground-glass opacities or consolidations

MR Findings

- IPA
 - Hypointense on T1WI
 - Hyperintense on T2WI
 - Uniform gadolinium enhancement during early stage
 - Peripheral gadolinium enhancement in late stage

Imaging Recommendations

- Best imaging tool
 - **Consider chest CT early in evaluation of febrile neutropenic patient** with normal or nonspecific chest radiographic findings
 - 50% of patients with normal radiographs have findings suggestive of pneumonia on CT
 - CT helps narrow differential diagnosis and guide workup and therapy

Image-Guided Biopsy

• CT-guided percutaneous needle aspiration or biopsy helpful in obtaining samples for pathologic diagnosis or microbiology culture

PATHOLOGY

General Features

- Etiology
 - Neutropenia + nodular opacities
 - IPA
 - Mucormycosis
 - Septic emboli
 - Organizing pneumonia
 - Neutropenia + ground-glass opacities
 - PCP
 - Viral infection
 - Pulmonary hemorrhage
 - Pulmonary alveolar proteinosis
 - Associated with hematologic malignancy
 - Inadequate or ineffective granulopoiesis
 - Aplastic anemia
 - Leukemia
 - Chemotherapy
 - Drug toxicity
 - Chloramphenicol
 - Sulfonamides
 - Chlorpromazine
 - Radiation

- o Accelerated removal or destruction of neutrophils
- Overwhelming bacterial or fungal infectionsSplenomegaly

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Malaise
 - o Chills
 - o Fever
- Other signs/symptoms
 - o Weakness
 - o Ulcerating, necrotizing lesions of oral cavity
- Fungitell [(1→3)-β-D-Glucan]: Elevated in angio- or bronchial invasive aspergillosis and PCP pneumonia, but not in mucormycosis; not elevated in bacterial or viral infections
- **Procalcitonin**: Elevated in bacterial infections but not in viral or fungal infections; higher levels correlate with sepsis

Demographics

- Epidemiology
 - Incidence of pneumonia in neutropenic cancer patients: 17-24%
 - Bacterial infection responsible for ~ 90% of infections in early neutropenia

Natural History & Prognosis

- Infection-related mortality rate: Up to 38%
- Survival rates in patients with IPA undergoing chemotherapy and bone marrow or stem cell transplant: < 10%
- Viral pneumonia: Mortality of 50% in neutropenic host

Treatment

- Control of infections
 - Antibiotics
 - Surgical drainage/resection
- Removal of offending drug
- Recombinant hematopoietic growth factors
 - o Granulocyte colony-stimulating factor (G-CSF)
 - Granulocyte-macrophage colony-stimulating factor (GM-CSF)

DIAGNOSTIC CHECKLIST

Consider

• Early imaging diagnosis of opportunistic infections in febrile neutropenic patients is crucial for appropriate antimicrobial therapy

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Neutropenia





(Left) PA chest radiograph of a 62-year-old patient with febrile neutropenia status post bone marrow transplantation shows a dense area of consolidation 🛃 in the superior segment of the left lower lobe. (Right) Axial NECT of the same patient shows a mass-like consolidation in the left lower lobe 🔁. Bronchoalveolar lavage fluid sampled with bronchoscopy showed Staphylococcus aureus. Neutropenia is a major predisposing factor for bacterial infections, including hospital-acquired infections.





(Left) Axial CECT of a 57-yearold febrile neutropenic patient with Pneumocystis jirovecii pneumonia shows characteristic subtle bilateral ground-glass attenuation ᠫ and thick interlobular septa (crazy-paving pattern). (Right) Coronal CECT of the same patient confirms ground-glass opacities 🔁 and underlying thick interlobular septa. Pneumocystis jirovecii was previously a frequent cause of infection in neutropenic patients, but is currently less common because of the routine use of prophylactic treatment.





(Left) Axial CECT of a 67-yearold febrile neutropenic patient with respiratory syncytial virus (RSV) pneumonia shows treein-bud *⊡* and ground-glass opacities 🔁. RSV and cytomegalovirus are common causes of viral infection in patients with neutropenic fever. (Right) Axial CECT of a 63-year-old neutropenic and thrombocytopenic patient who developed hemoptysis shows ground-glass opacities 🔁 in the right lung. Bronchoalveolar lavage showed macrophages with hemosiderin consistent with pulmonary hemorrhage.

KEY FACTS

TERMINOLOGY

- Idiopathic pulmonary hemorrhage
- Recurrent diffuse alveolar hemorrhage without underlying cause; diagnosis of exclusion
- **Clinical Triad**: Hemoptysis, iron deficiency anemia, bilateral airspace opacities

IMAGING

- Radiography
 - Bilateral airspace disease
- CT/HRCT
 - Multifocal bilateral ground-glass opacities
 - Temporal progression to pulmonary fibrosis

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary edema
- Pneumonia
- Autoimmune disorders and systemic vasculitides
- Acute respiratory distress syndrome

PATHOLOGY

- Lungs are diffusely brown in color
- Hemosiderin-laden alveolar macrophages
- Absence of vasculitis, capillaritis, granulomas, or immunoglobulin deposition

CLINICAL ISSUES

- Symptoms/signs
 - o Dyspnea, nonproductive cough, hemoptysis
 - Dyspnea on exertion and fatigue
 - 80% of cases in children, typically < 10 years
- 25% subsequently develop autoimmune disorder
- Treatment
 - o Glucocorticoids, rituximab
 - Lung transplantation for select patients

DIAGNOSTIC CHECKLIST

• Consider IPH in patient with hemoptysis, anemia, and bilateral airspace disease without underlying cause

(Left) PA chest radiograph of a 32-year-old woman with idiopathic pulmonary hemorrhage manifesting with dyspnea and daily hemoptysis shows faint mid and lower lung zone opacities and basilar linear fibrosis. (Right) Coronal NECT of the same patient shows diffusely distributed centrilobular ground-glass nodules, subtle mid to lower lung zone reticulations, and scattered cystic spaces. Oxidative stress of recurrent alveolar hemorrhage and free iron deposition leads to development of alveolar and parenchymal fibrosis.





(Left) PA chest radiograph of a 16-year-old girl with dyspnea on exertion and nonproductive cough shows diffuse, faint reticulonodular opacities in the absence of cardiomegaly or pleural effusions. (Right) Axial CECT of the same patient shows diffuse alveolar ground-glass opacities with areas of reticulation and scattered cystic spaces. Idiopathic pulmonary hemorrhage is a diagnosis of exclusion, as many systemic vasculitides and autoimmune processes may produce recurrent alveolar hemorrhage.





Abbreviations

• Idiopathic pulmonary hemosiderosis (IPH)

Synonyms

• Idiopathic pulmonary hemorrhage

Definitions

• Recurrent alveolar hemorrhage without underlying cause

Clinical Triad

• Hemoptysis, iron deficiency anemia, bilateral airspace opacities

IMAGING

General Features

- Best diagnostic clue
 - Bilateral airspace disease in patient with hemoptysis and iron deficiency anemia
- Location
- Mid to lower lung predominance; may be diffuse

Radiographic Findings

- Multifocal airspace disease
- Reticulonodular opacities

CT Findings

- HRCT
 - Multifocal ground-glass opacities: Centrilobular, geographic, diffuse
 - May progress to fibrosis: Reticulation, bronchiectasis, parenchymal cysts

Imaging Recommendations

- Best imaging tool
 - HRCT is imaging modality of choice

DIFFERENTIAL DIAGNOSIS

Pulmonary Edema

• Cardiomegaly, bilateral pleural effusions, bilateral interstitial and airspace opacities

Pneumonia

- Fever, productive cough, leukocytosis
- Focal or multifocal pulmonary consolidation

Goodpasture Syndrome

- Autoimmune IgG antibodies to alveolar and glomerular basement membranes
- May result in hemorrhagic interstitial pneumonitis characterized by diffuse airspace disease

Granulomatosis With Polyangiitis

- Systemic vasculitis often involving kidneys; c-ANCA
- Affected patients may present with airspace disease secondary to pulmonary hemorrhage

Acute Respiratory Distress Syndrome

- Typically known cause of lung injury (infection, trauma, inhalational injury)
- Diffuse bilateral airspace disease

Systemic Lupus Erythematosus

- Autoimmune disorder with multiorgan involvement
- Recurrent alveolar hemorrhage resulting from capillaritis

PATHOLOGY

General Features

- Etiology
 - Unknown; may relate to consanguinity or environmental factors
 - **Diagnosis of exclusion**: Many systemic vasculitides result in alveolar hemorrhage and hemosiderosis
- Associated abnormalities
 - Lane-Hamilton syndrome = pulmonary hemosiderosis and celiac disease

Gross Pathologic & Surgical Features

• Lungs are diffusely brown in color

Microscopic Features

- Hemosiderin-laden alveolar macrophages
- Free iron leads to oxidative stress on alveoli resulting in fibrosis
- Swollen vacuolated endothelial cells
- Absence of vasculitis, capillaritis, granulomas, or immunoglobulin deposition (which would indicate nonidiopathic etiology)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Dyspnea and nonproductive cough → hemoptysis
 - Dysphea and nonproductive cough –
 Dysphea on exertion and fatigue
 - Iron deficiency anemia
 - Precapillary pulmonary hypertension

Demographics

- Age
 - 80% of cases in **children**, typically < 10 years
- Epidemiology
 - Exceedingly rare: < 1 per million

Natural History & Prognosis

- 25% subsequently develop autoimmune disorder
- Massive acute pulmonary hemorrhage or chronic pulmonary fibrosis are most frequent causes of death

Treatment

- Glucocorticoids, rituximab, cyclophosphamide
- Lung transplantation for select patients
 - IPH may recur following lung transplantation

DIAGNOSTIC CHECKLIST

Consider

• IPH in patient with hemoptysis, anemia, and bilateral airspace disease of unknown etiology

- Saha BK: Idiopathic pulmonary hemosiderosis: a state of the art review. Respir Med. 176:106234, 2020
- Zhang Y et al: Clinical characteristics and prognosis of idiopathic pulmonary hemosiderosis in pediatric patients. J Int Med Res. 47(1):293-302, 2019

Goodpasture Syndrome

KEY FACTS

TERMINOLOGY

- Anti-glomerular basement membrane (Anti-GBM) disease
- Combined crescentic glomerulonephritis and diffuse alveolar hemorrhage (DAH) caused by anti-GBM antibodies
- Small vessel vasculitis with immune complex formation (type II hypersensitivity reaction)

IMAGING

- Acute: Onset < 24 hours
 - Bilateral, chiefly central opacities sparing lung periphery
- Subacute
 - Ground-glass opacities and consolidations with interlobular septal thickening
 - Pulmonary opacities resolve within 2 weeks
- Recurrent/chronic
- Pulmonary fibrosis with reticulation and architectural distortion
- Pleural effusion rare

TOP DIFFERENTIAL DIAGNOSES

- ANCA-associated vasculitides
- Systemic lupus erythematosus vasculitis
- Noncardiogenic pulmonary edema

CLINICAL ISSUES

- Symptoms/signs
 - Acute dyspnea, hemoptysis (90% of patients)
 - o Glomerulonephritis, hematuria, anemia (80-90%)
 - o Renal and lung involvement (40-60%)
- Bimodal distribution: Young men, older women
- Timely diagnosis and prompt treatment essential

DIAGNOSTIC CHECKLIST

- Consider Goodpasture syndrome in symptomatic young adult with new-onset renal disease and imaging findings suggestive of pulmonary hemorrhage
- Evolution of pulmonary opacities is important for diagnosis of pulmonary hemorrhage

(Left) AP chest radiograph of a young adult with Goodpasture syndrome, hemoptysis, respiratory failure, and renal failure shows extensive bilateral hazy ill-defined opacities that reflect diffuse alveolar hemorrhage, confirmed by bronchoscopic evaluation. (Right) Composite image with axial CECT of the same patient shows diffuse centrilobular ground-glass nodules and scattered nodular consolidations. A left-sided $pneumothorax \square developed$ after intubation. In this acute setting, thickened septal lines are absent.





(Left) AP chest radiograph of a young adult with Goodpasture syndrome and a one-week history of respiratory failure shows fluffy central peribronchovascular opacities on a background of widespread tiny nodules and reticular lines. (Right) Composite image with axial CECT of the same patient shows multifocal bilateral consolidations on a background of diffuse groundglass opacity, with lobular $sparing \supseteq$ and scatteredthickened interlobular septa \supseteq compatible with subacute pulmonary hemorrhage.





Abbreviations

- Anti-glomerular basement membrane (anti-GBM) disease
- Goodpasture disease

Definitions

- Goodpasture syndrome: Coexistent glomerulonephritis and diffuse alveolar hemorrhage (DAH)
 - Antibodies directed against glomerular basement membranes; cross reaction with alveolar basement membranes
 - Anti-GBM disease: Circulating antiglomerular basement membrane antibodies, glomerulonephritis, and DAH
- Pulmonary-renal syndromes: Acute glomerulonephritis and alveolar capillaritis (DAH)
 - Anti-GBM disease, granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), systemic lupus erythematosus (SLE)

IMAGING

General Features

- Best diagnostic clue
 - Acute onset of bilateral ground-glass opacities and consolidations in patient with hemoptysis and renal disease

Radiographic Findings

- Radiographic findings vary depending on chronicity of hemorrhagic episodes
 - Acute: Onset < 24 hours
 - Bilateral opacities, often airway-centered
 - Usually perihilar and basilar, with peripheral sparing
 - Unilateral or focal involvement rare

• Subacute

- Opacities gradually decrease after single episode of hemorrhage
- Pulmonary opacities often resolve within 2 weeks
- Recurrent/chronic
 - Architectural distortion from interstitial fibrosis
- Reticular opacities in areas of prior hemorrhage
- Pleural effusion rare; suggests alternative diagnosis

CT Findings

- HRCT
 - Acute
 - Bilateral patchy, diffuse, or centrilobular ground-glass opacities and consolidations
 - Interlobular septal thickening not evident
 - Distribution often central with peripheral sparing; findings more widespread/diffuse in severe disease
 - Subacute
 - Ground-glass opacities and consolidations with interlobular septal thickening, intralobular lines, ± lobular sparing
 - ± mediastinal and hilar lymphadenopathy
 - Opacities often resolve in 2-3 weeks with treatment

• Recurrent/chronic

- Pulmonary fibrosis: Reticular opacities, traction bronchiectasis, ± mild honeycombing, volume loss
- Lobular sparing may be present

MR Findings

- Role of MR in Goodpasture syndrome not defined
- Low signal in lungs secondary to paramagnetic properties of hemosiderin
 - Pulmonary edema and pneumonia demonstrate high signal intensity on T2WI
- Low signal intensity in reticuloendothelial system: Important clue for hemosiderosis

Imaging Recommendations

- Best imaging tool
 - CT for characterization of distribution and disease extent

DIFFERENTIAL DIAGNOSIS

Granulomatosis With Polyangiitis

- Systemic vasculitis, typically affects kidneys, upper and lower respiratory tracts
- Mass-like consolidations and nodules, ± cavitation
 - Less common: Acute diffuse bilateral consolidations, often early &/or in younger patients
 - DAH in GPA reflects capillaritis
- c-ANCA positive in 85-98% of patients with active disease
- Systemic symptoms: Fever, weight loss, arthralgias, peripheral neuropathy

Microscopic Polyangiitis

- Necrotizing vasculitis involving small vessels (arterioles, venules, capillaries); no immune complexes
- Involvement: Kidneys > 95%, lungs ~ 50%
- Onset may be rapid with fever, myalgias, arthralgias, and ear, nose, or throat symptoms
 - Extensive bilateral consolidations common; usually with lower lobe distribution
- > 80% with positive ANCA, usually p-ANCA

Eosinophilic Granulomatosis With Polyangiitis

- Multisystem disorder: Asthma/history of allergy, peripheral blood eosinophilia, systemic vasculitis
- Multifocal and evolving consolidations: 1 of 6 diagnostic criteria
 - Consolidations often surrounded by ground-glass opacity; peribronchovascular or peripheral
- Also known as Churg-Strauss Syndrome

Systemic Lupus Erythematosus

- Immune complex-mediated small vessel vasculitis
- Most common collagen vascular disease associated with DAH; only 2% of SLE patients develop DAH
 - May present with DAH closely resembling anti-GBM disease or idiopathic pulmonary hemorrhage
 - Renal involvement in 60-90%
- Pleural effusion in 50% of cases (rare in Goodpasture)

Noncardiogenic Pulmonary Edema

- Pleural effusion common, hemoptysis rare
- Common: Acute onset of diffuse ground-glass opacities and consolidations
- Associated with toxic exposures (including cocaine)

Idiopathic Pulmonary Hemosiderosis

• Diffuse pulmonary hemorrhage syndrome without identifiable cause

- Recurrent episodes of diffuse pulmonary hemorrhage, usually in young patients (< 10 years)
- Hemoptysis very common, may be quite severe
- No renal involvement; ANCAs and antibasement membrane antibodies absent

PATHOLOGY

General Features

- Etiology
 - Type II hypersensitivity reaction to glomerular basement membrane; also affects alveolar basement membrane
 - Anti-GBM antibodies detected by serum radioimmunoassay in > 90%
 - Antibodies directed at type IV collagen α-3 chain
 - Attack type IV collagen in glomerular and alveolar basement membranes
 - Suspected environmental factors for lung involvement: Smoking, hydrocarbon aerosols, drugs (e.g., alemtuzumab for multiple sclerosis), respiratory infection (e.g., Influenza A)
- Genetics
 - Anti-GBM disease reported in siblings, identical twins, and cousins; supports genetic predisposition
 - Strong association (80%) with class II human leukocyte antigen (HLA-DR2)
- Associated abnormalities
 - 20-35% have positive serum c- or p-ANCA, in addition to anti-GBM

Microscopic Features

- Renal biopsy demonstrates linear deposition of IgG and C3 along glomerular basement membranes by immunofluorescence
 - Renal biopsy is most common method to establish diagnosis
- Lung biopsy not common, but similar findings of linear IgG found along alveolar basement membranes
 - Intraalveolar erythrocytes, fibrin, hemosiderin-laden macrophages
 - Patchy neutrophilic capillaritis, but no extensive vasculitis
 - Interlobular septa expanded by hemosiderin-laden macrophages

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Majority (80-90%) present with rapidly progressive glomerulonephritis
 - o Renal and lung involvement in 40-60%
 - Acute onset cough (55%), dyspnea (65%), hemoptysis (90%)
 - Renal involvement alone in 20-40%
 - Lung involvement alone in < 10% (pulmonary hemorrhage)
 - o Iron deficiency anemia (> 90%)
- Other signs/symptoms
 - History of recent viral illness, smoking, drug or hydrocarbon exposure in some patients

Demographics

• Age

- Bimodal distribution
 - Most common: Young white men with lung and renal disease, peak: 20-30 years of age
 - Less common: Older women (6th-7th decades), predominant or isolated renal involvement
- Sex
 - o M:F at least 2:1; may be as high as 9:1 in younger patients
- Epidemiology
 Rare, occurs in 0.5-1.6 people/million/year

Natural History & Prognosis

- Diagnosis made by serum enzyme-linked immunosorbent assay (ELISA) or radioimmunoassay for anti-GBM antibodies
 - Serologic tests are performed urgently; highly sensitive (~ 95%) and specific (~ 97%)
 - If serologic tests negative (~ 10%), kidney biopsy with immunofluorescence staining
- DAH may be confirmed by bronchoscopy using serial lavage aliquots (not in critical patients)
- Usually acute onset and rapidly progressive
- Recurrent pulmonary hemorrhage
 - May lead to pulmonary hypertension, lung organization, pulmonary fibrosis
- Progressive renal regurgitation common; determines long-term prognosis
- Prompt therapy can produce rapid remission of both lung and renal disease
- Untreated Goodpasture syndrome often has fulminant course (> 90% fatal)

Treatment

- Urgent plasmapheresis to remove circulating antibodies
- Immediate high-dose corticosteroids and cyclophosphamide
- With treatment, > 90% recovery of lung hemorrhage and renal function; relapse uncommon
- End-stage kidney disease may require renal transplant

DIAGNOSTIC CHECKLIST

Consider

• Goodpasture syndrome in symptomatic young adult with renal disease and imaging findings of pulmonary hemorrhage

Image Interpretation Pearls

• Evolution of pulmonary opacities is important for diagnosis of pulmonary hemorrhage

- 1. Reisman S et al: A review of clinical and imaging features of diffuse pulmonary hemorrhage. AJR Am J Roentgenol. 1-10, 2021
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- Hellmark T et al: Diagnosis and classification of Goodpasture's disease (anti-GBM). J Autoimmun. 48-49:108-12, 2014
- Lichtenberger JP 3rd et al: Diffuse pulmonary hemorrhage: clues to the diagnosis. Curr Probl Diagn Radiol. 43(3):128-39, 2014

Goodpasture Syndrome





(Left) Composite image with axial CECT of a young adult with acute dyspnea and renal failure shows non-uniform ground-glass opacities in all five lobes. Occasionally, asymmetric patterns of lung opacity are found at presentation. (Right) Graphic shows diffuse bilateral consolidations with relative sparing of the peripheral and basilar lung parenchyma near the costophrenic angles, which are characteristic findings of Goodpasture syndrome.





(Left) PA chest radiograph of a patient with Goodpasture syndrome and cough shows patchy airspace disease ≥ in the right lower lung zone. (Right) Axial CECT of the same patient shows patchy groundglass and reticular opacities, consistent with subacute pulmonary hemorrhage. Pulmonary hemorrhage in Goodpasture syndrome is usually bilateral, but can be predominantly unilateral, as in this case.





(Left) PA chest radiograph of a patient with Goodpasture . syndrome and acute hemoptysis shows bilateral patchy airspace disease 🛃 representing pulmonary hemorrhage. The distribution is central, with sparing of the lung bases and apices. (Right) Axial HRCT of a patient with Goodpasture syndrome shows bilateral centrilobular groundglass opacities and no pleural effusions. Bronchoscopy demonstrated blood in the lavage fluid, and renal biopsy confirmed the diagnosis of anti-glomerular basement membrane disease.

KEY FACTS

TERMINOLOGY

- Granulomatosis with polyangiitis (GPA): Multisystem necrotizing granulomatous vasculitis of small to medium-sized vessels
- Upper respiratory tract, pulmonary, and renal involvement

IMAGING

- Radiography
 - Multiple lung nodules/masses ± cavitation
 - o Multifocal consolidations, may represent hemorrhage
- CT
 - Ground-glass opacity from hemorrhage
 - o Multifocal lung nodules/masses/consolidations
 - Cavitation more common in larger nodules
 - Air-fluid levels suggest secondary infection
 - Wedge-shaped peripheral opacities
 - o Halo sign, reversed halo sign, feeding vessel sign
 - Pulmonary fibrosis may occur

TOP DIFFERENTIAL DIAGNOSES

- Hematogenous metastases
- Septic emboli
- Lung abscess

CLINICAL ISSUES

- Symptoms/signs of bronchopulmonary disease: Cough, hemoptysis, dyspnea, chest pain
- Precedent upper airway inflammation/stenosis typical
- Laboratory: Cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA) positive in 90% with active GPA
- Diagnosis: Nasal, paranasal sinus, lung, or renal biopsy
- Treatment: Corticosteroids, cyclophosphamide, rituximab
 - Remission in ~ 90% with treatment

DIAGNOSTIC CHECKLIST

 Consider GPA in patients with multiple cavitary lung nodules or masses, and in patients who present with pulmonary hemorrhage

(Left) PA chest radiograph of a 42-year-old man with granulomatosis with polyangiitis shows bilateral cavitary lung masses 🖾. (Used with permission from AIRP.) (Right) Composite image with axial CECT of the same patient confirms an irregularly thickwalled cavitary mass \bowtie in the right lung and a thick-walled left upper lobe spherical cavitary nodule 🔁. Reactive lymphadenopathy is not present, and occurs in only 20% of affected patients. (Used with permission from AIRP.)





(Left) AP chest radiograph of an adult patient with hemoptysis, respiratory failure, and granulomatosis with polyangiitis shows widespread bilateral heterogeneous opacities, consistent with alveolar hemorrhage related to capillaritis and confirmed on bronchoscopy. (Right) Coronal NECT of the same patient confirms multilobar bilateral upper lung zone predominant consolidations with some subpleural sparing. Severe pulmonary hemorrhage may produce confluent mass-like consolidations, as in this case.





Abbreviations

• Wegener granulomatosis: Term no longer in use

Synonyms

• Granulomatosis and polyangiitis (GPA)

Definitions

- Multisystem necrotizing granulomatous vasculitis of small to medium-sized blood vessels (arteries, capillaries, veins)
- Idiopathic ANCA-associated vasculitis, likely autoimmune
- Upper respiratory tract, pulmonary, and renal involvement

IMAGING

General Features

- Best diagnostic clue
- Multiple cavitary lung nodules or massesLocation
- Bilateral; no zonal predilection
- Size
 - Range: Few mm-10 cm
- o Most lesions 2-4 cm
- Morphology
 - Nodules and masses ± cavitation
 - Mass-like consolidations ± cavitation
 - Ground glass opacities, septal lines

Radiographic Findings

- Radiography
 - Radiographs may be normal (20%)
 - Multiple nodules or masses
 - 40-70% of patients
 - Cavitation more common in larger nodules
 - □ Present in up to 50% of patients
 - □ 25% of nodules > 2 cm
 - Walls of variable thickness, contour
 - Air-fluid levels unusual; suggest infection

$\circ~$ Ground-glass opacities and consolidations

- Secondary to pulmonary hemorrhage, infarction, organizing pneumonia
- Wedge-shaped peripheral consolidations
- Central necrosis may be present
- May evolve into cavitary consolidations
- Often initially characterized as pneumonia; does not resolve with treatment
- Less common manifestations
 - Atelectasis
 - Reticular opacities
- Radiographs used to monitor response to treatment
 - Findings suggestive of relapse/recurrence
 - Increase in size &/or number of parenchymal findings
 - Findings suggestive of favorable response/improvement
 - Decrease in size of nodules/masses
 - Wall thinning of cavitary lesions

CT Findings

- Pulmonary nodules or masses (90%)
 - Multiple, bilateral (70%); sharp or poorly-defined margins
 - Nodules: Smooth or spiculated margins

- Masses: Sharp or ill-defined contours
- Air bronchograms often evident
- o Wedge-shaped peripheral consolidations (~ 70%)
- Cavitation: Up to 50% of larger nodules (> 2cm)
 Cavitary lesions initially irregularly thick-walled

Diseases, and Vasculitis

Connective Tissue Disorders, Immunological

615

- Wall thinning with treatment
- Air-fluid levels unusual; suggest infection
- Ground-glass opacity
 - Diffuse alveolar hemorrhage (10%)
 - Diffuse or patchy, ± subpleural sparing
 - Thick interlobular septa
 - May coalesce into hemorrhagic consolidations
 - Mosaic attenuation
 - Likely due to variations in regional perfusion
 - Inflammation: Superimposed infection or drug-related toxicity
- Halo sign
 - Ground-glass opacity surrounding nodules/consolidations: Hemorrhage
- Reversed halo sign
 - Dense rim of consolidation surrounding central groundglass opacity
 - Lung organization marginating area of pulmonary hemorrhage
 - Organizing pneumonia evolving from prior consolidation

• Feeding vessel sign

- Pulmonary artery appears to enter nodule/mass
- Pulmonary fibrosis
 - Subpleural reticular opacities, traction bronchiectasis, honeycomb lung
 - o ~15-20% of cases of GPA; may increase mortality risk
- Other pulmonary abnormalities
 - Parenchymal bands
 - o Atelectasis (lobar, segmental, subsegmental)
 - Septal thickening
- Tracheobronchial disease
 - Subglottic stenosis (up to 90%)
 - Tracheal wall thickening, ulceration, stenosis (16-23%)
 - Bronchial wall thickening (40-73%), multifocal ectasia,
- stenosis
- Pleural abnormalities
 - Pleural effusion is most common (often exudative)
- Mediastinal lymphadenopathy
 - Up to 20% of cases
 - Always concomitant with pulmonary abnormalities

Nuclear Medicine Findings

- Ga-67 scintigraphy
 - Lesions are typically gallium-avid
 - May be used to monitor disease activity

Imaging Recommendations

- Best imaging tool
 - Radiography and CT used to monitor response to treatment

DIFFERENTIAL DIAGNOSIS

Hematogenous Metastases

• Multiple bilateral pulmonary nodules or masses

- Hemorrhagic metastases (± surrounding ground-glass opacity): Renal cell carcinoma, melanoma, angiosarcoma, choriocarcinoma
- Squamous cell carcinoma, sarcomas, and adenocarcinomas may cavitate

Septic Emboli

- Poorly-defined angiocentric pulmonary nodules or masses
- Varying degrees of cavitation
- Endocarditis, bacteremia, or line infection

Lung Abscess

- Singular cavitary lung mass ± air-fluid levels
- ± adjacent consolidation or ground-glass opacity
- Aspiration, necrotizing, post-obstructive pneumonia

PATHOLOGY

General Features

- Etiology
 - Autoimmune syndrome of unknown etiology
 - Lung most commonly affected (50-90%)
 - o Paranasal sinuses (91%); Kidneys (85%)

Gross Pathologic & Surgical Features

- Gray-white or red-brown solid or necrotic-appearing nodules
 - Multiple lesions typical, often centered on bronchovascular bundles
 - Scattered consolidations (organizing pneumonia)
 - Diffuse or limited hemorrhage, even in absence of nodules/masses

Microscopic Features

- Necrotizing vasculitis
 - Variably involves arteries, veins, capillaries
 - Medial layer: Fibrinoid necrosis, microabscesses, scattered multinucleated giant cells
 - o Microabscess: Admixed neutrophils and histiocytes
 - Destruction of collagen fibers and elastic laminae
- Necrotizing granulomatous inflammation
 - o Variably involves lung, airways, pleura, vessels
 - Loose and palisading granulomas with inflammatory cell infiltrates
 - Microabscesses in lung and walls of large and small airways
 - Lung geographic necrosis with irregular/undulating margins

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Classic triad (original description)
 - Upper airway disease, lower respiratory tract involvement, and glomerulonephritis
 - Most common symptoms related to upper airway involvement (70-100%)
 - Sinusitis, otitis, rhinitis, oral, and nasal ulcers, saddlenose deformity, subglottic stenosis
 - Variable onset of symptoms related to bronchopulmonary involvement
 - Cough, fever, dyspnea, hemoptysis, chest pain

- Constitutional symptoms (50%): Arthralgias, fever, weight loss
- Other signs/symptoms
 - Renal disease in 40% at presentation, ~ 85% within 2 years
 - o Sensorimotor neuropathy (~ 33%)
 - o Cardiac involvement < 30%, often subclinical
 - Pericarditis, supraventricular arrhythmias; most common manifestations
 - Skin (10-50%), ocular (14-60%), gastrointestinal tract (5-11%) involvement
 - o \uparrow risk with a-1-antitrypsin deficiency
- Laboratory findings
 - $\circ~$ ~ 90% ANCA positivity in active GPA, ~ 50% positivity in remission
 - Cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA)
 - Detected by indirect immunofluorescence
 - Levels of c-ANCA correlate with disease activity
 Anemia (from diffuse alveolar hemorrhage or renal disease)

Demographics

- Age
 - Peak incidence: 4th-6th decades
- Sex
 - \circ M = F
- Epidemiology
- Incidence 2-10/million persons in Europe, < 1/million in USA

Diagnosis

• Nasal, paranasal sinus, lung, or renal biopsy

Treatment

- Immunosuppressive drugs to induce remission
 Glucocorticoids and cyclophosphamide
- Targeted therapy: Rituximab (others under investigation)

Natural History & Prognosis

- Nodules/masses increase in size and number with disease progression
- Remission rate ~ 90% with treatment; Relapses common
- Mean 5-year survival rate: 90-95%
 - Renal failure most common cause of death in untreated patients

DIAGNOSTIC CHECKLIST

Consider

• GPA in patients with multiple cavitary lung nodules or masses

Image Interpretation Pearls

• Pulmonary hemorrhage may be initial manifestation of GPA

- 1. Almaani S et al: ANCA-associated vasculitis: an update. J Clin Med. 10(7), 2021
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- Broncano J et al: CT and MR imaging of cardiothoracic vasculitis. Radiographics. 38(4):997-1021, 2018





(Left) Composite image with axial NECT of a patient with granulomatosis with polyangiitis shows central nodular bronchial wall localized right lower lobe bronchial wall abnormalities \blacksquare associated with segmental atelectasis. (Right) Axial CECT of a patient with granulomatosis with polyangiitis shows bilateral lower lobe mass-like lesions that exhibit of the CT halo sign ■. Note the left lower lobe subpleural wedge-shaped consolidation 🔁.





(Left) Axial CECT of patient with granulomatosis with polyangiitis shows bilateral consolidations with air bronchograms ⊡, which may represent hemorrhage, infarction, organizing pneumonia, &/or superimposed pneumonia. (Right) Axial CECT of patient with granulomatosis with polyangiitis shows a right perihilar consolidation, surrounding ground-glass opacity, and bilateral small lung nodules, one of which exhibits the feeding vessel sign Cround-glass opacity reflects alveolar hemorrhage.





(Left) Axial NECT of a patient with granulomatosis with polyangiitis shows multifocal nodular lesions with central ground-glass opacity and a rim of peripheral consolidation ➡, the so-called reversed halo sign, consistent with organizing pneumonia. (Right) Axial CECT of a patient with granulomatosis with polyangiitis and pulmonary interstitial fibrosis shows subpleural honeycombing \supseteq and a small right pneumothorax. Honeycombing *in this case may be related to* recurrent episodes of lung inflammation.

KEY FACTS

TERMINOLOGY

- Synonyms: Allergic granulomatosis, allergic granulomatous angiitis
- Formerly: Churg-Strauss syndrome

IMAGING

- Radiography
 - Peripheral, transient consolidation
 - Mimics eosinophilic pneumonia
- CT/HRCT
 - Peripheral consolidations and ground-glass opacities; often transient or migratory
 - Interlobular septal thickening
 - Pulmonary nodules and masses less common
 - Small pleural effusions
 - o Bronchial wall thickening/dilatation; air-trapping
- Cardiac CTA
 - o Cardiomegaly
 - Regional hypo- or akinesis; arteritis

TOP DIFFERENTIAL DIAGNOSES

- Eosinophilic pneumonia
- Allergic bronchopulmonary aspergillosis
- Pneumonia
- Granulomatosis with polyangiitis
- Cryptogenic organizing pneumonia
- Nonspecific interstitial pneumonia

PATHOLOGY

• Small vessel vasculitis

CLINICAL ISSUES

- Affected patients mostly middle-aged at diagnosis
- 5-year survival of 60-80%

DIAGNOSTIC CHECKLIST

 Consider eosinophilic granulomatosis and polyangiitis in patient with asthma, transient consolidations, and + p-ANCA

(Left) Axial HRCT of a patient with eosinophilic granulomatosis with polyangiitis asthma shows asymmetric bilateral ground $qlass opacities \rightarrow and$ consolidations *≥* with superimposed interlobular septal thickening. (Right) Coronal NECT of the same patient shows peripheral and upper lung predominant ground-glass opacities \supseteq , consolidations, interlobular septal thickening, and mild bronchial wall thickening $\mathbf{E}_{\mathbf{A}}$, suggestive of asthma-related large airways disease.





(Left) Axial HRCT of a patient with eosinophilic granulomatosis with polyangiitis shows groundglass opacities and consolidations \supseteq in the lung periphery. Associated interlobular septal thickening nay be related to eosinophilic infiltration or leftsided heart failure due to cardiac involvement. (Right) Axial CECT of a patient with eosinophilic granulomatosis with polyangiitis shows asymmetric bilateral patchy ground-glass opacities with more confluent involvement of the left lung.





Synonyms

- Allergic granulomatosis, allergic granulomatous angiitis
- Formerly: Churg-Strauss syndrome

IMAGING

General Features

- Best diagnostic clue
 - Transient, peripheral consolidation in patient with asthma and positive p-ANCA

Radiographic Findings

- Radiography
 - Peripheral, transient consolidations
 - Mimics eosinophilic pneumonia

CT Findings

- HRCT
 - Peripheral predominant consolidations and ground-glass opacities, often transient or migratory; no zonal predilection
 - Interlobular septal thickening either from heart failure or eosinophilic infiltration
 - Pulmonary nodules and masses less common; cavitation extremely rare as compared to polyangiitis and granulomatosis
 - o Bronchial wall thickening/dilatation, air-trapping
 - Small pleural effusions
- Cardiac gated CTA
 - Cardiomegaly
 - Regional hypo- or akinesis; arteritis

MR Findings

- Delayed enhancement
 - Abnormal focal delayed enhancement either representing scar or active inflammation
 - Myocardial infarct: Subendocardial to transmural delayed enhancement in coronary artery territory

DIFFERENTIAL DIAGNOSIS

Eosinophilic Pneumonia

- Simple: Fleeting, peripheral pulmonary opacities, selflimited, rapidly changing (days)
- Chronic: Fleeting peripheral consolidations and groundglass opacities, evolution over weeks, centripetal resolution

Allergic Bronchopulmonary Aspergillosis

- Central and upper lung predominant bronchiectasis and mucous plugging in patient with asthma
- Migratory pulmonary opacities may be seen before development of bronchiectasis

Pneumonia

- Focal or multifocal consolidation
- Cough, fever, chills, ↑ white blood cell count

Granulomatosis With Polyangiitis (GPA)

- Positive c-ANCA
- Cavitary nodules and masses > consolidations as compared to eosinophilic granulomatosis and polyangiitis

Organizing Pneumonia

- May have identical imaging appearance
- Reversed halo sign: Central ground-glass opacity with surrounding rim of consolidation

Nonspecific Interstitial Pneumonia (NSIP)

• Idiopathic or secondary to collagen vascular disorder

PATHOLOGY

General Features

- Etiology
 - o Small vessel vasculitis
 - Majority exhibit positive p-ANCA
- Associated abnormalities
 Typically asthma; marked peripheral eosinophilia

Microscopic Features

- 3 key findings, but unusual to find all 3 (20%)
 - o Vasculitis, necrotizing extravascular granulomas, tissue eosinophilia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Diagnostic criteria proposed by American College or
 - Rheumatology (4 of 6 required)
 - Asthma
 - Blood eosinophilia > 10%
 - Poly- or mononeuropathy
 - Migratory or fleeting pulmonary opacities
 - Paranasal sinus disease
 - Extravascular eosinophilia on biopsy
 - Cardiac involvement in up to 1/2 of patients: Myocardial infarction (coronary arteritis), myocarditis, heart failure, pericarditis
 - o Skin, renal, and gastrointestinal involvement

Demographics

- Epidemiology
 - Rare, 1-3 per million people
- Middle-aged patients; M > F

Natural History & Prognosis

- 5-year survival: 60-80%
- Cardiac involvement is leading cause of mortality

DIAGNOSTIC CHECKLIST

Consider

• Eosinophilic granulomatosis and polyangiitis in patient with asthma, transient, peripheral consolidation, and positive p-ANCA

- Trivioli G et al: Eosinophilic granulomatosis with polyangiitis: understanding the disease and its management. Rheumatology (Oxford). 59(Suppl 3):iii84-94, 2020
- 2. Furuta S et al: Update on eosinophilic granulomatosis with polyangiitis. Allergol Int. 68(4):430-6, 2019
- Nguyen Y et al: Eosinophilic granulomatosis with polyangiitis (Churg-Strauss). Semin Respir Crit Care Med. 39(4):471-81, 2018

Behçet Syndrome

KEY FACTS

TERMINOLOGY

- Idiopathic systemic necrotizing vasculitis
- Thoracic involvement may be severe and fatal
 Multiple vascular aneurysms ± luminal thrombus
 - Potential for aneurysm rupture, lung hemorrhage, infarcts, bronchial erosion, cardiac inflammation

IMAGING

- Radiography
 - Aneurysms of thoracic aorta and pulmonary arteries
- CT
 - Aortic aneurysm, pulmonary artery aneurysm ± thrombus
 - o Subpleural opacities (consider ischemia, infarction)o Ground-glass opacities, septal lines (hemorrhage)
- CT to evaluate extent/severity of vascular disease and pulmonary involvement
- MRA for delineation of aneurysms; MR for assessment of cardiac thrombus and inflammation

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary vasculitis
- Sarcoidosis
- Tuberculosis
- Hughes-Stovin syndrome

CLINICAL ISSUES

- Symptoms/signs
 - Clinical triad of oral and genital ulcers, uveitis
 - Thoracic symptoms (hemoptysis, chest pain, superior vena cava syndrome) prompt imaging evaluation
- Most prevalent in young men of eastern Mediterranean, Middle Eastern, or Asian descent
- Treatment: Immunosuppression

DIAGNOSTIC CHECKLIST

• Consider Behçet syndrome in patients with multiple pulmonary artery aneurysms, particularly young men of Mediterranean, Middle Eastern, or Asian ethnicity

(Left) Coronal CECT MIP reformatted image of a patient with hemoptysis and oral ulcers shows pulmonary artery aneurysms 🔁. Consolidations and groundglass opacities are consistent with pulmonary hemorrhage. (Right) Coronal CECT of the same patient after placement of endovascular coils 🔁 shows enlargement and thrombosis of the right lower lobe pulmonary artery aneurysm 🛃 and new sites of thrombosis 🛃. Surgical or endovascular intervention often flares vascular inflammation.





(Left) PA chest radiograph of the same patient after endovascular coil placement \bowtie confirms the abnormal lobular contour of the right hilum 🔁 and a right lower lobe mass \blacksquare , compatible with the documented pulmonary artery aneurysm. (Right) Coronal CECT of a patient with Behçet disease shows a lobulated left ventricular thrombus \mathbf{E} , a characteristic sign of cardiac involvement. Note multifocal subpleural cavitary consolidations 🔁 and nodules \blacksquare that suggest multifocal pulmonary infarcts.





Synonyms

• Behçet disease (BD), Silk Road disease

Definitions

- Idiopathic systemic necrotizing vasculitis of large, medium, and small vessels
 - Arteritis: Pulmonary arteries, aorta ± branches, coronaries (rare)
 - Thoracic manifestations: Vascular aneurysms ± in situ thrombosis

IMAGING

Radiographic Findings

- Aneurysmal dilatation of thoracic aorta, pulmonary arteries
- Multifocal opacities
- Pleural effusion

CT Findings

- Thoracic vasculature
 - Superior vena cava, inferior vena cava, subclavian and brachiocephalic veins: Venous in situ thrombosis ± obstruction
 - Pulmonary artery: Aneurysms ± thrombosis; most common cause of multifocal aneurysms
 - Pulmonary thromboembolism unusual (from extrapulmonary venous thrombus)
 - Aorta: Aneurysm, mural thickening, mobile thrombus
 - Brachiocephalic, subclavian arteries: Aneurysms/thrombosis
- Heart: Filling defect (thrombus), pericardial effusion
- Lungs
 - Subpleural wedge-shaped opacities; ischemia/infarction
 - Ground-glass opacities/interlobular septal thickening
 Consolidations ± nodules: Exclude infection
- Pleura: Nodules, effusions
- Mediastinum: Lymphadenopathy, inflammation, fibrosis

MR Findings

- MRA for delineation of aneurysms, occlusions, collaterals
- MR for identification of intracardiac thrombus, myocarditis, pericarditis

Imaging Recommendations

- Best imaging tool
 - CECT for optimal evaluation of disease extent and severity; vascular patency, pulmonary involvement
 - MRA for assessment of vascular disease; MR for assessment of cardiac disease

DIFFERENTIAL DIAGNOSIS

Pulmonary Vasculitis

- Takayasu arteritis: Large/medium size vessel arteritis
- Pulmonary hemorrhage syndromes
- Septic/mycotic vasculitis with pseudoaneurysms

Sarcoidosis

- Subpleural opacities may be similar; pulmonary artery aneurysms rare
- Calcified lymph nodes, upper lung zone distribution

Tuberculosis

• "Rasmussen" pulmonary artery aneurysms rare

Hughes-Stovin Syndrome

- Limited form of BD: No mucocutaneous features
- Pulmonary artery aneurysms, venous thrombophlebitis

PATHOLOGY

General Features

- Genetics
- Predisposition in patients with HLA-B51
- Associated abnormalities
 - o Superior vena cava syndromeo Abdominal aortic aneurysm (in 60%)

Gross Pathologic & Surgical Features

- Multiple saccular or fusiform pulmonary artery aneurysms
- Aneurysms of aorta, coronary arteries, subclavian artery

Microscopic Features

• Necrotizing lymphocytic vasculitis with in situ thrombi, intimal thickening, inflamed vasa vasorum, collateral vessels

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Aphthous ulcers, oral (> 95%) ± genital (> 65%)
 - Ocular lesions (~ 60%): Uveitis, retinal vasculitis, cataracts
 Superficial and deep venous thrombophlebitis
- Other signs/symptoms
 - Dyspnea, hemoptysis (may be massive), chest pain

Demographics

- Age
- o Mean: 20-30 years
- Sex
- M:F = 3:1 (with regional variations)
- Ethnicity
- Most patients of Middle Eastern or East Asian ethnicity
- Epidemiology
 - Most prevalent in eastern Mediterranean (Turkey)

Natural History & Prognosis

- Recurrence and remissions of multiorgan inflammation
- Pulmonary artery aneurysms: Risk of rupture, massive hemoptysis

Treatment

- Immunosuppression: Corticosteroids, cyclophosphamide
- Surgery may exacerbate vascular inflammation

DIAGNOSTIC CHECKLIST

Consider

• Behçet syndrome in patients with multiple pulmonary artery aneurysms, particularly young men of Middle Eastern or Asian ethnicity

SELECTED REFERENCES

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KEY FACTS

TERMINOLOGY

- Noncaseating granulomatous inflammation accompanied by granulomatous vasculitis and tissue necrosis
- Rare and controversial entity, possibly variant or later stage of nodular sarcoidosis

IMAGING

- Radiography
 - Bilateral pulmonary nodules and masses ± cavitation
 ± hilar lymphadenopathy
- CT
 - o Subpleural and peribronchovascular nodules/masseso Cavitation in up to 25%

TOP DIFFERENTIAL DIAGNOSES

- Granulomatous infection (mycobacterial, fungal)
- Granulomatosis with polyangiitis
- Hypersensitivity pneumonitis (subacute/chronic)
- Cavitary pulmonary metastases

PATHOLOGY

- Noncaseating sarcoid-like granulomas
- Granulomatous vasculitis
- Multifocal fibrinoid to widespread geographic necrosis

CLINICAL ISSUES

- Symptoms/signs
 - o Pleuritic chest pain, dyspnea
 - Cough, hemoptysis
 - o Fever, weight loss, fatigue
- Disease typically limited to thorax
- M:F = 1:2; onset: ~ 40-50 years of age
- Often regresses spontaneously or with corticosteroids

DIAGNOSTIC CHECKLIST

- Consider necrotizing sarcoid granulomatosis in patients with multiple cavitary nodules in perilymphatic distribution
- Fungal and mycobacterial infection must first be excluded

(Left) Composite image with axial NECT of a 52-year-old patient shows a spiculated right upper lobe nodule 🔁 with eccentric cavitation 🔁 surrounded by centrilobular rightarrow and subpleural ightarrowmicronodules. Biopsy confirmed necrotizing sarcoid granulomatosis. (Used with permission from AIRP.) (Right) Composite image with NECT of a 43-year-old patient with necrotizing sarcoid granulomatosis shows a left upper lobe peribronchovascular mass 🔿 and mediastinal lymphadenopathy 🔁.











Definitions

- Necrotizing sarcoid granulomatosis (NSG): Noncaseating granulomatous disease + lung necrosis and vasculitis
- Rare and controversial entity; possible variant or later stage of nodular sarcoidosis

IMAGING

General Features

- Best diagnostic clue
 - Multiple, bilateral lung nodules ± cavitation
 - Peribronchovascular and subpleural distribution

Radiographic Findings

- Single or multiple lung nodules and masses ± cavitation
- ± hilar lymphadenopathy

CT Findings

- Subpleural and peribronchovascular nodules/masses
 - Size: 0.5 5cm; cavitation (up to 25%); solitary nodule (up to 33%)
 - o Heterogeneous enhancement may reflect necrosis
- Miliary pattern may precede nodules/masses
- ± hilar lymphadenopathy (7-65%)

Nuclear Medicine Findings

- PET/CT
 - Evaluation of extent of disease and active lesions

Imaging Recommendations

- Best imaging tool
 - CT for optimal delineation of pulmonary disease

DIFFERENTIAL DIAGNOSIS

Infection

- Multifocal consolidations with necrosis/cavitation
- Tuberculosis and atypical mycobacterial infection
- Fungal infection (histoplasmosis, aspergillosis)

Granulomatosis With Polyangiitis (GPA)

- Multifocal cavitary nodules/masses (up to 50%)
- Systemic disease involving upper airways, kidneys, skin
- ANCA-positivity

Hypersensitivity Pneumonitis

- Fibrotic stage: Upper lobe architectural distortion
- Air-trapping ± peribronchovascular nodules
- Cavitation atypical
- Environmental/organic exposure

Pulmonary Metastases

- Multifocal lung nodules/masses; may be cavitary
- Cavitary metastases: Squamous cell carcinoma, sarcomas

PATHOLOGY

General Features

- Most likely variant of nodular (or classic) sarcoidosis
 - Shared histopathology, clinical, and radiologic manifestations

Gross Pathologic & Surgical Features

• Pale pulmonary nodules/masses with irregular margins ± satellite nodules

Microscopic Features

- Three defining histopathologic criteria
 - Granulomatous pneumonitis with sarcoid-like granulomas
 - Granulomatous vasculitis (muscular arteries and veins)
 - Zones of fibrinoid and infarct-like geographic necrosis
 - Perilymphatic distribution: Bronchovascular bundles, interlobular septa, subpleural
- Microbial stains and cultures to exclude fungi/acid-fast organisms

CLINICAL ISSUES

Presentation

٠

- Most common signs/symptoms
 - Pleuritic chest pain, dyspnea
 - o Cough, hemoptysis
 - o Fever, weight loss, fatigue
- Other signs/symptoms
 - Up to 25% of patients asymptomatic
 - o Extrapulmonary manifestations infrequent (< 15%)

Demographics

- Age
 - Range; 3rd to 7th decades; typically 40-50 years of age
- Sex
 M:F = 1:2

Natural History & Prognosis

- Diagnosis requires excisional biopsy
- Clinical course usually indolent
- Some lesions may regress spontaneously

Treatment

- Antituberculous therapy often instituted until infection excluded
- Corticosteroid therapy effective; up to 25% relapse

DIAGNOSTIC CHECKLIST

Consider

 NSG in patient with multiple cavitary nodules in a perilymphatic distribution

Image Interpretation Pearls

• Infection, cavitary metastases, and GPA should be excluded

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Introduction

The mediastinum is a thoracic region located between the lungs and pleural surfaces that extends from the thoracic inlet to the diaphragm and is bound anteriorly by the sternum and posteriorly by the thoracic vertebral bodies. It contains the thymus, heart and pericardium, thoracic great vessels, central airways, and esophagus. It also contains the thoracic duct, lymph nodes, various nerves, and mesenchymal tissues mostly comprised of mediastinal fat. Mediastinal abnormalities include primary (benign and malignant) and secondary (malignant) neoplasms, lymphadenopathies, cysts, vascular lesions (malformations, proliferations, aneurysms), glandular enlargement (thymus, thyroid), and intrathoracic herniation of abdominal contents. The diagnosis of mediastinal abnormalities requires understanding of and familiarity with normal mediastinal anatomy and imaging mediastinal compartments as well as typical features of mediastinal lesions.

The Mediastinal Compartments

Although various mediastinal compartmentalization schemes have been described over the years, it should be noted that most are not delineated by anatomic tissue planes. Localization of a particular lesion or process to a mediastinal compartment is usually undertaken for the purpose of formulating a focused imaging differential diagnosis.

Mediastinal Compartments According to Felson

The radiographic mediastinal compartments as described by Benjamin Felson are based on normal landmarks identified on lateral chest radiography. The Felson method divides the mediastinum into anterior, middle, and posterior compartments. The anterior mediastinum is located between the sternum and a line drawn along the anterior trachea and continued along the posterior margin of the heart. The posterior mediastinum includes the paravertebral region and is located posterior to a line drawn vertically along the anterior thirds of the thoracic vertebral bodies. The middle mediastinum is located between the anterior and posterior compartments.

Mediastinal Compartments According to the International Thymic Malignancy Interest Group (ITMIG)

Localization of a lesion to a radiographic mediastinal compartment allows the formulation of a differential diagnosis. In most cases, additional imaging is needed for further evaluation. Although most mediastinal abnormalities are assessed with contrast-enhanced chest computed tomography (CT) &/or magnetic resonance (MR) imaging, angiography, ultrasonography, and echocardiography may also be employed. The ITMIG developed a mediastinal compartmentalization system for thoracic cross-sectional imaging studies endorsed by a multidisciplinary group of experts, which defines prevascular, visceral, and paravertebral mediastinal compartments.

The **prevascular** mediastinum is bound anteriorly by the sternum and posteriorly by the arcuate border formed by the anterior margin of the pericardium. It contains the thymus, fat, lymph nodes, and the left brachiocephalic vein. The **visceral** mediastinum is bound anteriorly by the pericardium and posteriorly by the *visceral-paravertebral compartment boundary line*. The latter is an imaginary vertical line "drawn" through the thoracic vertebral bodies 1 cm posterior to their anterior margins. It contains the cardiovascular structures, trachea, carina, esophagus, lymph nodes, and fat. The **paravertebral**

mediastinum is defined anteriorly by the *visceral-paravertebral compartment boundary line* and posteriorly by imaginary vertical lines "drawn" along the posterior chest wall at the lateral aspects of the thoracic vertebral transverse processes.

Imaging of Mediastinal Abnormalities

Radiography

Mediastinal abnormalities are often detected on radiography based on identification of an abnormal mediastinal contour. Approximately 10% of mediastinal contour abnormalities are vascular and include anomalous vessels and aneurysms. Mediastinal masses may be focal and unilateral or diffuse and bilateral. Diffuse mediastinal enlargement should suggest lymphadenopathy, while focal enlargement is typical of primary neoplasms and cysts. Once a mediastinal abnormality is identified on frontal chest radiography it is localized to a radiographic mediastinal compartment (anterior, middle, posterior) based on the lateral radiograph. The radiographic features are then correlated with the patient's age, sex, and clinical presentation in order to provide a focused differential diagnosis and suggest the next most appropriate imaging study or management step. For example, a unilateral anterior mediastinal mass in a patient over the age of 40 years is often a thymoma. The next imaging study should be a contrastenhanced chest CT. On the other hand, a focal posterior mediastinal mass with benign pressure erosion on the adjacent skeleton in an asymptomatic adult is most often a neurogenic neoplasm, and the most appropriate next imaging study is MR to exclude intraspinal extension.

Cross-Sectional Imaging

Cross-sectional imaging with CT and MR allows further characterization of mediastinal abnormalities. Vascular lesions may be contiguous with other vascular structures and are optimally evaluated with intravenous contrast. Nonvascular lesions can be analyzed for their enhancement characteristics and the presence of absence of cystic change, calcification, fat, or necrosis. Adjacent structures can be assessed for identification of mass effect or local invasion. Diffuse mediastinal enlargement on radiography often represents lymphadenopathy on cross-sectional imaging, which can be identified based on involvement of one or more intrathoracic lymph node stations. Lymphadenopathy may manifest as discrete enlarged lymph nodes or as a diffuse soft tissue mass (nodal coalescence). FDG PET/CT complements morphologic imaging and allows distinction between benign and malignant lesions, clinical staging, and treatment planning.

The Radiologist's Role

Radiologists play a crucial role in the evaluation and management of mediastinal abnormalities. Radiographic localization of a lesion to a specific mediastinal compartment allows the formulation of a prospective differential diagnosis and helps guide further imaging. Differentiation between neoplastic and nonneoplastic lesions, and between surgical and nonsurgical lesions, should be attempted. Image-guided biopsy should be considered in nonsurgical lesions such as lymphomas and malignant germ cell neoplasms. In some cases, imaging findings are pathognomonic, and the radiologist can provide a definitive diagnosis.

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Approach to Mediastinal Abnormalities



Felson Mediastinal Compartments



(Left) Graphic illustrates the mediastinum, a space between the lungs and pleura that extends from the thoracic inlet to the diaphragm and contains the thymus, heart, pericardium, great vessels, central airways, and esophagus. (Right) The Felson scheme includes anterior, middle, and posterior mediastinal compartments. The imaginary lines that divide the mediastinum are drawn along the anterior trachea/posterior heart border and along the anterior 1/3 of the vertebral bodies.

ITMIG Mediastinal Compartments

ITMIG Mediastinal Compartments



(Left) The ITMIG mediastinal compartments [prevascular (magenta), visceral (blue), and paravertebral (yellow)] are outlined on this axial CECT. The green line represents the visceral-paravertebral compartment boundary line. (Right) The ITMIG mediastinal compartments [prevascular (magenta), visceral (blue), and paravertebral (yellow)] are outlined on this axial CECT. The green line represents the visceral-paravertebral compartment boundary line. The prevascular compartment wraps around the heart and pericardium.



ITMIG Mediastinal Compartments



ITMIG Mediastinal Compartments



(Left) The ITMIG mediastinal compartments [prevascular (magenta), visceral (blue), and paravertebral (yellow)] are outlined on this axial CECT. The green line represents the visceral-paravertebral compartment boundary line. The prevascular compartment wraps around the heart and pericardium. (Right) The ITMIG mediastinal compartments [prevascular (magenta), visceral (blue), and paravertebral (yellow)] are outlined on this sagittal CECT. The green line is the visceralparavertebral compartment boundary line.

Approach to Mediastinal Abnormalities

(Left) PA chest radiograph of a 58-year-old woman with chest pain shows a left mediastinal lobulated mass \square that was located in the anterior mediastinum on lateral radiography (not shown). Note a right perihilar nodular opacity → that exhibits the incomplete border sign. (Right) Axial CECT of the same patient shows a prevascular mediastinal mass 🔁 with intrinsic calcifications and a right posterior pleural drop metastasis 🔁. The findings are most consistent with invasive thymoma, confirmed on biopsy.

(Left) PA chest radiograph of a 54-year-old smoker with hemoptysis shows right lower and middle lobe volume loss with inferior displacement of the minor fissure 🖾. A right mediastinal abnormality 🔁 was located in the middle compartment on lateral radiography (not shown). (Right) Axial CECT of the same patient shows a lobulated visceral mediastinal mass 🖂 that narrows the bronchus intermedius \blacksquare and invades the right pulmonary artery \blacksquare . The most likely diagnosis is advanced lung cancer, small cell lung cancer in this case.

Lymphadenopathy

Thymoma



Thymoma

Lymphadenopathy



(Left) PA chest radiograph of an asymptomatic 21-year-old man shows a right paravertebral mass \supseteq that projected over the spine on lateral radiography (not shown). (Right) Axial CECT of the same patient shows a well-defined mass \blacksquare in the paravertebral compartment. Note that although the lesion extends anterior to the imaginary visceralparavertebral compartment boundary line, the bulk of the mass is paravertebral. The most likely diagnosis is neurogenic neoplasm, which was confirmed at surgery.

Neurogenic Neoplasm



Neurogenic Neoplasm



Focal Mediastinal Mass: Thymoma



Diffuse Mediastinal Enlargement: Lymphoma

Focal Mediastinal Mass: Thymoma



Diffuse Mediastinal Enlargement: Lymphoma

(Left) PA chest radiograph of an asymptomatic 58-year-old patient shows a focal rightsided mediastinal mass located in the anterior compartment on the lateral radiograph (not shown). The focal nature of the lesion . suggests a primary mediastinal neoplasm, and thymoma would be most likely given the demographic and clinical information. (Right) Axial CECT of the same patient shows a lobulated right anterior mediastinal soft tissue mass without associated lymphadenopathy.

(Left) PA chest radiograph of a 16-year-old boy shows diffuse mediastinal enlargement involving both sides of midline,

lymphadenopathy and likely related to lymphoma given demographic and imaging features. (Right) Composite image with axial CECT of the same patient shows

homogeneous mediastinal soft tissue involving multiple lymph node stations and encasing the vascular structures, consistent with coalescent lymphadenopathy. Hodgkin

consistent with



Vascular Lesion: Aneurysm





Enhancing Mediastinal Lesion: Ectopic Thyroid Tissue



lymphoma was confirmed at biopsy. (Left) Composite image with axial (left) and coronal (right) CECT shows a right-sided saccular aneurysm \triangleright of the descending thoracic aorta that produced a middle mediastinal mass on radiography (not shown). (Right) Composite image with axial (left) and oblique coronal (right) CECT of an asymptomatic patient with an ectopic mediastinal thyroid shows a prevascular mediastinal nodule 🔁 with intense contrast enhancement. The differential diagnosis should also include Castleman disease and

paraganglioma.
Thymoma

KEY FACTS

TERMINOLOGY

Most common primary anterior mediastinal neoplasm
 Considered malignant, may metastasize at any stage

IMAGING

• Radiography

- Anterior mediastinal mass with well-defined, smooth or lobulated borders; typically unilateral
- Invasive thymoma: Irregular borders, elevated ipsilateral hemidiaphragm, pleural nodules
- CT
 - Prevascular, spherical/ovoid, unilateral soft tissue mass
 - Smooth or lobulated borders
 - Low-attenuation foci from necrosis or cystic change
 - o Typically no lymphadenopathy
 - o Invasive thymoma: Local invasion, pleural nodules
- MR
 - T1WI: Low to intermediate signal intensity
 - o T2WI: High signal intensity, particularly in cystic change

TOP DIFFERENTIAL DIAGNOSES

- Thymic carcinoma
- Thymic carcinoid
- Lymphoma
- Malignant germ cell neoplasm
- Thymic hyperplasia

CLINICAL ISSUES

- 70% present in 5th and 6th decades
- M = F
- Symptoms/signs
 - Asymptomatic, incidental diagnosis
 - Compression/invasion of adjacent structures
 - Paraneoplastic syndromes
- Treatment
 - Stages I and II: Complete surgical excision
 - Stages III and IVa: Neoadjuvant chemotherapy and complete excision
 - Stage IVb: Palliative chemotherapy

(Left) PA chest radiograph of a patient with thymoma shows a right mediastinal mass 🔁 with well-defined lobulated borders. Thymomas typically manifest as an abnormal mediastinal contour on frontal chest radiography. (Right) Lateral chest radiograph of the same patient shows the anterior mediastinal location of the thymoma 🔁. Lateral chest radiography allows localization of a mediastinal mass to 1 of the 3 radiographic mediastinal compartments and the formulation of a focused differential diagnosis.





(Left) Axial CECT of an asymptomatic 65-year-old man evaluated for a radiographic abnormality shows a heterogeneously enhancing right prevascular mediastinal mass \supseteq with a preserved tissue plane 🔁 against the adjacent mediastinum. An encapsulated type A thymoma was diagnosed at surgery. (Right) Graphic demonstrates the morphologic features of thymoma. Thymoma 🔁 typically arises in one of the thymic lobes, which accounts for the unilateral location of most lesions.





Definitions

- Most common malignant thymic epithelial neoplasm
- Most common nonlymphomatous primary anterior/prevascular mediastinal neoplasm

IMAGING

General Features

- Best diagnostic clue
 - Unilateral spherical or ovoid anterior/prevascular mediastinal mass
- Location
 - o Prevascular mediastinum, typically unilateral
 - Anywhere from thoracic inlet to diaphragm
- Size
- Variable: 1-10 cm at diagnosis (mean: 5 cm)
- Morphology
 - Spherical or ovoid, smooth or lobulated borders

Radiographic Findings

- Normal radiography in small or occult thymomas
- Focal anterior mediastinal mass
 - Anywhere from thoracic inlet to cardiophrenic angle
 - Nodular thickening of anterior junction line
 - Contour abnormality on frontal chest radiography
 - o Well-marginated, smooth or lobulated borders
 - o Typically unilateral, less frequent bilateral growth
 - May exhibit calcification
 - Anterior mediastinal nodule/mass on lateral radiography
 - o Invasive thymoma
 - Lung invasion: Irregular or spiculated margins
 - Phrenic nerve invasion: Diaphragmatic elevation/paralysis
 - Pleural metastases: Pleural nodules; may progress to circumferential nodular pleural thickening

CT Findings

- CECT
 - Prevascular mediastinal soft tissue mass
 - Abuts superior pericardium and great vessels
 - Anywhere from thoracic inlet to cardiophrenic angle
 - Rarely in other mediastinal compartments
 - o Typically unilateral; origin in a thymic lobe
 - Variable size; spherical or ovoid; smooth or lobulated; well-defined borders
 - May exhibit homogeneous attenuation
 - Heterogeneous attenuation/enhancement
 - Necrosis or hemorrhage
 - Calcification: Curvilinear, coarse, punctate
 - Cystic: Fluid-attenuation content; ± intrinsic soft tissue mural nodule(s)
 - o Typically no associated lymphadenopathy
 - Exclusion of local invasion: Mediastinal fat, vessels, pericardium, heart, pleura, lung
 - Invasive thymoma
 - Tissue plane obliteration does not denote invasion
 - Higher frequency of
 - Low-attenuation tumor necrosis
 - □ Lobulated or irregular tumor contours

- Infiltration of surrounding fat
- □ Multifocal calcification in tumor substance □ Size \geq 7 cm
- Direct signs of invasion
 - Vascular invasion: Irregular vessel contour, encasement/obliteration, endoluminal tumor
 - Pleural nodule(s): Ipsilateral, bilateral, diffuse
 - $\hfill\square$ Pericardial thickening, invasion, nodules
 - Pulmonary involvement; rarely endobronchial

MR Findings

- T1WI
 - Low to intermediate signal intensity
 - o Isointense or higher signal than skeletal muscle
 - Low signal: Necrosis, cystic change, fibrous septa/capsule, Ca++
- T2WI
- High signal intensity, higher signal in cystic/necrotic areas
- T2WIFS
 - o Differentiation from adjacent fat
- Chemical shift imaging
 - No signal drop on opposed-phase imaging, unlike thymic hyperplasia
- Advantages of MR
 - Identification of invasive features if CECT contraindicated
 - o Identification of hemorrhage
 - Hemosiderin: Low signal on T1WI and T2WI
 - Acute/subacute hemorrhage: T1 hyperintensity
 - o Identification of mural nodules in cystic thymoma
 - o Identification of chest wall invasion

Nuclear Medicine Findings

- PET/CT
 - Not routinely performed
- Indium¹¹¹ octreotide scintigraphy: Advanced tumors unresponsive to chemotherapy; identification of patients who may respond to octreotide treatment

Imaging Recommendations

- Best imaging tool
 - CECT is modality of choice; assessment of invasion
 - Expanding role of MR
 - When CECT contraindicated
 - Attempts at correlation with histologic type, distinction of aggressive from early disease
- Postsurgical follow-up imaging recommendations
 - Complete resection: Annual CECT for 5 years, then annual CECT alternating with chest radiography until year 11, then annual chest radiography
 - Incomplete resection, resected stage III or IVa: CECT every 6 months for 3 years
- Radiology reports should include
 - Tumor size: Axial short and long axes, craniocaudad
 - Lesion location, borders, attenuation, calcification
 - Description of features of invasion
 - Fat infiltration, adjacent lung abnormality
 - Tumor abutting ≥ 50% of adjacent structure
 - Vessel/heart invasion, lymphadenopathy
 - Diaphragm elevation, pleural effusion/nodules
 - Distant metastases

DIFFERENTIAL DIAGNOSIS

Thymic Carcinoma

- Dominant prevascular mediastinal mass
 Lymphadenopathy, local invasion
- Histologic features of malignancy

Thymic Carcinoid

- Dominant prevascular mediastinal mass
 Lymphadenopathy, local invasion
- Histologic features of atypical carcinoid
- Clinical hormone syndrome, multiple endocrine neoplasia

Lymphoma

- Hodgkin and non-Hodgkin types
- Prevascular mediastinal mass and lymphadenopathy
- Local invasion, central necrosis, cystic change

Malignant Germ Cell Neoplasm

- Symptomatic men, < 40 years of age
- Seminoma: Homogeneous prevascular mediastinal mass
- Nonseminomatous germ cell neoplasm: Heterogeneous prevascular mass with central low attenuation/necrosis
- Dominant locally invasive mass and lymphadenopathy

Thymic Hyperplasia

- Diffuse or focal nodular thymic enlargement
- Signal drop on chemical shift MR

PATHOLOGY

Staging, Grading, & Classification

- 8th edition of Tumor-Node-Metastasis (TNM) Classification of Malignant Tumors: recently recognized by American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC)
 - Based on proposal of International Association for the Study of Lung Cancer (IASLC) and International Thymic Malignancy Interest Group (ITMIG)
 - Based on large retrospective database of thymic epithelial neoplasms

Gross Pathologic & Surgical Features

- Encapsulated thymoma
 - o Spherical/ovoid mass surrounded by fibrous capsuleo Intrinsic fibrous septa connected to capsule
- Necrosis, hemorrhage, cystic change (30-40%)
- Invasive thymoma
 - Invasion of tumor cells through tumor capsule
 - Invasion of mediastinal fat, cardiovascular structures, pleura, lung

Microscopic Features

- Tumor composition: Epithelial cells and lymphocytes in varying proportions
- WHO histologic classification of thymoma
 - Based on epithelial cell morphology, relative proportions of epithelial cells to lymphocytes, and resemblance to normal thymic architecture
 - o Type A histology: Round/epithelioid tumor cells
 - Type B histology: Oval/spindle tumor cells
 - WHO histologic classification
 Types A, AB, B1, B2, B3

- Poor reproducibility and clinical predictive value
- WHO subtypes may coexist in single tumor

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic, incidental imaging finding
 - Symptoms of compression or invasion of adjacent structures
 - Chest pain, dyspnea, cough
 - Dysphagia, diaphragm paralysis, superior vena cava syndrome
 - Paraneoplastic syndromes
 - Myasthenia gravis (MG) (30-50%)
 - □ 15% of patients with MG have thymoma
 - Hypogammaglobulinemia or Good syndrome (10%)
 - Pure red cell aplasia (5%)
- Other signs/symptoms
 - Autoimmune disorders: Systemic lupus erythematosus, polymyositis, myocarditis

Demographics

- Age
 - 70% of affected patients in 5th and 6th decades
- Sex
- o M=F
- Epidemiology
 - Rare malignancy
 - 0.2-1.5% of al malignancies
 - 1-5 cases/million/year in USA

Natural History & Prognosis

• Completeness of resection is most important prognostic indicator

Treatment

- Complete surgical excision when possible
 - Early-stage thymomas
 - Encapsulated and locally invasive (involving mediastinal pleura &/or pericardium) tumors
- Invasive and advanced thymoma
 - Controversially debated
 - Surgical cytoreduction + induction chemotherapy, adjuvant chemotherapy &/or postoperative radiotherapy

DIAGNOSTIC CHECKLIST

Consider

• Thymoma in patient over 40 years of age with unilateral anterior/prevascular mediastinal mass; particularly if symptomatic or with parathymic syndrome

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Thymoma





(Left) Axial NECT shows a large predominantly rightsided prevascular mediastinal mass with linear \blacksquare and rounded 🔁 low-attenuation areas that corresponded to intrinsic fibrous septa and areas of necrosis, respectively. (Right) Axial 2D FIESTA F/S MR of a 42-year-old woman shows a right prevascular mediastinal cystic lesion with large mural soft tissue masses An encapsulated type B1 thymoma was diagnosed at surgery. MR helps distinguish congenital and acquired mediastinal cysts from cystic neoplasms.





(Left) Axial CECT shows a left prevascular mediastinal thymoma with irregular borders and infiltration of the adjacent mediastinal fat 🔁 Mediastinal fat invasion was confirmed at surgery, but the mass was completely resected. (Right) Composite image with axial CECT shows an invasive thymoma that manifests as a large lobulated prevascular mediastinal mass with coarse calcifications (left) and diaphragmatic ➡ and $mediastinal \Longrightarrow pleural$ metastases (right).





(Left) Axial T1WI C+ SPGR MR of a 51-year-old man with a type B1 invasive thymoma who presented with chest pain and facial swelling shows a heterogeneously enhancing prevascular mediastinal mass and tumor thrombus \supseteq in the superior vena cava. (Right) Axial T1WI C+ SPGR MR of the same patient shows the heterogeneously enhancing mass, which invades the upper pericardium and possibly the pulmonary trunk. Note the low signal intensity focus 🔁 in the lesion that represented intrinsic cystic change.

KEY FACTS

TERMINOLOGY

- Thymic neuroendocrine neoplasm (TNEN)
- Thymic carcinoid (TC)

IMAGING

- Large heterogeneous anterior/prevascular mediastinal mass
- Frequent local invasion
- Mediastinal lymphadenopathy
- Distant metastases ~ 20%
- **PET/CT**: FDG and Ga-68 DOTATATE PET/CT for staging and surveillance

TOP DIFFERENTIAL DIAGNOSES

- Thymic epithelial neoplasm
- Lymphoma
- Malignant germ cell neoplasm
- Primary lung cancer
- Metastatic lymphadenopathy

PATHOLOGY

- Atypical carcinoid most common histology
- Well-differentiated neuroendocrine carcinomas: Typical and atypical carcinoid
- Poorly differentiated neuroendocrine carcinomas: Small cell and large cell carcinomas

CLINICAL ISSUES

- Most patients symptomatic from compression/invasion of mediastinal structures
- 50% of TNENs are functional with associated endocrinopathies: Cushing syndrome most common
- Multiple endocrine neoplasia-1 (MEN1) in 25% of patients with TNEN
- Complete surgical resection is treatment of choice

DIAGNOSTIC CHECKLIST

• Consider TNEN in patient with MEN1 + mediastinal mass

(Left) Axial CECT of a patient with a thymic neuroendocrine neoplasm shows a small ovoid prevascular mediastinal soft tissue lesion 🔁 with calcification and heterogeneous enhancement. Atypical carcinoid tumor was confirmed on surgical resection. (Right) Axial FDG-PET of the same patient shows focal FDG avidity 🔁 in the small prevascular mediastinal lesion, concerning for malignancy. The patient was asymptomatic and undergoing routine surveillance for multiple endocrine neoplasia-1 syndrome.





(Left) Coronal CECT of a patient with a thymic neuroendocrine neoplasm shows a large lobulated heterogeneously enhancing prevascular mediastinal mass *⊡*. Intrinsic foci of low attenuation indicate necrosis and cystic change. (Right) Coronal CECT of the same patient shows a left upper lobe lobulated mildly spiculated subpleural nodule *▶*, highly suspicious for malignancy. Tissue sampling confirmed metastatic poorlydifferentiated small cell thymic neuroendocrine neoplasm.





Synonyms

- Thymic neuroendocrine neoplasm (TNEN)
- Thymic carcinoid (TC)

Definitions

• Primary malignant neuroendocrine neoplasm

IMAGING

General Features

Best diagnostic clue
 Aggressive anterior/prevascular mediastinal mass

Radiographic Findings

• Large anterior mediastinal mass

CT Findings

- CECT
 - Large lobulated prevascular mediastinal mass
 - Heterogeneous attenuation/enhancement
 - Locally invasive; superior vena cava syndrome ~ 20%
 - Thoracic lymphadenopathy (50%)
 - o Metastases (20%): Liver, brain, lung, bone

MR Findings

- T1 intermediate signal; T2-hyperintense signal
- T1WI C+: Heterogenous enhancement

Nuclear Medicine Findings

- PET/CT
 - FDG uptake in primary tumor and metastases
 Intrinsic photopenia: Necrosis, hemorrhage, cysts

 - Ga-68 DOTATATE PET/CT
 - Highly sensitive for somatostatin receptor+ tumors
 - Imaging primary tumor, metastases; surveillance

Imaging Recommendations

- Best imaging tool
 - CECT or MR: Assessment of tumor, local invasion, metastases
 - PET/CT: Staging, restaging, surveillance

DIFFERENTIAL DIAGNOSIS

Thymic Epithelial Neoplasm

- Anterior/prevascular mediastinal mass; ± local invasion
- Lymphadenopathy and metastases favor TNEN or thymic carcinoma over thymoma

Lymphoma

• Locally invasive mediastinal mass; nodal coalescence

Primary Lung Cancer

• Large central mass ± local invasion/lymphadenopathy

Malignant Germ Cell Neoplasms

- Almost exclusively young men < 40 years
- Large locally invasive heterogeneous anterior/prevascular mediastinal mass

Metastatic Lymphadenopathy

• Various malignancies; mediastinal metastases

PATHOLOGY

General Features

- Two major histopathological categories
 - Well differentiated (atypical and typical TC)
 Atypical TC: Most common (intermediate grade)
 - Poorly-differentiated (high-grade small cell or large cell neuroendocrine carcinoma)
- Genetics

o MEN1~25%

Gross Pathologic & Surgical Features

- 2-4% of anterior/prevascular mediastinal tumors
- Large, usually circumscribed mass, frequent hemorrhage/necrosis and local invasion

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Compression/invasion of mediastinal structures: Cough, dyspnea, chest pain, superior vena cava syndrome
- Other signs/symptoms
 - o 50% of TNENs are functional
 - Cushing syndrome (most common); ectopic adrenocorticotropic hormone (ACTH)
 - Association with MEN1
 - ~ 1/3 asymptomatic; incidental finding

Demographics

- Epidemiology
 - o Incidence: 1/10 million/year
 - o M:F = 3:1
 - Average age: 43 years (range: 30-60 years); median age: 57 years

Natural History & Prognosis

- 5-year survival after complete resection: 28-84%
- Best prognostic indicators: Completeness of resection, stage
- TC is most lethal neoplasm in MEN1

Treatment

- Complete surgical resection; debulking surgery if unresectable
- Somatostatin analogs (SSAs) play fundamental role in therapy

DIAGNOSTIC CHECKLIST

Consider

• TNEN in patient with MEN1 + mediastinal mass

Image Interpretation Pearls

• Ga-68 DOTATATE PET/CT highly sensitive for diagnosis and surveillance

- Hsu CH et al: Trends in the incidence of thymoma, thymic carcinoma, and thymic neuroendocrine tumor in the United States. PLoS One. 14(12):e0227197, 2019
- 2. Araki T et al: Radiological features and metastatic patterns of thymic neuroendocrine tumours. Clin Radiol. 73(5):479-84, 2018

Thymic Carcinoma

KEY FACTS

TERMINOLOGY

• Malignant epithelial thymic neoplasm

IMAGING

- Thymic carcinoma not reliably distinguished from thymoma on imaging
- Radiography
 - Dominant anterior mediastinal mass
- CT
 - Prevascular mediastinal mass ± calcification &/or local invasion
 - Identification of lymphadenopathy and distant metastases
 - Pleural drop metastases less common than in thymoma
- MR
 - Necrosis, cystic change, hemorrhage may result in heterogeneous signal intensity
- **PET/CT**: Detection of metastases and surveillance

TOP DIFFERENTIAL DIAGNOSES

- Thymoma
- Malignant germ cell neoplasm
- Lymphoma
- Metastatic lymphadenopathy

PATHOLOGY

• Thymic carcinomas lack immature T-lymphocytes seen in thymoma

CLINICAL ISSUES

- Symptoms/signs: May relate to mass effect/invasion; superior vena cava syndrome
- Mean age: 50-60 years, with slight male predominance

DIAGNOSTIC CHECKLIST

- Thymic neoplasms not reliably differentiated on imaging
- Distant metastases and lymphadenopathy more common in thymic carcinoma

(Left) PA chest radiograph of a patient with thymic carcinoma shows a large mediastinal mass that extends to both sides of midline ⊇. (Right) Coronal FDG PET/CT of the same patient shows heterogeneous FDG avidity within the thymic mass and extensive hepatic metastases. Note foci of relative photopenia within the primary mass and metastases, indicative of tissue necrosis ⊇.





(Left) Axial CECT of a patient with thymic carcinoma shows a heterogeneous lobulated prevascular mediastinal mass with irregular borders 🖂 Mediastinal fat and pericardial invasion were confirmed at surgical resection. (Right) Axial CECT of a patient with thymic carcinoma shows a large heterogenous mass in the left prevascular mediastinum that directly invades the myocardium evidenced by complete loss of the subepicardial fat plane. $Lymphadenopathy \supseteq favors$ thymic carcinoma over thymoma.





Definitions

• Thymic carcinoma: Rare malignant thymic epithelial neoplasm

IMAGING

General Features

- Best diagnostic clue
 - Large prevascular mediastinal mass; frequent invasion of adjacent mediastinal structures
 - Not reliably distinguished from thymoma on imaging
 - Mediastinal lymphadenopathy &/or distant
 - metastases favors thymic carcinoma over thymoma
- Location
 - Prevascular mediastinum
- Size
 - o Large mass (mean size: 6.4 cm)
- Morphology
 - Ill-defined lobulated contours and intrinsic heterogeneity: Necrosis, hemorrhage, cystic change

Radiographic Findings

• Lobulated anterior mediastinal mass on PA and lateral chest radiography

CT Findings

- CECT
 - **Prevascular mediastinal mass** with lobulated contours, intrinsic heterogeneity, frequent invasion of surrounding structures, ± calcification
 - Pleural and pericardial effusions more common than in thymoma
 - Intrathoracic **lymphadenopathy and distant metastases**

MR Findings

- Variable T1 intermediate signal and T2-hyperintense signal
- T1WI C+: Heterogeneous enhancement and progressive DCE

• DWI: Diffusion restriction with low ADC values

Nuclear Medicine Findings

- PET/CT
 - FDG avidity of primary tumor and metastases

DIFFERENTIAL DIAGNOSIS

Thymoma

- Prevascular mediastinal mass; intrathoracic lymphadenopathy and pleural effusions highly unusual
- Paraneoplastic syndromes more common

Malignant Germ Cell Neoplasm

- Almost exclusively young adult men under 40 years
- Large invasive prevascular mediastinal mass, intrathoracic lymphadenopathy, distant metastases

Mediastinal Lymphoma

- Hodgkin or Non-Hodgkin lymphoma
- Prevascular mediastinal mass with nodal coalescence; may affect other compartments

Mediastinal Metastatic Lymphadenopathy

• Lymphadenopathy ± nodal coalescence

PATHOLOGY

General Features

• Loss of organotypical features of thymic differentiation and overt cytologic features of malignancy

Staging, Grading, & Classification

- TNM staging/classification system created by IASLC and ITMIG, adapted in 8th edition of AJCC manual
- Modified Masaoka-Koga staging system widely used for both thymoma and thymic carcinoma

Gross Pathologic & Surgical Features

• Large, firm, infiltrating mass with cystic change and necrosis, typically lacks capsule

Microscopic Features

- Cytologic atypia, cytoarchitectural features analogous to those seen in carcinomas of other organs
- Multiple histologic subtypes
 - o Squamous cell carcinoma subtype most common
 - Other subtypes (basaloid, mucoepidermoid, lymphoepithelioma-like, sarcomatoid subtypes, among others)
 - Subtypes may appear in combination

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Symptoms of mass effect/invasion: Cough, chest pain, phrenic nerve palsy, superior vena cava syndrome
- Other signs/symptoms
 - Paraneoplastic syndromes rare
 - Myasthenia gravis, pure red cell aplasia, hypogammaglobulinemia

Demographics

- Epidemiology
- ~ 20% of thymic epithelial neoplasms
 Mean age at diagnosis: 50-60 years; slight male
- Mean age at diagnosis: 50-60 years; slight male predominance

Natural History & Prognosis

- Survival rates heavily influenced by stage and resectability
- 5-year survival range: 100% in stage I disease to 17% in stage IVb disease

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Thymic carcinoma, thymic carcinoid, and thymoma not reliably differentiated on imaging
- Distant metastases, lymphadenopathy, and pleural/pericardial effusions common

- Berghmans T et al: Systemic treatments for thymoma and thymic carcinoma: a systematic review. Lung Cancer. 126:25-31, 2018
- Scorsetti M et al: Thymoma and thymic carcinomas. Crit Rev Oncol Hematol. 99:332-50, 2016

KEY FACTS

TERMINOLOGY

• Rare, benign primary thymic neoplasm

IMAGING

- Radiography
 - o Large unilateral or bilateral anterior mediastinal mass
 - o Involvement of inferior anterior mediastinum
 - Smooth or lobulated, well-defined borders
 - May mimic cardiomegaly &/or hemidiaphragm elevation
- CT
 - Well-defined prevascular mediastinal fat-attenuation mass with intrinsic soft tissue elements
 - Rarely predominant soft tissue or fat attenuation
 - Anatomic connection to thymus
 - o Unilateral or bilateral mediastinal involvement
- MR
 - T1-hyperintense fat components
 - Intermediate signal intensity soft tissue components on T1WI and T2WI

TOP DIFFERENTIAL DIAGNOSES

- Lipoma
- Mediastinal lipomatosis
- Teratoma
- Mediastinal fat
- Morgagni hernia
- Liposarcoma

CLINICAL ISSUES

- Symptoms/signs
 - Most patients asymptomatic
 - Symptoms related to mass effect
- Mean age: 26.7 years
- Surgical resection curative

DIAGNOSTIC CHECKLIST

• Consider thymolipoma in young patient with large, pliable, noninvasive, noncystic prevascular mediastinal mass with fat and soft tissue components

(Left) PA chest radiograph of a 17-year-old male patient with a long history of cough and dyspnea shows a thymolipoma that manifests as a large left mediastinal mass that conforms to the shape of the heart and mimics cardiomegaly 🔁. (Right) Lateral chest radiograph of the same patient shows that the mass also conforms to the shape of the left hemidiaphragm and mimics diaphragmatic elevation 🖂 Thymolipomas are soft pliable tumors that often conform to the shape of adjacent organs.





(Left) Coronal CECT of the same patient shows a large mediastinal mass of predominant fat attenuation with intrinsic soft tissueattenuation elements 🔁. The mass conforms to the adjacent $mediastinum \ge and mimics$ cardiomegaly on radiography. (Right) Sagittal CECT of the same patient shows a predominant fat-attenuation mass with intrinsic soft tissue and documents an anatomic connection to the thymus \supseteq . The mass conforms to the left $hemidiaphragm \square and mimics$ diaphragmatic elevation on radiography.





Definitions

• Rare, benign primary thymic neoplasm

IMAGING

General Features

- Best diagnostic clue
 Anterior/prevascular mediastinal mass with fat and soft tissue components
- Location
- Typically inferior anterior/prevascular mediastinum
- Size
 - Typically large; average size of 20 cm
- Morphology
 - Well circumscribed
 - o Pliable mass, conforms to shape of adjacent organs
 - May exhibit positional change in shape

Radiographic Findings

- Large unilateral or bilateral anterior mediastinal mass
- Preferential involvement of inferior anterior mediastinum
- Smooth or lobulated, well-defined borders
- Conforms to shape of adjacent structures; may mimic cardiomegaly &/or hemidiaphragm elevation

CT Findings

- Well-defined prevascular mediastinal fat-attenuation mass with intrinsic soft tissue elements
 - Rarely predominant soft tissue attenuation
 - Rarely predominant fat attenuation with small soft tissue attenuation foci
- Anatomic connection to thymus

MR Findings

- T1-hyperintense fat components
- Intermediate signal intensity soft tissue components on T1WI and T2WI
- Chemical shift MR: Signal loss of solid components on outof-phase MR

Imaging Recommendations

- Best imaging tool
 - CT for assessment of disease extent and surgical planning
 - MR may help confirm presence of fat tissue

DIFFERENTIAL DIAGNOSIS

Lipoma

- Homogeneous, well-circumscribed fat-attenuation mass
- Absent or small linear soft tissue components
- 2% of primary mediastinal neoplasms

Mediastinal Lipomatosis

- Unencapsulated mediastinal fat
- Associated with obesity and steroid use

Teratoma

- Unilateral prevascular mediastinal mass
- Multilocular cystic lesion ± calcification &/or fat

Mediastinal Fat

- Located at cardiophrenic angles
- Associated with obesity, steroids, Cushing syndrome

Morgagni Hernia

- Herniated abdominal contents through anteromedial diaphragmatic defect
- May contain omental fat, omental vessels, liver, colon

Liposarcoma

- Most commonly in visceral/paravertebral mediastinum
- Conspicuous irregular soft tissue components
- Rapid growth, local invasion, lymphadenopathy, metastases
- Thymic liposarcoma has been reported

PATHOLOGY

Gross Pathologic & Surgical Features

• Lobulated encapsulated soft, yellow mass

Microscopic Features

• Admixture of mature adipose tissue and thymic tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms

 Most patients asymptomatic
- Other signs/symptoms
 - o Dyspnea, cough, paroxysmal tachycardia
 - Related to mass effect
 - Reported cases of associated parathymic syndromes in adult patients with thymolipoma

Demographics

- Age
 - Mean age: 26.7 years; wide age range
 - Most patients < 50 years
- Sex
- No sex predilection
- Epidemiology
 - < 5% of primary thymic neoplasmsIncidence: 0.12 cases/100,000 persons/year

Treatment

• Curative surgical resection for symptomatic or enlarging lesions

DIAGNOSTIC CHECKLIST

Consider

 Thymolipoma in young patient with large, pliable, noninvasive, noncystic prevascular mediastinal mass with fat and soft tissue components

Image Interpretation Pearls

• Cross-sectional imaging for documentation of anatomic connection to thymus

- 1. Varma V et al: Thymic masses and mimics in adults: review of common and uncommon pathologies. Clin Imaging. 77:98-110, 2021
- Miranda A et al: Persistent radiologic thoracic hypotransparency: a case report and review of the literature. Arch Pediatr. 25(8):489-92, 2018

Mediastinal Teratoma

KEY FACTS

TERMINOLOGY

• Primary germ cell neoplasm (GCN) containing tissues derived from ≥ 2 germinal layers

IMAGING

- Radiography
 - Well-defined spherical or ovoid anterior mediastinal mass with smooth or lobulated borders
 - Radiographic calcification (20%)

• CT

- Heterogeneous multilocular cystic prevascular mediastinal mass
- Smooth or lobulated borders
- Fluid-attenuation cysts (90%)
- Fat (75%); fat-fluid levels (10%)
- o Calcification (50%)
- MR
 - Superior for tissue characterization and for confirmation of intrinsic fat

TOP DIFFERENTIAL DIAGNOSES

- Thymic cyst
- Cystic thymic neoplasm
- Mediastinal lymphangioma

PATHOLOGY

- Macroscopic cysts in majority of cases
- Lipid-rich sebaceous material

CLINICAL ISSUES

- Symptoms/signs
 - Most patients asymptomatic
 - Cough, dyspnea, chest pain
- Excellent prognosis
 - Nearly 100% 5-year survival

DIAGNOSTIC CHECKLIST

• Cystic prevascular mediastinal mass containing fat is considered diagnostic of mature teratoma

(Left) Coned-down PA chest radiograph of a 25-year-old man with a mature cystic teratoma shows a smoothly marginated right anterior mediastinal mass 🔁 that exhibits the hilum overlay sign with visualization of the right interlobar pulmonary artery through the lesion. (Right) Lateral chest radiograph of the same patient shows that the mass projects over the heart, confirming the anterior mediastinal location of the lesion 🔁. Patients with mature teratoma are typically men or women in the first through fourth decades of life.





(Left) PA chest radiograph of a patient with mature teratoma shows a lobulated left anterior mediastinal mass \supseteq with intrinsic curvilinear calcification 🔁. Calcifications are detected radiographically in 20% of mature teratomas. (Right) Coronal CECT of the same patient shows an ovoid lobulated left prevascular mediastinal mass with curvilinear calcifications and heterogeneous attenuation. Mature teratoma should be considered based on the morphologic features of the lesion and the pattern of calcification.





Synonyms

• Germ cell neoplasm (GCN)

Definitions

• Primary GCN containing tissues derived from at least 2 germinal layers

IMAGING

General Features

- Best diagnostic clue
 - Multilocular cystic prevascular mediastinal mass
 Fluid, fat, soft tissue, and calcification
 - Fat-fluid level in 10% of cases
 - Formed teeth and bone diagnostic but rare
- Location
 - Anterior/prevascular mediastinum
 - Other mediastinal compartment (5%)
- Size
 - May be large and multicompartmental
- Morphology
 - Spherical, well circumscribed
 - Most exhibit multilocular cystic components

Radiographic Findings

- Anterior mediastinal mass
 Mediastinal widening
 May mimic cardiomegaly
- Well-defined, smooth or lobulated margins
- Spherical or ovoid shape
- Radiographic calcification in 20% (linear, rim-like, coarse)
- Difficult identification of intrinsic fat on radiography
- Adjacent airspace disease: Atelectasis &/or consolidation
- Pleural effusion

CT Findings

- Well-defined, unilateral, prevascular mediastinal mass
- Smooth or lobulated borders
- Unilocular or multilocular cystic lesion
- Heterogeneous attenuation

• Fluid attenuation cysts (90%)

- Typically thin-walled
- Soft tissue components, including cyst walls and septa
 May exhibit contrast enhancement
- Fat-attenuation cyst content (75%)
 - Fat-fluid level diagnostic (10%)
- $\circ~$ Calcification best detected on CT (50%)
 - Rim-like or coarse
 - Rarely related to teeth or bone
- No lymphadenopathy
- Adjacent atelectasis, consolidation
- Pleural &/or pericardial effusion
- Teratoma with malignant component: Malignant GCN
 - Dominant solid soft tissue components
 - Thick, enhancing cyst capsule
 - Poorly-defined margins
 - Mass effect, local invasion
 - Lymphadenopathy, metastases
 - Less frequent fat content

MR Findings

- T1WI
 - Fat components are T1 hyperintense
 - Proteinaceous fluid and hemorrhage may be T1 hyperintense
- T1WIFS
- Confirmation of fat components
- Heterogeneous prevascular mediastinal mass
- Cystic components exhibit low signal intensity on T1WI and high signal intensity on T2WI

Ultrasonographic Findings

• Encapsulated mass with heterogeneously echogenic components

Imaging Recommendations

- Best imaging tool
 - CT optimally demonstrates multicompartmental extension and calcification
 - MR superior for tissue characterization, confirmation of fat

DIFFERENTIAL DIAGNOSIS

Thymic Cyst

- Cyst with fluid attenuation, unilocular or multilocular
- High-attenuation content from hemorrhage, infection

Cystic Thymic Neoplasm

- Cystic thymoma
 - Prevascular mediastinal cystic lesion with mural nodule(s)
- Thymic carcinoma or carcinoid
 - Prevascular mediastinal mass
 - o Lymphadenopathy, local invasion

Mediastinal Lymphangioma

- Multilocular cystic mass
- Involvement of neck, chest wall, axilla

Other Germ Cell Neoplasms

- 10% of primary mediastinal masses
- Seminoma, embryonal carcinoma, endodermal sinus (yolk sac) tumor, choriocarcinoma, mixed types
 Seminoma typically homogeneous
- Serum tumor markers
 - ο β-human chorionic gonadotropin, α-fetoprotein

Lipoma

- Homogeneous, encapsulated mass of adipose tissue
- Fat attenuation with soft tissue wisps and vessels

Mediastinal Lipomatosis

- Unencapsulated fat infiltration of mediastinum
- Associated with obesity and steroid use

Mediastinal Fat

- Associated with obesity, steroids, Cushing syndrome
- Cardiophrenic angle fat, no soft tissue or calcification

Morgagni Hernia

- Herniation of abdominal contents through anterior diaphragmatic foramen
- May contain omental fat, liver, bowel

Thymolipoma

- Rare, benign primary thymic neoplasm
- Typically large, averaging 20 cm
- Soft, pliable tumor without aggressive features
- Anatomic connection to thymus

Liposarcoma

- Most commonly in visceral/paravertebral mediastinum
- Aggressive features: Local invasion, lymphadenopathy, metastases
- May exhibit rapid growth

Metastatic Disease

- Malignant teratoma may metastasize to mediastinum
- Gonadal source usually excluded when malignant teratoma diagnosed in mediastinum

PATHOLOGY

General Features

- Etiology
 - Postulated origin in rests of primitive germ cells left in mediastinum during migration of yolk sac endoderm to urogenital ridge
 - Mediastinum most common location of extragonadal GCNs
- Associated abnormalities
- Rare association of malignant mediastinal GCN with Klinefelter syndrome
- Tissues derived from ≥ 2 germinal layers
- o Ectoderm
 - Typically predominates: Hair, skin, teeth
- o Mesoderm
- Cartilage, bone, muscle
- o Endoderm
 - Bronchial or gastrointestinal epithelium, mucus glands
 - Pancreatic tissue

Staging, Grading, & Classification

- Pathologic classification
 - Mature teratoma
 - Most common; 70% of mediastinal GCNs
 - Well-differentiated tissues
 - Immature teratoma
 - Immature elements (neuroectoderm)
 - Typically benign course in children, more aggressive in adults
 - Teratoma with malignant component
 - Seminoma
 - Yolk sac tumor
 - Embryonal carcinoma
 - More common in men
 - o Teratoma with malignant mesenchymal component
 - Angiosarcoma
 - Rhabdomyosarcoma
 - Osteosarcoma
 - Chondrosarcoma
 - Malignant immature teratoma
 - Histologically benign teratoma that subsequently metastasizes

Gross Pathologic & Surgical Features

- Macroscopic cysts in majority of cases
- Lipid-rich sebaceous material
- Soft tissue components; hair, bone, teeth

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Most patients asymptomatic unless lesions are large
 - Teratoma with malignant component is more likely to cause symptoms
- Other signs/symptoms
 - Cough, dyspnea, chest pain
 - Upper respiratory complaints, fever
 - Rupture and infection reported
 - Fistulous tract from digestive enzymes reported

Demographics

- Age
 - o Most common in children and young adults
- Sex

Natural History & Prognosis

- Mature teratomas are benign and slow growing
 Nearly 100% 5-year survival
- Malignant teratoma carries very poor prognosis

Treatment

- Options, risks, complications
 - Rupture into adjacent pleural or pericardial space in up to 30% of cases
 - May also rupture into lung/bronchi
- Mature teratoma
 - Surgical excision curative
- Mediastinal growing teratoma syndrome
 - Continued slow growth of benign mature teratoma components after chemotherapy

DIAGNOSTIC CHECKLIST

Consider

- Teratoma in patient with cystic prevascular mediastinal mass
- Malignant GCN if dominant solid component, local invasion, &/or lymphadenopathy
- Exclusion of metastasis from gonadal source in cases of mediastinal teratoma with malignant component

Image Interpretation Pearls

- Unilocular or multilocular cystic prevascular mediastinal mass with fat is considered diagnostic of mature teratoma
- Fat-fluid levels and teeth are rare but diagnostic of mature teratoma

- 1. Park JW et al: Pictorial review of mediastinal masses with an emphasis on magnetic resonance imaging. Korean J Radiol. 22(1):139-54, 2021
- Prosch H et al: The role of radiological imaging for masses in the prevascular mediastinum in clinical practice. J Thorac Dis. 12(12):7591-7, 2020
- Al-Khalifa M et al: A giant primary mediastinal teratocarcinoma in a male adult. Case Rep Surg. 2019:7123241, 2019

Mediastinal Teratoma





(Left) Axial CECT of a 16-yearold boy shows a right prevascular mediastinal mass with intrinsic soft tissue, fluid, and fat components. Mature teratomas are typically cystic, and 75% exhibit fat attenuation. (Right) Cut section of a mature teratoma shows multiple cystic areas 🔁 intermixed with solid soft tissue components. The heterogeneous nature of these neoplasms results in characteristic findings on cross-sectional imaging studies. (Courtesy C. Moran, MD.)





(Left) Composite image with axial CECT of a young woman with mature teratoma shows a multilocular cystic right prevascular mediastinal mass that produces mass effect on the superior vena cava 🔁. Although the lesion exhibits predominant fluid attenuation, intrinsic fat attenuation \blacksquare allows a confident prospective diagnosis of mature teratoma. (Right) Axial T2WI MR of the same patient confirms the multilocular cystic nature of the lesion and demonstrates an intrinsic fluid-fluid level ᠫ that was not visible on CT.





(Left) Axial CECT of a 40-yearold woman with a mature teratoma shows a heterogeneous prevascular mediastinal mass with cystic and soft tissue elements as well as rim-like calcifications \square If biopsy is required, the soft tissue component should be targeted. Surgical resection is curative in mature teratomas. (Right) Axial CECT of a patient with a mature teratoma shows a large left prevascular mediastinal mass containing soft tissue, fluid, fat 🔁, and calcification 🔁. CT optimally demonstrates lesional calcification.

Mediastinal Seminoma

KEY FACTS

TERMINOLOGY

• Primary malignant mediastinal germ cell neoplasm (MGCN)

IMAGING

- Radiography
 - o Large lobular anterior mediastinal mass
- CT
 - o Large lobular prevascular mediastinal soft tissue mass
 - o Relatively homogeneous with mild enhancement
 - Mass effect on adjacent structures
 - o Mediastinal lymphadenopathy; nodal coalescence
 - o Metastases common (regional lymph nodes, lung, bone)
- MR
 - Relatively homogeneous prevascular mediastinal mass
 - T2 hypointense; T1 C+ shows enhancing septa
- FDG PET/CT
 - FDG-avid mass in prevascular mediastinum
 - Post treatment assessment of tumor viability

TOP DIFFERENTIAL DIAGNOSES

- Lymphoma
- Thymoma
- Teratoma

PATHOLOGY

• Tumor cell aggregates circumscribed by fibrous septa, lymphocytic infiltrate, occasional necrotic foci

CLINICAL ISSUES

- Symptoms/signs
 - Chest pain, dyspnea, cough, fever, weight loss
 - o Elevated serum β-HCG, normal α-fetoprotein level
- 90% of seminomas in men aged 20-40 years

DIAGNOSTIC CHECKLIST

• Consider seminoma in symptomatic male patient with homogeneous prevascular mediastinal mass

(Left) PA chest radiograph shows a young adult man who presented with a one-month history of fever and pleuritic chest pain secondary to a large mediastinal seminoma that manifests as a large predominantly right-sided mediastinal mass 🛃 that obscures the right cardiomediastinal border. (Used with permission from AIRP.) (Right) Lateral chest radiograph of the same patient shows the large homogeneous mass 🔁 located in the anterior mediastinum. (Used with permission from AIRP.)





(Left) Axial CECT of the same patient shows a large right prevascular mediastinal soft tissue mass \blacksquare that produces mass effect on the right heart and the adjacent right lung with resultant relaxation atelectasis 🛃. (Used with permission from AIRP.) (Right) Coronal CECT of the same patient shows the large mildly heterogeneous prevascular mediastinal mass, which produces mass effect on adjacent cardiovascular structures 🛃 as well as adjacent mediastinal lymphadenopathy 🔁. (Used with permission from AIRP.)





Definitions

- Primary mediastinal malignant germ cell neoplasm (MGCN)
 - Extragonadal germ cell tumors (GCTs) typically develop in midline structures
 - Seminoma second MGCN in frequency, after teratoma

IMAGING

General Features

- Best diagnostic clue
 - Large prevascular mediastinal mass in young man
- Location
 - Anterior/prevascular mediastinum
- Size
 - Typically large (> 5 cm)
- Morphology
 - Homogeneous, lobular borders

Radiographic Findings

- Radiography
 - o Large lobulated anterior mediastinal mass

CT Findings

- CECT
 - Large lobulated prevascular mediastinal soft tissue mass
 Typical homogeneous attenuation, mild enhancement
 - Typical nomogeneous acce
 Rare cysts or calcification
 - Mass effect on adjacent structures
 - Mediastinal lymphadenopathy; nodal coalescence
 - Metastases (intrathoracic nodes, lung, bone) common

MR Findings

Mass hypointense on T2WI; T1 C+ may show enhancing septa

Nuclear Medicine Findings

- PET/CT
 - FDG-avid mass in prevascular mediastinum
 - Detection of residual disease following initial treatment

Imaging Recommendations

- Best imaging tool
 - Contrast-enhanced CT is imaging modality of choice

DIFFERENTIAL DIAGNOSIS

Lymphoma

- Multiple lymph node groups/mediastinal compartments involved
- Pleural effusions common
- Rarely calcifies prior to treatment

Thymoma

- Prevascular lobular mass; frequent cysts/necrosis
- Patients typically > 40 years of age

Teratoma

• Heterogeneous cystic mass with fat, calcium, soft tissue

PATHOLOGY

General Features

- Associated abnormalities
 - GCT biomarkers
 - ↑ β-human chorionic gonadotropin (β-HCG); secreted by tumor in 10-30%
 - α-fetoprotein (AFP) level typically normal
 ↑ serum lactate dehydrogenase (LDH)

Gross Pathologic & Surgical Features

- Large fleshy lobulated soft tissue mass
- Limited hemorrhage, necrosis, cysts may be present
- May be entirely within thymus

Microscopic Features

- Uniform round or polygonal cells
 - Tumor cell nests marginated by fibrous septa, lymphocytic infiltrate, granulomatous inflammation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain, dyspnea, cough
 - o Fever, weakness, weight loss (over weeks/months)
 - o Asymptomatic (25%)
 - Superior vena cava syndrome (10%)

Demographics

- Epidemiology
 - o 2-4% of all mediastinal masses
 - 2% of all extragonadal GCTs found in adults, M > F
 - Seminoma most common primary mediastinal MGCN of single histology (25-50% of all MGCN)
- Age/sex: 20-40 years; range: 13-79 years; 90% are men

Natural History & Prognosis

- Tissue diagnosis: Fine-needle aspiration or core biopsy
- Majority metastatic at diagnosis
 Regional lymph nodes, lung, bone, liver, brain
- 5-year survival rate: ~ 88%
- Patients > 37 years: Less favorable outcomes
- Frequent residual mass on CT following treatment
 Typically necrotic tissue or desmoplastic reaction
 PET/CT assists surveillance for recurrent disease

Treatment

- Cisplatin, etoposide, and bleomycin (3 or 4 cycles)
- External beam radiation (35-50 Gy)
- Highly sensitive to chemotherapy and radiotherapy

DIAGNOSTIC CHECKLIST

Consider

 Seminoma in symptomatic male patient with homogeneous anterior/prevascular mediastinal mass

- Garrana SH et al: Imaging of the anterior/prevascular mediastinum. Radiol Clin North Am. 59(2):155-68, 2021
- Prosch H et al: The role of radiological imaging for masses in the prevascular mediastinum in clinical practice. J Thorac Dis. 12(12):7591-7, 2020

KEY FACTS

TERMINOLOGY

- Malignant germ cell neoplasm (MGCN)
- Primary mediastinal yolk sac tumor, choriocarcinoma, embryonal carcinoma, mixed-type germ cell neoplasm (GCN)

IMAGING

Radiography

- Large anterior mediastinal mass
- Mass effect on adjacent structures
- CT
 - o Large heterogeneous prevascular mediastinal mass
 - Nodular peripheral enhancement
 - Central low attenuation: Hemorrhage, necrosis
 - Mass effect and local invasion
 - Lymphadenopathy, metastases
- MR
 - Large heterogeneously enhancing prevascular mediastinal mass with infiltrative margins

TOP DIFFERENTIAL DIAGNOSES

- Seminoma
- Thymoma
- Lymphoma

PATHOLOGY

- Large necrotic soft tissue mass, invasive at margins
- Varied histologies recapitulate embryonic tissues
- Elevation of serum β -human chorionic gonadotropin &/or α -fetoprotein in ~ 90% of patients

CLINICAL ISSUES

- Symptoms/signs: Chest pain, dyspnea, superior vena cava syndrome
- Treatment: Chemotherapy and resection of residual mass

DIAGNOSTIC CHECKLIST

• Consider nonseminomatous MGCN in male patient with large, locally invasive, heterogeneous anterior/prevascular mediastinal mass

(Left) PA chest radiograph of a young man with mixed-type mediastinal malignant germ cell neoplasm who presented with chest pain shows a large left mediastinal mass ➡ that obscures the left mediastinum. (Right) Axial CECT of the same patient shows a

heterogeneously enhancing left prevascular mediastinal mass with infiltrative margins ➡ that produces marked mass effect on adjacent structures. Intrinsic lowattenuation areas represent necrosis &/or hemorrhage, and intratumoral gas ➡ reflects airway invasion.





(Left) Coronal CECT of the same patient shows that the mass compresses adjacent mediastinal structures and evidence of contiguous pleural \triangleright and pericardial \triangleright involvement. Intrinsic gas foci within a low-attenuation area of tumor necrosis are related to airway invasion. (Right) Steady-state free precession (SSFP) axial MR of the same patient confirms internal heterogeneity related to widespread necrosis and hemorrhage. Biopsy confirmed elements of embryonal carcinoma and yolk sac tumor.





Nonseminomatous Malignant Germ Cell Neoplasm

TERMINOLOGY

Abbreviations

- Malignant germ cell neoplasm (MGCN)
- Nonseminomatous germ cell tumor (NSGCT)

Definitions

- Primary malignant mediastinal MGCN
 - o Yolk sac (endodermal sinus) tumor
 - o Choriocarcinoma
 - o Embryonal carcinoma
 - Mixed-type germ cell neoplasm (GCN)

IMAGING

General Features

- Best diagnostic clue
 - o Large, heterogeneous anterior/prevascular mediastinal mass in young man

Radiographic Findings

- Large anterior mediastinal mass; may grow to both sides of midline
- Mass effect on adjacent structures
- Pleural effusion

CT Findings

- Large heterogeneous prevascular mediastinal mass
- Peripheral nodular soft tissue enhancement
- Central low attenuation: Hemorrhage, necrosis, cysts
- Compression and invasion of adjacent structures
- Regional lymphadenopathy
- Pleural ± pericardial thickening/nodules/effusion
- Pulmonary metastases: Ground-glass opacity margins; hemorrhagic metastatic choriocarcinoma

MR Findings

- Large heterogeneous prevascular mediastinal mass
- T1WI: Identification of local invasion
- T1 hyperintense foci correspond to hemorrhage
- T1WI + C: Heterogeneous enhancement

Imaging Recommendations

• Best imaging tool • CECT is imaging modality of choice

DIFFERENTIAL DIAGNOSIS

Lymphoma

• Multiple lymph node groups and mediastinal compartments; nodal coalescence

Seminoma

- Large homogeneous prevascular mediastinal mass
- Rarely cystic or necrotic

Thymoma

- Unilateral prevascular mediastinal mass
- Absence of serum tumor markers

Teratoma

• Multilocular cystic mass with fluid, fat, calcium, soft tissue

PATHOLOGY

General Features

- Associated abnormalities
 - ο Elevated serum β-human chorionic gonadotropin (β-HCG) &/or a-fetoprotein (AFP) in ~ 90%
 - o Strong association with Klinefelter syndrome

Gross Pathologic & Surgical Features

• Large soft solid mass with necrosis and hemorrhage

Microscopic Features

- Yolk sac tumor
 - Recapitulates yolk sac, allantois, extra-embryonic mesenchyme
- Embryonal carcinoma
 - Recapitulates embryonic germ disk with solid, papillary, and glandular structures
- Choriocarcinoma
 - Most rare and aggressive GCN
- Mixed-type GCNs (at least 2 types of GCN)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain, dyspnea, cough, hoarseness
 - Superior vena cava syndrome
- Other signs/symptoms
 - o Male gynecomastia or female virilism: Elevated β-HCG

Demographics

Age

- Sex
 - Postpubertal patients, almost exclusively males
 - Epidemiology
 - o Less common than seminoma and teratoma

Typically 20-40 years (range: 14-80 years)

Natural History & Prognosis

- Biopsy required for definitive diagnosis
- Associated hematologic malignancies (2-6% of MGCNs), carcinomas, sarcomas
 - Poor prognosis: Median survival < 6 months

Treatment

- Cisplatin-based chemotherapy followed by surgical resection of residual mass
 - o 50% 5-year progression-free survival (in adults)

DIAGNOSTIC CHECKLIST

Consider

 Nonseminomatous MGCN in male patient with large, locally invasive, heterogeneous anterior/prevascular mediastinal mass

Image Interpretation Pearls

Testicular ultrasound excludes testicular primary MGCN

SELECTED REFERENCES

Stram AR et al: Mediastinal germ cell tumors: updates in diagnosis and 1 management. Surg Oncol Clin N Am. 29(4):571-9, 2020

KEY FACTS

TERMINOLOGY

- Peripheral nerve sheath tumors (PNST)
 Schwannoma and neurofibroma
- Malignant peripheral nerve sheath tumor (MPNST)

IMAGING

- Radiography
 - o Spherical paravertebral mass
 - Wide neural foramen
 - Benign pressure erosion of adjacent skeleton
 - Neurofibromatosis: Multifocal neurogenic neoplasms
- CT
 - Spherical paravertebral mass
 - Dumbbell tumor extension into spinal canal (10%)Variable contrast enhancement
- **MR**: Optimal assessment of intraspinal/extradural extension and spinal cord involvement

TOP DIFFERENTIAL DIAGNOSES

- Sympathetic ganglion tumor
- Paraganglioma
- Lateral thoracic meningocele

CLINICAL ISSUES

- Often asymptomatic
- Demographics: M = F
 - Schwannoma: 5th decade
 - o Neurofibroma: 2nd-4th decades
- Treatment: Surgical excision
- Prognosis
 - Indolent slow growth
 - o 5-year survival of patients with MPNST: 35%

DIAGNOSTIC CHECKLIST

• Consider PNST in adult patient with spherical paravertebral mass and skeletal pressure erosion

(Left) Graphic shows the morphologic features of peripheral nerve sheath tumor, which typically manifests as a spherical paravertebral soft tissue mass that may produce benign skeletal pressure erosion 🖂 and widening of the adjacent neural foramen \supseteq . (Right) Axial CECT of an asymptomatic patient shows a well-defined homogeneously enhancing right apical partially paravertebral soft tissue mass, a characteristic appearance and location of schwannoma.





(Left) Coned-down PA chest radiograph of an asymptomatic 40-year-old man shows a large schwannoma that manifests as a lobulated left mediastinal mass 🔁 with well-defined borders that extends above the clavicle, consistent with its paravertebral location. (Right) Axial NECT of the same patient shows a left paravertebral soft tissue mass \square with well-defined borders and intrinsic areas of low attenuation. Such lesions may produce benign pressure erosion of adjacent ribs and vertebrae.





Definitions

- Peripheral nerve sheath tumor (PNST)
 - o Schwannoma
 - o Neurofibroma
- Malignant peripheral nerve sheath tumor (MPNST) • Spindle cell sarcoma of nerve sheath origin

IMAGING

General Features

- Best diagnostic clue
 - Paravertebral mass with widened neural foramen
- Location
 - May occur along any peripheral nerve
 - Most commonly intercostal nerve; growth along undersurface of rib
 - May be centered on neural foramen and grow into spinal canal
 - Involvement of phrenic and vagus nerves less common
 - Primary airway neoplasm (rare)
- Morphology
 - o Spherical shape and horizontal axis

Radiographic Findings

- Spherical or oblong well-marginated paravertebral mass, spans 1-2 rib interspaces
 - Often centered at neural foramen, ± wide neural foramen on lateral radiography
 - Benign pressure erosion of adjacent skeleton: Posterior ribs, vertebrae
- May follow axis of involved nerve
- Horizontal extension along intercostal nerve
- Incomplete border due to extrapulmonary location
- Apical paravertebral location: Lung-mass interface may extend above clavicle
- Neurofibromatosis: Multifocal neurogenic neoplasms
 Associated abnormalities: Benign pressure erosion,
 - skeletal dysplasia, scoliosis

CT Findings

- NECT
 - Spherical or elongate paravertebral soft tissue mass
 - Decreased attenuation on CT due to lipid or cystic degeneration
 - Calcification in 10% of schwannomas
 - **Skeletal findings**: Benign pressure erosion of rib &/or vertebrae
 - **Dumbbell morphology** with extension into spinal canal (10%)
 - **Split fat sign**: Fat attenuation surrounding soft tissue neoplasm
 - Neurofibromatosis
 - Multifocal neurogenic neoplasms
 - Cutaneous nodules: Often multiple, well circumscribed
 - Skeletal manifestations
 - Well-marginated rib erosions from plexiform neurofibromas

- □ Rib deformity from associated osseous dysplasia
- □ Short segment, acute angle scoliosis
- Posterior scalloping of vertebral bodies from dural ectasia
- Pulmonary manifestations
 - □ Thin-walled upper lobe bullae associated with basilar predominant fibrosis (rare)
 - Pulmonary metastases due to malignant degeneration
- CECT
 - Decreased attenuation due to lipid or cystic degeneration
 - Variable contrast enhancement (homogeneous, heterogeneous)
 - Neurofibroma
 - □ Typically homogeneous enhancement
 - □ May exhibit early central contrast blush
 - Heterogeneity related to regions of cellular and acellular (myxoid) components
 - Local invasion, osseous destruction, and pleural effusion suggest MPNST
 - Low-attenuation regions due to hemorrhage and hyaline degeneration

MR Findings

- T1WI
 - o Variable signal intensity, often isointense to spinal cord
 - Neurofibromas may exhibit central high signal due to collagen deposition
- T2WI
 - Intermediate to high T2 signal intensity
 - Tumor may be obscured by high signal intensity cerebrospinal fluid
 - Neurofibroma: May exhibit central low signal due to collagen deposition
 - **Target sign**: Central low signal surrounded by peripheral high signal
 - Schwannoma: Fascicular sign, multiple hypointense small ring-like structures, correspond to histologic fascicular bundles
- T1WIC+FS
 - Enhancement pattern mimics that of CECT
 - Neurofibromas may exhibit target appearance
- Peripheral enhancement, cystic components, and fluid-fluid levels in neurogenic neoplasms; allow differentiation from paravertebral cysts

Imaging Recommendations

- Best imaging tool
- MR for optimal assessment of intraspinal/extradural extension and spinal cord involvement
- Protocol advice
 Gadolinium helpful for delineating intradural neoplasm

DIFFERENTIAL DIAGNOSIS

Autonomic Ganglion Tumors

• Elongate; vertical axis: Spans 3-5 interspaces

May exhibit calcification

Lateral Thoracic Meningocele

• Fluid-attenuation lesion contiguous with thecal sac

• May coexist with neurofibroma in neurofibromatosis

Paraganglioma

• Intense contrast enhancement

Neurenteric Cyst

- Rare; fluid attenuation lesion
- Associated with congenital vertebral body anomalies

Spondylodiscitis

- Centered on disc rather than on neural foramen
- May surround spine

Paraspinal Hematoma

- Following trauma
- Associated with spinal fracture

PATHOLOGY

General Features

- Genetics
 - 30% of neurofibromas associated with neurofibromatosis 1 (von Recklinghausen disease)
 - Deletion on chromosome 17
 - Neurofibromatosis 2
 - Chromosome 22q deletion
- 90% of all paravertebral masses are of neurogenic origin
 - 40% are nerve sheath tumors
 - Schwannoma to neurofibroma ratio = 3:1

Gross Pathologic & Surgical Features

- Schwannoma
 - Encapsulated nerve sheath tumor
 - Eccentric growth
 - Nerve compression
 - Frequent cystic degeneration and hemorrhage
- Neurofibroma
 - Unencapsulated disorganized proliferation of all nerve elements
 - Centrally positioned in nerve
 - Cystic degeneration and hypocellularity uncommon
 - Localized, diffuse, or plexiform
- MPNST
 - May arise de novo or within preexisting plexiform neurofibroma
 - Rare in preexisting schwannoma
 - o Usually > 5 cm

Microscopic Features

- Schwannoma
 - Antoni A (hypercellular spindle cells organized in bundles or interlacing fascicles)
 - o Antoni B (hypocellular myxoid tissue)
 - Stain positive for protein S100
- Neurofibroma
- o Myelinated and unmyelinated axons, collagen, reticulin
- MPNST
 - o Highly cellular with pleomorphic spindle cells
 - Difficult differentiation from sarcoma

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Often asymptomatic
- Other signs/symptoms
 - Symptoms of mass effect or nerve entrapment
 - Pain should raise suspicion for malignant degeneration
 - Higher incidence of malignant degeneration in neurofibromatosis 1

Demographics

- Age
 - Schwannoma: 5th decade
 - Neurofibroma: 2nd-4th decades
 - MPNST: 2nd-4th decades
- Sex
 - o M=F
- Epidemiology
 - Most common cause of paravertebral mass
 - 90% of PNST are solitary
 - Solitary PNSTs rarely undergo malignant degeneration
 - Neurofibromatosis: Malignant degeneration in approximately 4%
 - Neurofibromatosis 1: Prevalence of 1 in 3,000
 - Multiple neurogenic tumors or single plexiform neurofibroma
 - Other neoplasms: Pheochromocytoma, chronic myelogenous leukemia, optic nerve glioma, astrocytoma
 - Neurofibromatosis 2: Prevalence of 1 in 1 million
 - o MPNSTs account for 5-10% of all soft tissue sarcomas

Natural History & Prognosis

- Indolent slow growth: Rare recurrence post excision
- 5-year survival of patients with MPNST is 35%

Treatment

- Surgical excision
- Radiation not indicated, may induce malignant degeneration

DIAGNOSTIC CHECKLIST

Consider

- PNST in patient with spherical paravertebral mass and benign skeletal pressure erosion
- MPNST in paravertebral mass with locally aggressive behavior, rapid enlargement, or ill-defined margins
- MPNST in patient with new symptom of pain related to known nerve sheath tumor

Image Interpretation Pearls

- Split fat sign: Suggests neurogenic tumor
- Target sign: Typical of neurofibroma
- Fascicular sign: More common in schwannoma

- 1. Dewey BJ et al: FDG PET/CT and MRI features of pathologically proven schwannomas. Clin Nucl Med. 46(4):289-96, 2021
- Wilson MP et al: Diagnostic accuracy of MRI for the detection of malignant peripheral nerve sheath tumors: a systematic review and meta-analysis. AJR Am J Roentgenol. 1-9, 2021





(Left) CECT of a patient with a mediastinal schwannoma shows a right paravertebral mass \implies that extends through and widens the adjacent neural foramen 🔁 and produces characteristic skeletal pressure erosion 🖂 (Right) Composite image with axial T1WI MR pre- (left) and post- (right) contrast of the same patient shows that the T1-hypointense mass 🖂 demonstrates marked contrast $enhancement \square, extends$ through the adjacent neural foramen into the spinal canal, and produces mass effect on the spinal cord 🔁.





(Left) Axial NECT of an asymptomatic patient shows a right chest wall neurofibroma that exhibits characteristic benign pressure erosion 🔁 on an adjacent rib. (Right) Composite image with PA chest radiograph (left) and axial CECT (right) shows a right paravertebral neurofibroma 🔁 that manifests with a dense right hilum 🖂 on radiography and exhibits intrinsic fat attenuation and widening of the adjacent neural foramen $\overline{}$





(Left) Axial CECT of a patient with a malignant peripheral nerve sheath tumor shows a large heterogenous right paravertebral mass 🖻 that widens the adjacent neural foramen and a smaller left paravertebral neurogenic neoplasm 🔁. Malignant peripheral nerve sheath tumors are aggressive rapidly growing lesions. (Right) Composite image with axial CECT (left) and FDG PET/CT (right) shows an FDG-avid left paravertebral malignant peripheral nerve sheath tumor that produces pressure erosion of an adjacent rib 🖂

KEY FACTS

TERMINOLOGY

- Ganglioneuroma: Benign neoplasm of sympathetic ganglia
- Ganglioneuroblastoma, neuroblastoma: Malignant neoplasms of sympathetic ganglia
- Paraganglioma: Neoplasm of paraganglion cells in sympathetic or parasympathetic chains

IMAGING

- Radiography
 - Elongated paravertebral mass
 - Rib displacement, skeletal pressure erosion
- CT
 - o Homogeneous or heterogeneous paravertebral masso Paragangliomas exhibit intense contrast enhancement
- MR
 - Optimal evaluation of intraspinal extension
- Ga-68 DOTATATE PET/CT: ↑ uptake in paragangliomas

TOP DIFFERENTIAL DIAGNOSES

- Neurogenic neoplasm of nerve sheath
- Neuroenteric cyst
- Lateral thoracic meningocele
- Extramedullary hematopoiesis
- Paraspinal abscess or hematoma

CLINICAL ISSUES

- Neuroblastoma: Children < 3 years
- Ganglioneuroblastoma: Children < 10 years
- Ganglioneuroma: Adolescents and young adults

DIAGNOSTIC CHECKLIST

- Consider ganglioneuroma in adolescent or young adult with elongate paravertebral mass ± skeletal pressure erosion
- Consider neuroblastoma in infant with paravertebral soft tissue mass ± calcification

(Left) PA chest radiograph of a 30-year-old woman with a ganglioneuroma shows a large, vertically oriented right paravertebral mass that produces splaying of the right posterior 5th and 6th ribs and produces the hilum overlay sign. (Right) Lateral chest radiograph of the same patient confirms the paravertebral location of the mass. Ganglioneuromas are benign neoplasms that typically affect asymptomatic adolescents and young adults, and many are incidentally discovered on imaging.





(Left) Composite image with axial (left) and coronal (right) CECT of a 27-year-old man with a paraganglioma shows an enhancing left paravertebral mass \triangleright with an elongated morphology on coronal imaging that spans at least 3 vertebral levels. (Right) Composite image with axial T2WI MR (top left), axial T1WI C+ FS MR (bottom left), and posterior MIBG scintigram (right) of the same patient shows a T2-hyperintense soft tissue mass with internal flow voids 🔁, heterogeneous enhancement , and intenseMIBG uptake 😂.





Definitions

- Ganglioneuroma: Benign neoplasm of sympathetic ganglia
- Ganglioneuroblastoma, neuroblastoma: Malignant neoplasms of sympathetic ganglia
- Paraganglioma: Neoplasm of paraganglion cells in sympathetic or parasympathetic chains

IMAGING

General Features

• Best diagnostic clue

o **Elongated**, vertically oriented paravertebral mass

- Location
 - Sympathetic chains run vertically near costovertebral junction
 - Paragangliomas may be located along sympathetic chain, vagus nerve, or about heart
- Morphology

• Well-circumscribed smooth or lobular soft tissue mass

Radiographic Findings

- Elongated paravertebral mass spanning 2-5 vertebrae
- Rib displacement, pressure erosion of ribs and vertebrae
- Radiographic calcification in 10% of neuroblastomas

CT Findings

- Elongate paravertebral soft tissue mass
 - Homogeneous or heterogeneous
 - Neuroblastoma: Hemorrhage, cystic degeneration, necrosis
 - Approximately 85% of neuroblastomas exhibit calcification on CT
- Paragangliomas exhibit intense contrast enhancement

MR Findings

- Optimal evaluation of intraspinal extension
- Neuroblastoma: Heterogeneous signal intensity
- Ganglioneuroblastoma and ganglioneuroma: Homogeneous intermediate T1 and T2 signal
 Homogeneous enhancement
- Paraganglioma: Intense enhancement
 Relatively high T1 signal with flow voids

Nuclear Medicine Findings

- PET
- FDG-PET: Moderate sensitivity for paragangliomasMIBG scintigraphy
 - Assessment of disease extent &/or surveillance
 Up to 30% of neuroblastomas are not MIBG avid
- Ga-68 DOTATATE PET/CT
 - Increased uptake in paragangliomas

Imaging Recommendations

- Best imaging tool
 - MR optimal modality for evaluation of intraspinal growth of mediastinal neurogenic neoplasms

DIFFERENTIAL DIAGNOSIS

Neurogenic Neoplasm of Nerve Sheath

• Schwannoma, neurofibroma

• Horizontal axis, rounded, centered on neural foramen

Neuroenteric Cyst

• Fluid characteristics at MR &/or CT

Lateral Thoracic Meningocele

• Fluid characteristics; contiguous with thecal sac

PATHOLOGY

General Features

- Etiology
 - Neuroblastoma: Derived from neural crest cells
 - Paraganglioma: Neuroendocrine tumor of chromaffin cell origin
- Genetics
 - Paragangliomas may be associated with multiple endocrine neoplasia and von Hippel-Lindau

Staging, Grading, & Classification

- Staging: Neuroblastoma (Evans anatomic staging)
 - 1: Confined to organ of origin
 - 2: Growth beyond organ of origin without crossing midline
 - 3: Growth across midline
 - o 4: Distant metastases
 - 4S: Age < 1 year, metastases confined to skin, liver, bone marrow

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Neuroblastoma: Painless mass, paraneoplastic syndrome
 - o Ganglioneuroblastoma and ganglioneuroma: May be asymptomatic
 - Paraganglioma: Hypertension, blushing, headaches due to circulating catecholamines

Demographics

- Age
 - Neuroblastoma: Children < 3 years
 - Ganglioneuroblastoma: Children < 10 years
 - Ganglioneuroma: Adolescents and young adults

Natural History & Prognosis

- Ganglioneuroma: Favorable prognosis
- Chest neuroblastoma: Better prognosis than other sites

Treatment

• Surgical resection ± adjuvant chemotherapy and radiation

DIAGNOSTIC CHECKLIST

Consider

- Ganglioneuroma in adolescent or young adult with elongate paravertebral mass ± skeletal erosion
- Neuroblastoma in infant with paravertebral soft tissue mass ± calcification

SELECTED REFERENCES

1. Carter BW et al: Imaging of the posterior/paravertebral mediastinum. Radiol Clin North Am. 59(2):243-9, 2021

Neurofibromatosis

KEY FACTS

TERMINOLOGY

• Neurofibromatosis type 1 (NF1): Hereditary, neurocutaneous disorder; rarely involves lungs

IMAGING

- Radiography
 - Lung cysts, bullae; interstitial lung disease, metastases from malignant neurogenic neoplasm
 - Posterior mediastinum neurogenic neoplasm
 - Pulmonary hypertension
- CT
 - Upper lung predominant bullae and cysts
 - Basilar predominant interstitial lung disease
 - Intrapulmonary neurofibroma: Well-defined intraparenchymal nodule/mass
 - Neurofibroma: Well-defined paravertebral mass, spherical or fusiform
 - Meningocele: Water attenuation, well-circumscribed paravertebral mass

TOP DIFFERENTIAL DIAGNOSES

- Bullous emphysema
- Interstitial lung disease

PATHOLOGY

• 50-70% of NF1 cases exhibit autosomal dominant inheritance; mutation in neurofibromin gene

CLINICAL ISSUES

- NF1: 1 in 3,000 individuals; M = F
- Pulmonary disease uncommon; < 70 cases reported
- Signs/symptoms: Dyspnea, cough, chest pain; pneumothorax; dyspnea and syncope from pulmonary hypertension
- Treatment: Surgical resection of symptomatic bullae/cysts

DIAGNOSTIC CHECKLIST

• Consider NF1 in patients with cystic lung disease and multiple neurogenic neoplasms

(Left) Axial CECT of a 26-yearold woman with neurofibromatosis type 1 shows multiple small, thinwalled upper lobe cysts 3. Note spinal hardware 3 for treatment of thoracic scoliosis. (Right) Coronal CECT of the same patient shows the classic upper lobe distribution of the cystic lung lesions 3 in patients with neurofibromatosis type 1. Pulmonary involvement occurs

in up to 20% of affected adults. It has been suggested that lung cysts or bullae in these patients may represent smoking-related emphysema.





(Left) Axial HRCT of a 20-yearold woman with neurofibromatosis type 1 shows a small, thin-walled right lower lobe cyst 🔁 Bullae and cysts in affected patients have been reported to exhibit an upper lobe predominance. (Right) Axial CECT of a 31-year-old man shows soft tissue lesions in the mediastinum 🔁, subcutaneous tissues 🖂, and intercostal spaces \bowtie , consistent with neurofibromas. Such peripheral neurogenic tumors are a pathognomonic feature of neurofibromatosis type 1.





- Abbreviations
- Neurofibromatosis type 1 (NF1)

Synonyms

- von Recklinghausen disease
- Peripheral neurofibromatosis

Definitions

• NF1: Hereditary, neurocutaneous disorder with systemic manifestations including lung involvement (10-20% of affected adults)

IMAGING

Radiographic Findings

- Lung
 - Cysts and bullae: Radiolucent foci
 - Interstitial lung disease: Bilateral, symmetric reticular opacities; basilar predominance
 - o Intrapulmonary neurofibroma: Lung nodule or mass
 - Multiple lung nodules/masses due to metastases from malignant degeneration of neurogenic neoplasm
- Mediastinum
 - Neurogenic neoplasm (posterior mediastinum): Mediastinal widening; extraparenchymal soft tissue mass with well-defined borders
 - Pulmonary hypertension (associated with lung disease or with plexiform lesions involving vascular intima): Dilated right ventricle, enlarged central pulmonary arteries
- Bone: Rib separation and pressure erosion, scoliosis, posterior scalloping of vertebral bodies, enlarged neuroforamina

CT Findings

- Lungs
 - Asymmetric, thin-walled bullae/cysts
 - Solitary or multiple; may be large
 - Upper lobe predominant
 - Interstitial lung disease: Reticulation, linear opacities (peripheral and lower lobe predominance)
 - Honeycombing uncommon
 - Intrapulmonary neurofibroma: Well-defined lung nodule or mass
 - Multiple nodules/masses due to metastases from malignant degeneration of neurogenic neoplasm
- Mediastinum
 - Neurogenic neoplasm: Well-defined paravertebral mass, spherical or fusiform, variable contrast enhancement
 - Meningocele: Water attenuation, well-circumscribed paravertebral mass
 - Pulmonary hypertension: Pulmonary trunk > 29 mm, mosaic attenuation
- Bone
 - o Scoliosis: Most common osseous complication of NF1
 - Vertebral scalloping, neuroforaminal widening, transverse process spindling, rib penciling of neuroforamen
 - o Pectus excavatum and carinatum, kyphoscoliosis

MR Findings

• Evaluation of intraspinal involvement of neurogenic neoplasm

Imaging Recommendations

- Best imaging tool
 - HRCT for evaluation of lung abnormalities
 - CECT for evaluation of pulmonary trunk size

DIFFERENTIAL DIAGNOSIS

Bullous Emphysema

- Cigarette smoking is risk factor
- Centrilobular emphysema

Interstitial Lung Disease

• Absence of extrapulmonary NF1 findings

PATHOLOGY

General Features

- Etiology
 - NF1: Mutations in neurofibromin gene (long arm of chromosome 17)
- Genetics
 - 50-70% of NF1 cases exhibit autosomal dominant inheritance
- Diagnostic criteria
 - At least 2 criteria: Café au lait spots, axillary or groin freckling, neurofibromas, optic glioma, iris hamartomas (Lisch nodules), bone abnormalities (sphenoid wing dysplasia, long bone cortical thinning ± pseudoarthrosis), 1st-degree relative with NF1

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Pulmonary disease uncommon; < 70 cases reported
 - Dyspnea, cough, chest pain
 - Pneumothorax from cyst or bulla rupture
 - o Dyspnea and syncope from pulmonary hypertension

Demographics

- Epidemiology
 - NF1: 1 in 3,000 individuals; M = F

Treatment

• Surgical resection of symptomatic bullae/cysts

DIAGNOSTIC CHECKLIST

Consider

 NF1 in patients with cystic lung disease and multiple neurogenic neoplasms

- Alves Júnior SF et al: Neurofibromatosis type 1: state-of-the-art review with emphasis on pulmonary involvement. Respir Med. 149:9-15, 2019
- Casal A et al: Neurofibromatosis type I with lung involvement in a cancer patient. Pulmonology. 24(4):269-71, 2018

KEY FACTS

IMAGING

- Best diagnostic clue: Thoracic lymph nodes ≥ 10 mm on CT + FDG uptake on PET/CT
- Radiography
 - Abnormal mediastinal contours
 - o Abnormal lines, stripes, and interfaces
- CT
 - o Most common finding is lymph node enlargement
 - o Abnormal when lymph nodes ≥ 10 mm
 - Hypoattenuation, enhancement, &/or calcification
 - Specific lymphatic drainage pathways for intrathoracic and some extrathoracic malignancies
- **PET/CT**: FDG uptake in lymph node metastases
 - Improved detection of lymph node metastases in lung cancer and regional lymph node metastases in esophageal cancer
 - False-positives: Granulomatous diseases and infectious/inflammatory processes

TOP DIFFERENTIAL DIAGNOSES

- Lymphoma
- Sarcoidosis

PATHOLOGY

• Lymph node metastases more common from intrathoracic than extrathoracic malignancies

CLINICAL ISSUES

- Lymph node staging in intrathoracic and extrathoracic malignancy important for prognosis and treatment
 - Lung cancer: Advanced nodal disease precludes surgical resection
 - Breast cancer: Advanced nodal disease necessitates preoperative chemotherapy

DIAGNOSTIC CHECKLIST

• Consider metastatic disease in patients with cancer and intrathoracic lymphadenopathy

(Left) Graphic demonstrates typical features of advanced malignancy with multifocal bilateral pulmonary nodules representing hematogenous metastases, bilateral malignant pleural effusions, and metastatic disease to hilar \square and mediastinal \square lymph nodes. (Right) Coronal CECT of a patient with esophageal cancer 🔁 demonstrates multiple mediastinal lymph node metastases 🔁. In cases of esophageal cancer, lymph node staging involves determining the specific number of lymph nodes affected.





(Left) Axial CECT of a patient with metastatic hepatocellular carcinoma demonstrates multiple enlarged heterogeneous mediastinal lymph node metastases 🔁. Lymph node metastases from extrathoracic malignancies are much less common than those from intrathoracic malignancies. (Right) Composite image with axial NECT in soft tissue (left) and lung window (right) shows a metastatic aortopulmonary window node 🛃 from a primary left upper lobe lung cancer \rightarrow .





IMAGING

General Features

- Best diagnostic clue
 o Intrathoracic lymph nodes ≥ 10 mm on CT
 o FDG uptake within lymph nodes on FDG PET/CT
- Location
 - o Most commonly involves mediastinal lymph nodes
- Morphology
 - o Hypoattenuation, enhancement, &/or calcification

Radiographic Findings

- Radiography
 - Lymphadenopathy may produce **abnormal mediastinal contours**
 - Right paratracheal lymph nodes
 Thickening of right paratracheal stripe
 - □ Convexity of superior vena cava interface
 - Left paratracheal lymph nodes
 Thickening of left paratracheal stripe
 - Convexity of left subclavian artery interface
 - Prevascular lymph nodes
 Anterior mediastinal mass
 Thickening of anterior junction line
 - Subcarinal lymph nodes: Convexity of upper azygoesophageal recess
 - Hilar lymph nodes: Hilar enlargement and lobulation
 - Aortopulmonary lymph nodes: Convexity of
 - aortopulmonary window

CT Findings

- Lymph node enlargement, most common finding
- Short-axis lymph node diameter is most reproducible measurement
 - Low paratracheal and subcarinal: > 11 mm
 - High paratracheal and superior mediastinal: > 7 mm
 - Right hilar and paraesophageal: > 10 mm
 - Left hilar and paraesophageal: > 7 mm
 - Peridiaphragmatic: > 5 mm
- o General
 - Paratracheal, hilar, subcarinal, paraesophageal, paraaortic, and subaortic lymph nodes: ≥ 10 mm
 - Internal mammary, retrocrural, and extrapleural lymph nodes: No size criteria
 - Visualization is considered abnormal
- Lymph node size is not always reliable
 - 13% of lymph nodes that measure < 10 mm contain metastatic foci
 - Meta-analysis for lung cancer
 - □ Sensitivity: 57%
 - □ Specificity: 82%
 - □ Positive predictive value (PPV): 56%
 - □ Negative predictive value (NPV): 83%
- Sensitivity for axillary metastases: 50-60%
- Various imaging appearances based on primary tumor of origin
 - Hypoattenuation
 - Lung cancer
 - Extrathoracic malignancy: Seminoma, ovarian, thyroid, and gastric cancers

- Enhancement
- Lung cancer
- Extrathoracic malignancy: Renal cell and thyroid cancers, melanoma, sarcoma
- Calcification
 - Mucinous adenocarcinomas of colon and ovary, thyroid cancer, osteosarcoma
- Intrathoracic malignancy may spread along specific lymphatic drainage pathways
 - o Lung cancer
 - Most tumors initially drain to hilar lymph nodes
 - Subsequent spread depends on lobe of origin
 - Right upper lobe
 Right paratracheal and prevascular mediastinal
 - lymph nodes – Right middle and lower lobes
 - Subcarinal, right paratracheal, and prevascular mediastinal lymph nodes
 - Left upper lobe
 - Subaortic and paraaortic lymph nodes
 - Left lower lobe
 - Subcarinal and subaortic lymph nodes
 - Esophageal cancer
 - Upper and middle esophagus
 - Lymphatics drain cephalad
 - Paratracheal lymph nodes
 - Lower esophagus
 - Lymphatics drain toward abdomen
 - □ Gastrohepatic ligament lymph nodes
 - Nodal disease may be extensive at presentation
 - "Skip" metastases are common
 - Direct communication between esophageal lymphatics and thoracic duct
 - Malignant pleural mesothelioma
 - Drainage pathways differ by location of pleural and diaphragmatic involvement
 - Pleura
 - Anterior: Internal mammary (upper and middle thorax) and peridiaphragmatic lymph nodes (lower thorax)
 - Posterior: Extrapleural lymph nodes
 - Diaphragm
 - Anterior and lateral: Internal mammary and anterior peridiaphragmatic lymph nodes
 - Posterior: Paraaortic and posterior mediastinal lymph nodes
- Some extrathoracic malignancies may spread along specific lymphatic drainage pathways
 - Breast cancer
 - 3 primary routes of spread: Axillary, transpectoral, and internal mammary pathways

Nuclear Medicine Findings

- PET/CT
 - FDG uptake within lymph nodes
 - Improved detection of metastatic lymph nodes in lung cancer
 - □ Sensitivity: 84%
 - □ Specificity: 89%
 - □ PPV: 79%

Metastatic Disease, Lymphadenopathy

Clinical Lymph Node Staging

Lung Cancer	
NX	Regional lymph nodes cannot be assessed
NO	No regional lymph nodes
N1	Ipsilateral peribronchial &/or ipsilateral hilar and intrapulmonary lymph nodes
N2	Ipsilateral mediastinal &/or subcarinal lymph nodes
N3	Contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes
Esophageal Cancer	
NX	Regional lymph nodes cannot be assessed
NO	No regional lymph nodes
N1	Metastasis in 1-2 regional lymph nodes
N2	Metastasis in 3-6 regional lymph nodes
N3	Metastasis in \geq 7 regional lymph nodes
Malignant Mesothelioma	
NX	Regional lymph nodes cannot be assessed
NO	No regional lymph nodes
N1	Ipsilateral intrathoracic lymph nodes
N2	Contralateral intrathoracic lymph nodes, or contralateral or ipsilateral supraclavicular lymph nodes

□ NPV: 93%

- Improved detection of metastatic regional lymph nodes in esophageal cancer
 - □ PPV of regional lymph nodes: 93.8% (vs. 62.5-73.7% for CT)
- False-positive findings: Granulomatous disease, infection, inflammation

MR Findings

- Accuracy similar to that of CT
- Gadolinium contrast administration improves staging accuracy

Imaging Recommendations

- Best imaging tool
 - CT optimal for identifying lymphadenopathy: Lymph node size not always reliable as indicator of metastasis
 - FDG PET/CT improves accuracy

DIFFERENTIAL DIAGNOSIS

Lymphoma

- Enlarged lymph nodes; may or may not enhance
- Untreated lymphoma does not calcify
- Treated lymphoma may calcify
- Hodgkin lymphoma more commonly involves thorax than non-Hodgkin lymphoma

Sarcoidosis

- Multisystem chronic inflammatory disorder characterized by noncaseating granulomas
- Bilateral symmetric hilar and right paratracheal lymphadenopathy
- Calcified lymph nodes may be present
- FDG PET/CT may be used to assess treatment response • False-positive in evaluation of intrathoracic metastatic lymphadenopathy

PATHOLOGY

General Features

- Etiology
 - Lymph node metastases more common from intrathoracic than extrathoracic malignancies
 - Intrathoracic: Lung and esophageal cancers, malignant pleural mesothelioma
 - Extrathoracic: Head and neck, genitourinary tract, and breast cancers, melanoma

CLINICAL ISSUES

Treatment

- Lung cancer
 - N1: Resectable in absence of mediastinal tumor invasion, malignant pleural effusion, satellite nodules, or metastases
 - o N2: Possibly amenable to resection; chemotherapy and radiation also used
 - N3: Not amenable to resection
- Malignant pleural mesothelioma
 - Most patients have advanced disease at presentation
 - Some may benefit from surgery and chemotherapy

DIAGNOSTIC CHECKLIST

Consider

• Metastatic disease in patients with cancer and intrathoracic lymphadenopathy

- Wang A et al: Lymph node metastatic patterns and its clinical significance for thoracic superficial esophageal squamous cell carcinoma. J Cardiothorac Surg. 15(1):262, 2020
- Carter BW et al: Revisions to the TNM staging of lung cancer: rationale, 2. significance, and clinical application. Radiographics. 38(2):374-91, 2018





(Left) Axial CECT of a patient with thyroid cancer demonstrates heterogeneously enhancing lymph nodes \supseteq in the visceral mediastinum adjacent to the trachea and esophagus. Enhancing lymph node metastases may be due to lung, renal cell, and thyroid cancers, melanoma, and sarcoma. (Right) Axial CECT shows metastatic ovarian cancer manifesting as calcified mediastinal lymph nodes 🖂 Calcified lymph node metastases may be due to colon, ovarian, and thyroid cancers, and osteosarcoma.





(Left) Axial CECT shows extensive left pleural thickening due to malignant pleural mesothelioma 🖾 and metastatic ipsilateral and contralateral mediastinal lymphadenopathy 🖂 (Right) Fused axial FDG PET/CT of a patient with FDG-avid malignant pleural mesothelioma 🖘 demonstrates an FDG-avid left paratracheal lymph node 🔁, consistent with metastasis. FDG PET/CT added value in this case by identifying FDG avidity in a mediastinal lymph node that was normal in size.





(Left) Axial CECT of a patient with esophageal cancer (not shown) demonstrates multiple enlarged heterogeneously enhancing right mediastinal lymph nodes 🖂 (Right) Whole-body FDG PET of the same patient shows increased FDG uptake in the primary esophageal cancer \supseteq , mediastinal lymph nodes 🖂, and right axillary lymph nodes ∠ Demonstration of FDG avidity in right axillary lymph nodes resulted in accurate staging for this patient.

Mediastinal Lymphoma

KEY FACTS

TERMINOLOGY

- Non-Hodgkin lymphoma (NHL)
- Hodgkin lymphoma (HL)
- Lymphoma arising primarily within or secondarily involving mediastinum

IMAGING

- **Radiography**: Anterior mediastinal mass; extends to both sides of midline; often large
- CT
 - Large heterogeneous mass &/or lymphadenopathy in prevascular mediastinum
 - Frequent involvement of multiple mediastinal compartments and lymph node stations
 - Infiltration between or encasement of vascular structures, ± mass effect or local invasion
- **PET/CT**: Imaging modality of choice for initial staging and ongoing surveillance

TOP DIFFERENTIAL DIAGNOSES

- Metastatic disease
- Thymic neoplasms (epithelial and neuroendocrine neoplasms)
- Malignant germ cell neoplasms
- Thymic hyperplasia
- Infection (tuberculosis, other granulomatous infection)
- Sarcoidosis

PATHOLOGY

• Core-needle biopsy for diagnosis: Cellular morphology and immunohistochemistry determine subtype

CLINICAL ISSUES

• Lymphoma favored in younger patients < 40 years with mediastinal mass and associated lymphadenopathy

DIAGNOSTIC CHECKLIST

• Consider malignant germ cell neoplasms in young man < 40 years with large invasive prevascular mediastinal mass

(Left) PA chest radiograph of a patient with diffuse large Bcell lymphoma shows a large left mediastinal mass that produces mass effect on the trachea with rightward deviation ⇒ and a small left pleural effusion. (Right) Axial fused FDG PET/CT of the same patient shows a large heterogeneous prevascular and visceral mediastinal FDGavid mass that compresses &/or invades the great vessels and the adjacent left lung.





(Left) Axial NECT of a patient with Hodgkin lymphoma shows a large prevascular mediastinal mass with indistinct tissue planes with the adjacent anterior chest wall concerning for direct chest wall invasion \supseteq and right upper paratracheal lymphadenopathy 🔁. (Right) Coronal fused FDG PET/CT of the same patient shows marked FDG avidity within the predominantly left-sided mediastinal mass 🔁 and additional FDG avid left supraclavicular lymphadenopathy 🔁.





Abbreviations

- Non-Hodgkin lymphoma (NHL)
- Hodgkin lymphoma (HL)

Synonyms

• Primary mediastinal lymphoma

Definitions

- Lymphoma arising primarily within or secondarily involving mediastinum
- Primary mediastinal lymphomas
 - Rare, comprise approximately 1% of all lymphomas; most common primary mediastinal malignancies

IMAGING

General Features

- Best diagnostic clue
 - Large mediastinal mass ± lymphadenopathy; often involves multiple mediastinal compartments
- Location
 - Prevascular mediastinum most commonly affected; frequent involvement of multiple mediastinal compartments
- Size
 - Usually large bulky masses > 10 cm
- Morphology
 - Lobulated heterogenous soft tissue masses, frequently encase mediastinal structures, ± mass effect or invasion

Radiographic Findings

- Mediastinal mass on frontal chest radiography; extension to both sides of midline; effacement of mediastinal lines, stripes, interfaces
 - ± narrowing or shift of trachea
- ± hilar lymphadenopathy

CT Findings

- Large heterogeneous mass &/or lymphadenopathy in prevascular mediastinum
- Frequent involvement of multiple mediastinal compartments and lymph node stations
- Infiltration between &/or encasement of vascular structures, ± mass effect or local invasion
- ± pulmonary opacities
 - Consolidation ± atelectasis: Post-obstructive pneumonia &/or lymphomatous involvement
 - Nodules &/or masses, ± cavitation
 - May represent lymphoma or infection (including atypical or opportunistic pathogens)
- Pleural &/or pericardial disease
 - Unilateral > bilateral pleural effusions, exudative
 - Pericardial effusion
 - Pleural or pericardial nodular thickening suggests lymphomatous involvement

MR Findings

• Variable T1-hypointense and T2-hyperintense signal in comparison to skeletal muscle

- DWI: Diffusion restriction with low ADC values suggests malignancy; cannot differentiate lymphoma from other malignancy
- T1WI C+: Mildly heterogeneous contrast enhancement
 - Dynamic contrast enhancement (DCE): Persistent or progressive enhancement

Nuclear Medicine Findings

- PET/CT
 - PET/CT: Imaging modality of choice for initial staging and surveillance
 - FDG uptake in lymph nodes &/or extranodal sites corresponds to active disease

Imaging Recommendations

- Best imaging tool
 - CECT for lesion characterization and assessment of mass effect/invasion of adjacent structures
 - PET/CT modality of choice for initial staging, assessment of treatment response, and ongoing surveillance
- Protocol advice
 - CECT images acquired at 60-90 seconds to allow opacification of arterial and venous structures

DIFFERENTIAL DIAGNOSIS

Mediastinal Metastases

- Direct extension from primary lung cancer
- Nodal metastases from various other malignancies

Thymic Neoplasms

- Patients > 40 years
- Epithelial neoplasms (thymoma, thymic carcinoma), neuroendocrine neoplasms

Malignant Germ Cell Neoplasms

- May be indistinguishable from lymphoma on imaging
- Seminoma
 - o Almost exclusively young men aged 20-40 years
- Non-seminomatous malignant germ cell neoplasms (NSMGCN)
 - Almost exclusively young men; mean age of 30 years at presentation
 - ↑ a-fetoprotein (AFP) and β-human chorionic gonadotropin (β-HCG) in > 50% of patients

Thymic Hyperplasia

- True thymic hyperplasia vs. lymphoid hyperplasia
 - Signal drop on opposed-phase chemical shift GRE T1WI MR

Infection

- Granulomatous infections (tuberculosis, histoplasmosis)
- Concurrent pulmonary consolidations ± cavitation suggests infectious etiology; may also be seen in lymphoma

Sarcoidosis

- Diagnosis of exclusion
- Bilateral hilar and right paratracheal lymphadenopathy in > 95% of patients
 - Prevascular mediastinal lymphadenopathy &/or masses uncommon
- Pulmonary perilymphatic micronodularity ± fibrosis favors sarcoidosis

PATHOLOGY

General Features

- Etiology
 - Lymphomas: Heterogeneous neoplasms with frequent intrathoracic involvement; 4.8% of newly diagnosed malignancies
 - Lymphoma may arise primarily in mediastinum or involve it secondarily
 - o Primary mediastinal lymphoma
 - Involvement of mediastinal lymph nodes &/or thymus; no evidence of extranodal &/or systemic disease at presentation
- Histologic subtypes
 - Diffuse large B-cell lymphoma (DLBCL)
 - 33% of primary mediastinal malignancies; 65% of primary mediastinal lymphomas
 - Primary mediastinal and systemic DLBCL are histologically indistinguishable
 - Primary mediastinal (thymic) B-cell lymphoma (PMBCL)
 - Subtype of DLBCL: High-grade extranodal thymic Bcell lymphoma
 - Difficult clinical distinction from classic HL (CHL): Both may manifest as anterior/prevascular mediastinal mass in young woman
 - o HL
 - Systemic HL with mediastinal involvement or primary mediastinal HL
 - Two major subtypes: CHL and nodular lymphocyte predominant HL (NLP-HL)
 - Gray zone lymphoma (GZL)
 - Aggressive subtype
 - Diagnosis based on cell morphology and immunohistochemistry
 - o T-cell lymphoblastic lymphoma (TCLL)
 - Aggressive subtype
 - Thymic extranodal marginal-zone B-cell lymphoma
 - Rare low-grade extranodal lymphoma of mucosaassociated lymphoid tissue (MALT) arising in thymus
 - Strong association with autoimmune disease, particularly Sjögren syndrome

Staging, Grading, & Classification

- Revised Ann-Arbor staging system
 - Limited stage (I-II) vs. advanced stage (III-IV)
 - Sub-classifications for "bulky" and "extranodal" disease
 - Extent of disease determined by CT or PET/CT
- Deauville criteria
 - 5-point scale based on visual assessment of FDG uptake on PET and PET/CT
 - Range: 1 (no uptake) to 5 (markedly elevated uptake above liver &/or new sites of disease)
- Lugano Criteria
 - Clinical and imaging findings to define extension
 - PET/CT for staging and monitoring
 - CECT for more accurate lymph node measurement, vascular involvement, and radiation planning
 - Response categories: Complete response (CR), partial response (PR), stable disease/no response (NR), progressive disease (PD)

Gross Pathologic & Surgical Features

- Mass often bulky (usually > 10 cm)
- Most frequently diagnosed on core-needle biopsy
 - Mediastinal lymphomas are generally non-resectable, unusual to have resection specimen

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Symptoms from mass effect/invasion of mediastinal structures: Cough, dyspnea, superior vena cava syndrome, effusions
 - o Systemic "B" symptoms: Fever, night sweats, weight loss
- Other signs/symptoms
 - 30-50% of young adult patients with CHL may be asymptomatic at diagnosis

Demographics

- DLBCL: 9% of NHL; older patients > 70 years, less frequently children; slight male predilection
- PMBCL: < 5% of all NHL; M:F = 1:2; median age: 30-40 years
- HL: Bimodal age distribution; young adults (more often females) between 20 and 40 years, and older patients > 70 years
- GZL: Rare (less common than CHL, DLBCL, PMBCL); M > F
- TCLL: Most common T-cell lymphoma; 2-4% of adult NHL; adolescent males, but affects all ages
- Thymic MALT lymphoma: Rare; F > M

Natural History & Prognosis

- Varies based on histologic subtypes and disease stage
 HL better prognosis than NHL
 - PMBCL more favorable prognosis compared to DLBCL.
 - DLBCL, GZL, and TCLL more aggressive, with poorer prognoses

Treatment

- Multi-agent chemotherapy based on histology and stage ± immunotherapy/targeted therapy ± radiation
- Refractory disease: Salvage chemotherapy ± radiation ± autologous stem cell transplantation

DIAGNOSTIC CHECKLIST

Consider

- Malignant germ cell neoplasm in young man < 40 years with large invasive prevascular mediastinal mass
- Thymic epithelial neoplasm in patients > 40 years with prevascular mediastinal mass ± parathymic syndrome

Image Interpretation Pearls

• Large mediastinal mass ± lymphadenopathy which often involves multiple mediastinal compartments

- 1. Pfau D et al: Primary Mediastinal large B-cell lymphoma: a review for radiologists. AJR Am J Roentgenol. 213(5):W194-210, 2019
- Ceriani L et al: Positron emission tomography/computed tomography assessment after immunochemotherapy and irradiation using the Lugano classification criteria in the IELSG-26 study of primary mediastinal B-cell lymphoma. Int J Radiat Oncol Biol Phys. 97(1):42-9, 2017

Mediastinal Lymphoma





(Left) PA chest radiograph of a patient with primary mediastinal B-cell lymphoma shows a large lobulated mediastinal mass that extends to both sides of midline 🔁 and a small left pleural effusion 🖾 (Right) Axial CECT of the same patient shows an infiltrative mediastinal soft tissue mass that involves the prevascular and visceral compartments, encases the thoracic great vessels, and obliterates the bilateral brachiocephalic veins. Chest wall collaterals \implies are consistent with superior vena cava obstruction.





(Left) Axial CECT of a patient with gray zone lymphoma shows a large heterogeneous prevascular mediastinal mass with intrinsic necrosis \supseteq and right hilar 🔁 and subcarinal Iymphadenopathy. (Right) Axial fused FDG PET/CT of the same patient shows a large heterogeneous FDG-avid prevascular mediastinal mass with direct invasion of the adjacent chest wall 差. Note areas of intrinsic photopenia ➡ that likely correspond to necrosis.





(Left) Axial fused FDG PET/CT of a patient with T-cell lymphoblastic lymphoma shows a large heterogeneous FDG-avid prevascular mediastinal mass with areas of photopenia \supseteq indicative of internal necrosis and FDG-avid subcarinal lymphadenopathy Axial NECT of a patient with Sjögren syndrome, lymphoid interstitial pneumonia, and mucosa-associated lymphoid tissue lymphoma shows a homogeneous left prevascular mediastinal mass \supseteq that involves the thymus.

Fibrosing Mediastinitis

KEY FACTS

TERMINOLOGY

- Fibrosing mediastinitis (FM)
- Benign condition characterized by proliferation of dense fibrous tissue in mediastinum

IMAGING

- Radiography
 - Abnormalities often subtle and nonspecific
 - Mediastinal widening, hilar enlargement ± calcification
- CT
 - Infiltrative mediastinal soft tissue ± calcification
 - Encasement and obstruction of central airways and vasculature
 - Superior vena cava (SVC) obstruction/syndrome
- MR
 - Intermediate signal intensity on T1WI and T2WI, heterogeneous enhancement
- **CECT** for optimal evaluation of extent of involvement and complications

TOP DIFFERENTIAL DIAGNOSES

- Lymphoma
- Metastatic disease
- Primary mediastinal neoplasm
- Tuberculosis
- Primary lung cancer

CLINICAL ISSUES

- Etiology: *Histoplasma capsulatum*, other fungi, tuberculosis, autoimmunity, IgG4-related disease
- Cough, dyspnea, infection, hemoptysis, chest pain
- Prognosis: Unpredictable course, slow progression
- Medical treatment: Corticosteroids for nongranulomatous FM, emerging role of immunomodulatory therapy
- Non-surgical/surgical procedures: Symptomatic patients

DIAGNOSTIC CHECKLIST

• Consider mediastinal fibrosis in young patients with obstructive mediastinal soft tissue and calcification

(Left) Axial CECT of a patient with fibrosing mediastinitis shows partially calcified right lower paratracheal lymphadenopathy 🖂 (Right) Axial CECT of the same patient shows partially calcified right lower paratracheal, subcarinal, and hilar lymphadenopathy that produces partial encasement and narrowing of the bronchus intermedius \square , the distal right pulmonary artery 🔁, and the proximal right interlobar pulmonary artery.





(Left) PA chest radiograph of a patient with fibrosing mediastinitis shows partially calcified left hilar soft tissue \square , low left lung volume and left basilar linear opacities. The enlarged right interlobar pulmonary artery $rac{1}{2}$ suggests pulmonary hypertension. (Right) Coronal CECT of the same patient shows encasement/stenosis of left central bronchovascular structures by calcified soft tissue 🖾, and diminutive left lung vasculature. Note subpleural opacities \square due to venolymphatic congestion.





- Abbreviations
- Fibrosing mediastinitis (FM)

Synonyms

• FM, mediastinal fibrosis, sclerosing mediastinitis

Definitions

• Rare benign but potentially life-threatening condition characterized by proliferation of infiltrative mediastinal fibrous tissue

IMAGING

General Features

- Best diagnostic clue
 - Mediastinal/hilar soft tissue with calcification + findings of vascular or airway obstruction
- Location
 - Mediastinum: Right paratracheal and subcarinal regions most commonly affected
 - o Unilateral > bilateral hilar involvement

Radiographic Findings

- Chest radiographs usually show abnormalities; may be subtle and nonspecific
- Abnormal mediastinal widening, loss of normal lines, stripes, interfaces
- ± unilateral or bilateral hilar enlargement
- Mediastinal &/or hilar calcification
- Secondary pulmonary manifestations, depending on disease severity
 - o Volume loss/atelectasis
 - Interstitial opacities and peribronchial cuffing
 - Hyperlucency from pulmonary artery obstruction with ↓ perfusion, &/or air-trapping
 - o Pulmonary infarct: Peripheral wedge-shaped opacity

CT Findings

- CECT
 - o General
 - Localized or Infiltrative mediastinal soft tissue that encases mediastinal structures and obliterates tissue planes
 - Two distinct subtypes
 - Granulomatous (focal): 80-90% of cases
 - □ Localized or infiltrative soft tissue: Right paratracheal and subcarinal, hilar
 - □ Calcification common: Stippled or dense
 - Signs of prior granulomatous infection: Calcified granulomas, broncholithiasis, splenic and hepatic calcifications
 - Soft tissue component may be minimal or absent; calcification associated with vascular &/or airway stenosis may be dominant finding
 - Nongranulomatous (diffuse): 10-20% of cases
 - Ill-defined infiltrative soft tissue involving multiple mediastinal compartments
 - Calcification typically absent

- Concurrent extrathoracic manifestations: Retroperitoneal fibrosis, sclerosing cholangitis, and pancreatitis (pancreatitis)
- Tracheobronchial stenosis
 - Post-obstructive atelectasis and recurrent pneumonia: Endobronchial mucus plugs, bronchiectasis, pulmonary fibrosis
- o Pulmonary vascular involvement
 - Pulmonary arteries
 - Encasement of central pulmonary arteries; narrowing or obliteration of affected vessels and peripheral branches
 - □ Collateral vascularity: Bronchial artery hypertrophy, transpleural/systemic collaterals
 - Pulmonary veins
 - Encasement of central pulmonary veins; resultant venous and lymphatic congestion (focal venoocclusive disease)
 - □ Ground-glass opacities, interlobular septal thickening, bronchial wall thickening
 - Pleural effusion ± thickening (unilateral > bilateral)
 - Pulmonary hypertension: Enlarged pulmonary trunk and branches
 - Pulmonary infarct (chronic arterial or venous obstruction): Peripheral, subpleural, wedge-shaped opacity

• Superior vena cava (SVC) obstruction/syndrome

- Most frequent serious complication of mediastinal fibrosis
- SVC stenosis/obliteration
- Chest wall and mediastinal collateral vessels
- Enhancing hepatic pseudolesion in segment IV from vascular shunt
- Pericardial thickening ± calcification
- Focal esophageal stenosis
- Diaphragmatic paralysis

MR Findings

- Variable intermediate signal on T1WI and T2WI
- T1WI C+: Variable heterogeneous enhancement

Fluoroscopic Findings

- Esophagram
 - Esophageal involvement
 - Mid-esophagus most commonly affected, typically near trachea or mainstem bronchi
 - Focal circumferential narrowing, long-segment strictures

Nuclear Medicine Findings

- PET/CT
- Variable FDG uptake, areas of active inflammation
- V/Q scan
 - Ventilation scintigraphy with Xe-133 or Tc-99m-DTPA
 - Partial or complete airway obstruction: Ventilation defects, delayed washout of Xe-133
 - Perfusion scintigraphy with Tc-99m-MAA
 - Pulmonary arterial or venous obstruction: Focal or diffuse perfusion defects
Angiographic Findings

• Focal or long-segment vascular stenoses, vary with disease severity

Imaging Recommendations

- Best imaging tool
 - CECT for optimal evaluation of extent of involvement and complications

DIFFERENTIAL DIAGNOSIS

Lymphoma

- Treated lymphoma (particularly Hodgkin lymphoma) may exhibit calcification
- Sclerosing lymphoma subtypes may mimic nongranulomatous MF

Metastatic Disease

• Soft tissue masses may exhibit sclerosing features and calcification

Primary Mediastinal Neoplasm

• Mediastinal sarcomas, desmoid tumors

Tuberculosis

• Concurrent pulmonary manifestations of active or latent infection

Primary Lung Cancer

 Asymmetric hilar/pulmonary mass with mediastinal involvement

Castleman Disease

• Typically no features of airway or vascular obstruction

PATHOLOGY

General Features

- Etiology
 - Granulomatous (focal) subtype: (80-90% of cases)
 - Abnormal immunologic response to antigenic stimulation
 - Most cases due to Histoplasma capsulatum
 - Rarely, inflammatory conditions, such as sarcoidosis
 - Nongranulomatous (diffuse) subtype: (10-20% of cases)
 Associated with autoimmune diseases
 - Associated with addominine diseases
 Immunoglobulin G4-related disease (IgG4-RD)
 - Multi-organ involvement (retroperitoneal fibrosis, sclerosing cholangitis, autoimmune pancreatitis, Riedel thyroiditis, orbital pseudotumor)
 - Drug toxicity (e.g., methysergide)
 - Complication of radiation therapy
- Genetics
 - Abnormal fibroinflammatory response to antigenic stimulation; may affect genetically susceptible individuals

Staging, Grading, & Classification

- Granulomatous FM: Localized mediastinal or hilar fibrosis + extensive calcification
- Nongranulomatous FM: Multicompartmental mediastinal fibrosis without calcification

Gross Pathologic & Surgical Features

• Localized mass or Ill-defined infiltrative dense, white, fibrous soft tissue

Microscopic Features

• Infiltration and obliteration of mediastinal fat by fibrous tissue and mononuclear cell infiltrate

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Cough, dyspnea, recurrent infection, hemoptysis, chest pain
- Other signs/symptoms
- Fever and weight loss

Demographics

- Age
 - Granulomatous FM: Most patients young at presentation (mean age: 35-46 years)
 - Nongranulomatous FM: Middle-aged and older patients
- Sex
 - Granulomatous FM: M = F
 - Nongranulomatous FM: M > F

Natural History & Prognosis

- Unpredictable course: Majority of patients have slowly progressive disease
- Bilateral mediastinal involvement associated with worse prognosis
- Secondary pulmonary hypertension and cor pulmonale are dreaded long-term complications

Treatment

- Medical therapy
 - o Corticosteroids: Nongranulomatous FM
 - Systemic antifungals: Insufficient evidence to support use
 - Immunomodulators: Ongoing research regarding emerging role of therapy targeted to B-lymphocytes (e.g., rituximab)
- Non-surgical procedures: Angioplasty, endobronchial and endovascular stenting
- Surgical intervention
 - Open debulking &/or decompression
 - Spiral vein grafting for SVC syndrome, polytetrafluoroethylene grafts or vascular bypass for arterial compromise
 - Pulmonary resection for recurrent postobstructive pneumonitis and intractable/recurrent hemoptysis

DIAGNOSTIC CHECKLIST

Consider

• FM in young patient with obstructive mediastinal soft tissue and calcification in appropriate clinical setting

SELECTED REFERENCES

 Garrana SH et al: Multimodality imaging of focal and diffuse fibrosing mediastinitis. Radiographics. 39(3):651-67, 2019

Fibrosing Mediastinitis





(Left) Axial NECT of a patient with granulomatous fibrosing mediastinitis shows dense right hilar calcifications → with mass effect and incompletely characterized obliteration of the right upper lobe bronchus and right pulmonary artery. (Right) Axial NECT of the same patient shows right upper lobe volume loss and retraction of the minor fissure → secondary to bronchial obliteration by central calcified soft tissue.





(Left) Coronal CECT of a patient with granulomatous fibrosing mediastinitis shows superior vena cava and left brachiocephalic vein stents \supseteq for treatment of chronic obstruction and multiple enlarged mediastinal $collateral vessels \boxtimes$ (Right) Catheter venogram of the same patient shows markedly diminished flow within the left brachiocephalic vein \supseteq and the superior vena cava 🖾 due to in-stent stenoses &/or thrombosis.





(Left) Axial CECT of a patient with nongranulomatous IgG4related fibrosing mediastinitis shows a non-calcified prevascular mediastinal soft tissue mass 🔁. Abdomen CT of this patient (not shown) showed associated retroperitoneal fibrosis. (Right) Axial CECT of a patient with granulomatous fibrosing mediastinitis shows bilateral superior pulmonary vein stents \square surrounded by abnormal soft tissue. Intimal hyperplasia resulted in bilateral partial stent luminal obstruction.

KEY FACTS

TERMINOLOGY

• Castleman disease (CD)

IMAGING

- Location: 70% of CD occurs in thorax
- Tracheobronchial, hilar, mediastinal lymph nodesRadiography
 - Smooth or lobulated hilar mass most common
 - Mediastinal: Middle compartment
- CT
 - Solitary or multiple enlarged lymph nodes
 - Smooth or lobulated margins
 - Intense contrast enhancement is characteristic
- MR
 - o T1WI: Low to intermediate signal intensity
 - o T2WI: Hyperintense
 - o T1WI C+: Intense enhancement

TOP DIFFERENTIAL DIAGNOSES

- Kaposi sarcoma
- Lymphoma and leukemia
- Metastatic lymphadenopathy
- Paraganglioma

PATHOLOGY

- Etiology unknown; several proposed theories
 - Chronic inflammation, immunodeficiency, hamartomatous process, autoimmunity
- 2 classification systems
 - o Histology: Hyaline vascular, plasma cell, mixed
 - Distribution: Unicentric, multicentric

CLINICAL ISSUES

- Most asymptomatic; symptoms from mass effect rare
- Complete surgical excision is usually curative
- Variable response to chemotherapy and radiation

(Left) Graphic demonstrates the morphologic features of Castleman disease. The affected right hilar lymph node 🔁 exhibits hypervascularity, which accounts for the intense enhancement seen on contrast-enhanced CT and MR. (Right) Axial CECT of a patient with multicentric Castleman disease demonstrates several enlarged and enhancing lymph nodes in the right anterior phrenic \square and internal mammary 🔁 regions.





(Left) Axial CECT of a patient with unicentric Castleman disease shows a large, enhancing, infiltrative mass in the visceral mediastinum with vascular encasement. Infiltration into surrounding fat or invasion of adjacent structures is a less common finding than a well-defined solid mass. (Right) Whole-body FDG PET demonstrates multiple FDG-avid lymph nodes in the axillae \square . Biopsy revealed multicentric Castleman disease, which typically manifests as thoracic, upper abdominal, &/or lower neck lymphadenopathy.





- Abbreviations
- Castleman disease (CD)

Synonyms

- Angiofollicular lymph node hyperplasia
- Giant lymph node hyperplasia

IMAGING

General Features

- Best diagnostic clue
 - o Enhancing solitary or multiple lymph nodes
- Location
 - o Unicentric
 - 70% occurs in thorax
 - May occur anywhere lymphatic tissue is present
 Mediastinum is most commonly affected site
 - Other sites: Hila, axillae, pleura, chest wall, extrapleural soft tissues
 - □ Rare involvement of trachea, esophagus, lungs
- Size
 - o Variable, often 2-6 cm

Radiographic Findings

- Unicentric
 - o Well-defined opacity with lobulated or smooth contours
 - Mediastinal involvement: Usually middle mediastinum
 - Associated findings
 - Displacement of adjacent structures
 - Ipsilateral pleural effusion
 - Periosteal reaction
- Multicentric
 - Findings depend on distribution and size of affected lymph nodes
 - Mediastinal or hilar lymphadenopathy usually detected in thoracic involvement

CT Findings

- NECT
 - o Unicentric
 - Homogeneous soft tissue mass
 - Low-density regions are common
 - Correspond to fibrosis, edema, or necrosis
 Punctate internal calcifications in 5-10%
 - o Multicentric
 - Homogeneous lymph node enlargement
- CECT
 - o Unicentric
 - Soft tissue mass is most common
 - □ Average size: 5–7 cm; maximum diameter: 25 cm
 - □ Lobulated with well-defined borders
 - Infiltration into fat, local invasion less common; may mimic aggressive malignancy
 - Localized lymphadenopathy with dominant mass less common
 - Enhancement
 - Intense during arterial phase; decreases during portal venous phase

- Enlarged feeding arteries and draining veins in ~ 50%
- Non- or poorly-enhancing areas common; focal fibrosis, edema, &/or necrosis
- Atypical enhancement patterns: Peripheral nodular enhancement, enhancement of feeding vessels with mild enhancement of dominant lesion
- Small subset show only mild enhancement
 Associated pleural effusion not uncommon
- Multicentric
 - Diffuse lymphadenopathy in mediastinum, hila, axillae
 - Cervical and upper abdominal lymphadenopathy, splenomegaly often present
 - Moderate to avid enhancement is typical; mild in some cases
 - Lung abnormalities
 - Scattered centrilobular nodules
 - Thick septa and bronchovascular bundles (plasma cell and lymphocytic infiltration)
 - □ Thin-walled cysts and ground-glass opacity
 - □ Large nodules or masses and confluent consolidations less common
 - Pleural and pericardial effusions not uncommon
 - Large effusion should raise suspicion for primary effusion lymphoma [non-Hodgkin B-cell lymphoma associated with human herpesvirus-8 (HHV-8)]
 - Findings related to Kaposi sarcoma may be present (association with HIV and HHV-8)
 - Enhancing lymphadenopathy + osseous lesions suggests POEMS syndrome
 - Osteosclerotic lesions or mixed lytic and osteosclerotic lesions
 - Splenomegaly, hepatomegaly

MR Findings

- T1WI
 - Slightly hypointense to slightly hyperintense compared to skeletal muscle
- T2WI
 - Slightly to markedly hyperintense to skeletal muscle
 Depends on composition and degree of T2 weighting
- DWI
 - Restricted diffusion; signal intensity increases with b value
- T1WIC+
 - Intense enhancement
 - Heterogeneous due to necrosis, edema, fibrosis
 - Flow voids due to prominent feeding vessels

Nuclear Medicine Findings

- PET/CT
 - o Unicentric
 - Moderately increased FDG uptake
 - Wide range of reported SUVs
 - o Multicentric
 - FDG-avid lymphadenopathy
 Median SUV range: 4.8-6
 - Increased FDG uptake in spleen and bone marrow in most patients
 - FDG PET/CT not diagnostic but useful in determining treatment response

Imaging Recommendations

- Best imaging tool
 - CECT is optimal imaging modality

DIFFERENTIAL DIAGNOSIS

Kaposi Sarcoma

- Kaposi sarcoma and CD may coexist in HIV(+) patients
- Enlarged lymph nodes may avidly enhance

Lymphoma and Leukemia

- Lymphadenopathy ± enhancement
- Overlap of clinical and imaging features

Metastatic Lymphadenopathy

- Intense enhancement of enlarged lymph nodes
- Renal cell and thyroid carcinomas, melanoma, sarcoma

Paraganglioma

- Uncommon mediastinal neoplasm; most paravertebral
- Solitary mass with intense enhancement

PATHOLOGY

General Features

- Etiology
 - o Classified as lymphoproliferative disorder
 - Etiology unknown; several proposed theories
 - Chronic inflammation, immunodeficiency, hamartomatous process, autoimmunity
 - o HHV-8 and HIV associated with multicentric disease
- Associated abnormalities
- Systemic disorders
 - POEMS syndrome
 - Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes
 - □ Up to 37% of patients with MCD have POEMS syndrome; 9-24% of those with POEMS syndrome have MCD
 - □ Coexistent HHV-8 infection in majority of patients
- Autoimmune disorders
 - Rheumatoid arthritis
 - Myasthenia gravis
 - Wiskott-Aldrich syndrome
 - Scleroderma
 - Sjögren syndrome
 - Polymyositis
 - Paraneoplastic pemphigus
 - Mixed connective tissue disease
 - Undifferentiated connective tissue disease
- Renal dysfunction
- o Neoplasms
 - Kaposi sarcoma
 - Lymphoma
 - Non-Hodgkin lymphoma: Most common malignancy associated with multicentric disease
 Primary effusion lymphoma
- Staging, Grading, & Classification
- Clinical classification
 - o Unicentric (68-96%): Most commonly in mediastinum
 - Multicentric: Systemic disease that affects lymph nodes

- Histologic classification
 - Hyaline vascular variant (90%): More likely unicentricPlasma cell variant (9%): More likely multicentric

Gross Pathologic & Surgical Features

- Lymph nodes
 - Enlarged: 6-7 cm (range: 1-25 cm)
 - Cut surfaces are soft and cream-colored, similar to lymphoma
- Thick fibrous capsule in hyaline vascular type

Microscopic Features

- Hyaline vascular variant
 - Germinal centers with many mature lymphocytes
 - Concentric hyaline sclerosis and onion-skin lymphocyte layer
 - Prominent interfollicular capillary proliferation
 - Areas of necrosis, especially in lymph nodes > 5 cm
- Plasma cell variant
 - Sheets of mature plasma cells between hyperplastic germinal centers
 - Variable capillary proliferation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Clinical manifestation depends on several factors
 - Distribution (unicentric, multicentric)
 - Histologic type (hyaline vascular, plasma cell)
 - Coexistent infection (HHV8, HIV)
 - Associated systemic disorder (POEMS syndrome, collagen vascular disease)
 - Unicentric: Most asymptomatic
 - o Multicentric: Most have systemic symptoms
 - Fever, weight loss, night sweats
 - Associated findings
 - Lymphadenopathy, organomegaly, renal dysfunction, pleural effusion, pulmonary edema, skin rash, endocrine dysfunction
 - Patients with coexisting infections (HIV, HHV-8) and systemic conditions (POEMS syndrome) tend to have more severe symptoms

Demographics

- Age
 - Unicentric: 3rd-5th decades
 - Multicentric: Older than patients with unicentric disease; median age: 5th-6th decades
- Sex
 - Unicentric and multicentric: M = F

Treatment

- Complete surgical excision is usually curative
- Variable results with chemotherapy and radiation

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Castleman Disease





(Left) PA chest radiograph of a patient with Castleman disease shows a wellmarginated lobulated right paratracheal mass 🔁. (Right) Axial CECT of the same patient shows a large, intensely enhancing right paratracheal lymph node 🛃 in the visceral mediastinum with pretracheal extension. 70% of cases of Castleman disease affect the thorax, and the most common imaging manifestation is mediastinal &/or hilar lymphadenopathy.





(Left) Axial CECT of a patient with multicentric Castleman disease demonstrates a lowattenuation soft tissue mass \blacksquare in the prevascular mediastinum and several conspicuous mediastinal lymph nodes 🛃 (Right) Fused axial FDG PET/CT of the same patient shows low-grade increased FDG uptake in the mass and less uptake in the mediastinal lymph nodes. FDG PET/CT findings are not diagnostic of Castleman disease but have been shown to be useful in determining response to therapy.





(Left) Axial CECT of a patient with multicentric Castleman disease demonstrates a right lung mass \supseteq with foci of enhancement and subcarinal lymphadenopathy 🔁. Most lesions of Castleman disease demonstrate intense enhancement, although nonor poorly-enhancing areas are common and represent focal fibrosis, edema, &/or necrosis. (Right) Whole-body FDG PET of the same patient demonstrates increased FDG uptake in the right lung mass \square as well as FDG-avid lymph nodes in the mediastinum and right hilum 🔁.

Bronchogenic Cyst

KEY FACTS

TERMINOLOGY

• Abnormal ventral foregut budding forms pouch (26- to 40- days gestation)

IMAGING

• Radiography

- o Middle mediastinal mass
- o Sharply marginated, spherical soft tissue lesion
- CT
 - Majority in visceral mediastinum (80%)
 - Well-defined, unilocular, spherical cyst
 - Thin wall may exhibit enhancement, calcification
 - Variable attenuation ranging from fluid to soft tissue
 - No enhancement of cyst content
- MR
 - Variable signal on T1WI
 - High signal on T2WI, closely parallels that of CSF

TOP DIFFERENTIAL DIAGNOSES

- Congenital thoracic cystic lesions
 - Pericardial, thymic, esophageal duplication cyst
- Mediastinal cystic neoplasms
 - o Mature teratoma, thymoma, lymphoma

PATHOLOGY

- Lined with respiratory epithelium
- Mural smooth muscle layer with mucous glands, cartilage

CLINICAL ISSUES

- Treatment
 - Asymptomatic simple cysts: Observation
 - o Symptomatic cysts: Aspiration, ablation, resection

DIAGNOSTIC CHECKLIST

• Consider bronchogenic cyst in asymptomatic patient with spherical fluid-filled subcarinal lesion

(Left) PA chest radiograph of a patient who presented with dysphagia shows a large, elongated well-marginated right-sided mediastinal mass \blacksquare , which was diagnosed as a bronchogenic cyst. (Right) Axial CECT of the same patient shows a wellcircumscribed, fluidattenuation ovoid mass \implies in the visceral and right paravertebral mediastinum, just below the level of the tracheal bifurcation. The lesion produced mass effect on the adjacent bronchus intermedius and esophagus.





(Left) Composite image with sagittal CECT (left) and lateral barium esophagram (right) of the same patient shows the ovoid fluid-attenuation subcarinal bronchogenic cyst \blacksquare located in the visceral mediastinum. Note mass effect on and posterior displacement of the adjacent esophagus 🔁. (Right) Graphic shows the classic morphologic features of bronchogenic cyst. These are thin-walled unilocular spherical cysts that typically abut the trachea &/or carina. A subcarinal location is typical.





Definitions

- Bronchogenic cyst (BC)
 - Abnormal ventral foregut bud with resultant discrete fluid-filled pouch (26- to 40-days gestation)
 - o Most common congenital foregut duplication cyst (60%)
- Other foregut cysts
 - Esophageal duplication cyst, neurenteric cyst
- Other thoracic congenital cystic lesions
- Lymphatic: Lymphangioma
- o Mesothelial: Pericardial cyst, mesothelial cyst
- o Thymopharyngeal duct: Congenital thymic cyst
- Leptomeningeal: Meningocele

IMAGING

General Features

- Best diagnostic clue
 - Spherical, thin-walled, unilocular cyst near tracheal carina
- Location
 - o Mediastinal BC: Middle/visceral mediastinum
 - Pulmonary BC: Lower lobe medial 1/3
- Size
 - Variable diameter: Range: 1.5-11 cm
- Morphology
 - o Spherical, unilocular, smoothly marginated

Radiographic Findings

- Rounded or ovoid middle mediastinal mass
 - Sharply marginated, typically subcarinal
 - o Right-sided convexity, upper azygoesophageal recess
 - May displace carina and central bronchi
 - o Fluid-fluid level if milk of calcium cyst content
- Air-filled cyst or air-fluid level suggests infection
- Intrapulmonary BC: Medial 1/3 of lower lobe

Fluoroscopic Findings

- Esophagram
 - Extrinsic esophageal compression

CT Findings

- NECT
 - o Well-defined spherical or ovoid lesion
 - Majority in visceral mediastinum (80%)
 - Subcarinal, paratracheal, paraesophageal
 - Atypical: Anterior mediastinum, lung
 - Rare: Pleura, diaphragm, pericardium, neck
 - o Thin wall: May exhibit mural calcification (10%)
 - Cyst content attenuation
 - Typically homogeneous fluid attenuation (0-20 HU)
 - Soft tissue attenuation due to mucous, blood, or calcium (40%)
 - Rarely milk of calcium-fluid level
 - Malleable, rarely causes obstruction
 - Mass effect on bronchi, esophagus, heart, vessels
 - Uncommon associated atelectasis/consolidation
 - Cyst infection: Enhancing irregular wall
 - Acquired airway communication: Air, air-fluid level
 - Intrapulmonary BC
 - Solitary, well-defined, unilocular, spherical/ovoid

- Central lower lobe, rarely upper lobe
- 3- to 5-cm diameter
- Variable attenuation (9-40 HU)
- Infection: Irregular enhancing wall; may contain air

Mediastinal Abnormalities

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- Adjacent mosaic attenuation or linear bands
- CECT
 - May exhibit uniform thin linear mural enhancement
 - Unilocular morphology
 - No internal enhancement of cyst content

MR Findings

- T1WI
 - Often low signal intensity, parallels cerebrospinal fluid
 - Variably increased signal intensity
 - Protein, blood, mucus
- T2WI
 - High signal intensity, iso- or hyperintense to CSF
 Visualization of low signal intensity cyst wall
 - T1WIC+
 - ± cyst wall enhancement; nonenhancing content

Ultrasonographic Findings

- Grayscale ultrasound
 - Transesophageal echocardiogram: Anechoic unilocular thin-walled cyst with increased through transmission

Imaging Recommendations

- Best imaging tool
 - CT is diagnostic in fluid-attenuation lesions
 - o MR useful for assessment of indeterminate lesions

DIFFERENTIAL DIAGNOSIS

Congenital Thoracic Cystic Lesions

- Pericardial cyst
 - Right cardiophrenic angle, abuts pericardium
 - Fluid attenuation, imperceptible wall
- Thymic cyst
 - Anterior/prevascular mediastinum; thymic bed
 - Unilocular or multilocular
 - o Fluid attenuation; may exhibit mural calcification
- Esophageal duplication cyst
 - Abuts esophagus, often right-sided
 - Mass effect on esophagus
 - Cyst wall may be thick
- Neurenteric cyst
 - Right-sided; elongated lesion
 - Associated vertebral anomalies cephalad to cyst
- Lymphangioma (cystic hygroma)
 - Unilocular, multilocular; thin septa
 - May involve neck/chest wall

Mediastinal Cystic Neoplasms

multilocular cystic lesion

• Meningocele

Mature teratoma

Herniation of leptomeninges through intervertebral foramen or vertebral body defect
Fluid attenuation/signal, continuity with thecal sac

o Anterior/prevascular mediastinal unilocular or

• May contain soft tissue, fluid, fat, calcium

Bronchogenic Cyst

- Thymoma
 - Anterior/prevascular mediastinal mass
- May exhibit cystic changes, septations, mural nodulesNeurogenic neoplasm
 - Spherical posterior/paravertebral mediastinal soft tissue mass
 - Pressure erosion of adjacent skeleton
 - May exhibit cystic degeneration
- Mediastinal Hodgkin lymphoma
 - Lymphadenopathy; nodal coalescence
 - Cystic degeneration may follow treatment

Pancreatic Pseudocyst

- History of pancreatitis
- Abdominal pseudocyst not always present

Mediastinal Abscess

• Signs/symptoms of infection/sepsis

Pulmonary Cystic or Cavitary Lesions

- Pulmonary airway malformation
- Neonates and infants with multilocular air-filled lesionBulla
- Multifocal pulmonary involvement
- May become infected and develop air-fluid level
- Pneumatocele
 - Spontaneous resolution
- Lung abscess
 - o Usually develops within consolidated lung
- Lung cancer
 - Smooth thin-walled cavities uncommon
 - Image-guided biopsy for diagnosis
- Intralobar sequestration
 - o Heterogeneous lesion with complex cystic component
 - o Systemic arterial supply, pulmonary venous drainage

PATHOLOGY

General Features

- Etiology
 - Congenital cyst
 - Foregut malformation
 - Abnormal budding from ventral foregut
 Precursor of trachea and major bronchi
 - □ Early anomalous budding = mediastinal cyst
 - □ Late anomalous budding = pulmonary cyst
 - Notochord adjacent to foregut may give rise to neurenteric cyst
- Associated abnormalities
 - Extralobar sequestration
 - Congenital lobar emphysema

Gross Pathologic & Surgical Features

- BC: 1/5 of mediastinal masses
 - 85% mediastinal; 15% in lung, pleura, diaphragm, or pericardium
- Unilocular cyst, no tracheobronchial communication
- Variable cyst content
 - Clear serous fluid, mucoid material, purulent material, milk of calcium, hemorrhagic fluid
- Stalk or pedicle attaches cyst to tracheobronchial tree (50%)

• Extrathoracic extension into neck or abdomen: Dumbbell cysts

Microscopic Features

- Lining: Columnar or cuboidal respiratory epithelium
- Wall: Fibromuscular connective tissue, cartilage, mucous glands

CLINICAL ISSUES

Presentation

Most common signs/symptoms

Most often asymptomatic

- Other signs/symptoms
 - Chest pain, cough, dyspnea, wheezing
 - Fever, purulent sputum, dysphagia
 - Life-threatening emergency
 - Airway compression, infection, hemorrhage, rupture, pneumothorax
 - Rarely: Arrhythmia, air embolus, superior vena cava syndrome

Demographics

- Age
 - Discovered at any age, usually < 35 years
- Sex
- o M:F = 1:1

Natural History & Prognosis

- Increasing cyst size: Consider hemorrhage, infection
- Rare malignant transformation of pulmonary congenital cystic lesions

Treatment

- Small asymptomatic lesions
 - o Observation
 - Resection of selected asymptomatic cysts in young patients
 - Low surgical risk; potential for late complications, infection, hemorrhage
- Symptomatic lesions
 - Aspiration/drainage/ablation (cyst may recur)
 - Surgical resection definitive
 - Thoracotomy or video-assisted thoracoscopic surgery

DIAGNOSTIC CHECKLIST

Consider

 BC in asymptomatic patient with spherical subcarinal or paratracheal lesion

Image Interpretation Pearls

 Mediastinal BC should be suspected based on morphology and location

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Bronchogenic Cyst





(Left) PA chest radiograph of an adult who presented with cough and dyspnea shows a large, well-marginated right mediastinal soft tissue mass. (Right) Axial NECT of the same patient shows a large fluidattenuation lesion 🔁 in the visceral mediastinum that extends to the precarinal region and small bilateral pleural effusions ➡. Given progressive symptoms, the lesion was surgically excised. Bronchogenic cysts may be entirely asymptomatic, but symptomatic lesions should be treated with aspiration, ablation, or excision.





(Left) Axial NECT of an asymptomatic patient with a bronchogenic cyst shows a right visceral mediastinal paratracheal spherical lesion ➡ of water attenuation. Note absence of mass effect on the adjacent structures. (Right) Composite image with lateral barium esophagram (left) and axial CECT (right) of a patient with a bronchogenic cyst and dysphagia shows smooth mass effect on the esophagus 🛃 produced by the spherical subcarinal fluid-attenuation cyst oxdots, which is intimatelyrelated to the mid esophagus \rightarrow





(Left) Axial NECT of a patient with chronic renal regurgitation shows a large soft tissue-attenuation subcarinal mass 🛃 that displaces the upper azygoesophageal recess laterally. (Right) Axial T2WI MR of the same patient shows that the lesion is a large fluidfilled unilocular cyst \mathbf{E} with homogeneous high signal intensity content. Although the lesion exhibited soft tissue attenuation on CT, a presumptive diagnosis of bronchogenic cyst can be made based on location, morphology, and MR features.

KEY FACTS

TERMINOLOGY

- Abbreviations
 - Enteric cyst (EC)
 - Esophageal duplication cyst (EDC)
- Synonyms
 - Foregut or enterogenous cyst
- Due to anomalous budding of dorsal foregut (3-6 weeks)

IMAGING

- Radiography
 - Spherical lower middle mediastinal mass
- CT
 - Paraesophageal unilocular fluid-filled cyst
 - Variable attenuation of internal content
 - Uniformly thin cyst wall; may enhance
- MR
 - o Variable signal on T1WI; high signal on T2WI
 - o T2WI may show internal fluid-fluid levels

TOP DIFFERENTIAL DIAGNOSES

- Bronchogenic cyst
- Benign esophageal neoplasm
- Esophageal diverticulum

PATHOLOGY

- Discrete unilocular cyst with variable fluid content
- Lining: Enteric or respiratory epithelium
- Cyst wall: Two smooth muscle layers, no cartilage
- Ectopic gastric mucosa in 50%

CLINICAL ISSUES

- Age/sex: 75% occur in children; M ~ F
- Symptoms: Dysphagia, dyspnea, chest pain
- Treatment: Surgical excision with excellent prognosis

DIAGNOSTIC CHECKLIST

• Consider EDC in patient with lower right paraesophageal unilocular fluid-filled cystic lesion

(Left) PA chest radiograph of an adult patient who presented with chest pain shows a large esophageal duplication cyst that manifested as a wellcircumscribed, oblong retrocardiac mass 🛃 located in the middle mediastinum. (Right) Axial CECT of the same patient shows a large, thinwalled, fluid-attenuation mass \blacksquare , which partly surrounds the lower esophagus \square and a small left pleural effusion ₽. Affected patients may present with symptoms related to presence of ectopic gastric mucosa in the cyst wall.





(Left) Coronal CECT of the same patient confirms the presence of a large, oblong, unilocular esophageal duplication cyst 🖻 in the visceral mediastinum directly adjacent to the lower third of the esophagus. (Right) Graphic shows the characteristic anatomic location of esophageal duplication cyst \blacksquare in the inferior aspect of the middle/visceral mediastinum, typically located to the right of the distal esophagus and within or adjacent to the esophageal wall.





Abbreviations

- Enteric cyst (EC)
- Esophageal duplication cyst (EDC)
- Foregut duplication cyst (FDC)

Synonyms

• Foregut or enterogenous cyst

Definitions

- FDC: Anomalous budding of embryonic foregut (weeks 3-6)
- FDC: Arises from dorsal foregut
- EDC or neuroenteric cyst formation

IMAGING

General Features

- Best diagnostic clue
 - o Well-defined lower paraesophageal cyst
- Location
 - o Most EC arise from distal ileum or duodenum
 - o 10-15% arise from esophagus (distal 1/3, right-sided)
 - o Multiple EC along gastrointestinal (GI) tract may occur
- Size
- o ≤5 cm
- Morphology

• Spherical, ovoid, tubular; unilocular

Radiographic Findings

• Spherical/ovoid mass or esophageal contour abnormality, lower paraesophageal mediastinum

CT Findings

- NECT
 - Spherical or oblong lower paraesophageal lesion
 - Unilocular cyst of variable attenuation
 - May exhibit soft tissue attenuation content
 - May exhibit intrinsic fluid-fluid level
 - May communicate with GI tract below diaphragm
- CECT
 - Uniformly thin cyst wall; may enhance
 - No internal enhancement of cyst content

MR Findings

- T1WI
 - High or low signal intensity cyst content
 - May exhibit fluid-fluid or blood-fluid levels
- T2WIFS
- High signal intensity cyst content

Ultrasonographic Findings

• Cyst wall muscle layers may merge with esophageal muscle

Nuclear Medicine Findings

• 99mTc pertechnetate detects ectopic gastric mucosa

DIFFERENTIAL DIAGNOSIS

Bronchogenic Cyst

• More common than EDC; cartilage differentiates from EDC

Benign Esophageal Neoplasm

- Leiomyoma: Solid esophageal mass
- Fibrovascular polyp: Endoluminal, on stalk, upper esophagus

Esophageal Diverticulum

• Communicates with esophageal lumen

Esophageal Carcinoma

Irregular mural thickening or soft tissue mass

Neurenteric Cyst

• Associated vertebral anomalies

PATHOLOGY

General Features

- Etiology
 - Primitive esophageal vacuoles form patent esophagus
 - Persistent isolated vacuole may give rise to EDC
- Associated abnormalities
 - o EC may be multiple; congenital GI anomalies in 12%
 o Esophageal atresia, vertebral anomalies, bronchogenic cyst

Gross Pathologic & Surgical Features

- Intramural esophageal or paraesophageal cystic lesion
 Esophageal communication in 10%
- Discrete unilocular cyst with variable fluid content
 Proteinaceous fluid, hemorrhagic fluid

Microscopic Features

- Lined by enteric or respiratory epithelium
- Cyst wall: 2 layers of muscularis propria, no cartilage
- Ectopic gastric mucosa in 50%; pancreatic tissue in 5%
- Rare malignant degeneration

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dysphagia, chest pain, stridor, wheezing
 - Compression of airways &/or esophagus
 - Bleeding, infection, perforation

Demographics

- Age
 - o 75% occur in children
- Sex
 Variably reported: M ~ F

Treatment

• Surgical excision with excellent prognosis

DIAGNOSTIC CHECKLIST

Consider

• EDC in patient with lower right paraesophageal unilocular fluid-filled cystic lesion

SELECTED REFERENCES

1. Chan M et al: Esophageal Cyst 2021

Pericardial Cyst

KEY FACTS

TERMINOLOGY

• Congenital: Anomalous nonunion of embryologic pericardial lacunae

IMAGING

• Radiography

- Well-defined right cardiophrenic angle massSpherical, ovoid, teardrop-shaped
- CT
 - Abuts pericardium
 - Homogeneous simple fluid attenuation
 - Thin/imperceptible wall without nodularity
- MR
 - Homogeneous high signal intensity on T2WI
 - No internal enhancement or mural nodularity
- Echocardiography
 - Modality of choice for evaluation of pericardium
 - Differentiates solid from cystic mass

TOP DIFFERENTIAL DIAGNOSES

- Chest radiography
- o Mediastinal fat; Morgagni hernia
- CT/MR
 - Bronchogenic cyst; thymic cyst

PATHOLOGY

- Fibrous wall lined by single mesothelial layer
- Adjacent to pericardium but no patent communication
- Simple fluid content, occasional thin septations

CLINICAL ISSUES

- Asymptomatic, incidental imaging finding
- No treatment required

DIAGNOSTIC CHECKLIST

• Imaging diagnosis of pericardial cyst is based on location, morphology, and CT/MR characteristics

(Left) PA chest radiograph of an asymptomatic young woman with a pericardial cyst demonstrates abnormal fullness of the right cardiac contour ➡. (Right) Lateral chest radiograph of the same patient shows a rounded opacity ➡ superimposed over the anterior cardiac silhouette, localizing the lesion to the right cardiophrenic angle.





(Left) Axial CECT of the same patient shows a unilocular pericardial cyst 🛃 of homogeneous water attenuation (< 15 HU by ROI analysis) with typical features of cardiophrenic angle location, unilocular cyst morphology, and imperceptible wall. (Right) Graphic shows the characteristic morphologic features and location of pericardial cyst. The lesion abuts the pericardium, is located at the right cardiophrenic angle, and exhibits a thin wall and clear fluid content.





Definitions

- Congenital: Anomalous nonunion of embryologic pericardial lacunae
- Acquired
 - o Inflammation
 - Cardiac surgery
 - o Trauma

IMAGING

General Features

- Best diagnostic clue
 - Cardiophrenic angle mass abutting heart
 - Smoothly marginated
 - Thin or imperceptible wall
 - Simple fluid attenuation (0-20 HU) on CT
 - High signal intensity on T2W1; lack of enhancement with Gadolinium
- Location
 - Cardiophrenic angle
 - Right (70%); left (10-40%)
- Size
 - o Variable: 2-30 cm; most < 5 cm
- Morphology
 - Spherical, ovoid, teardrop-shaped
 - o Unilocular (80%)
 - o Multilocular (20%)

Radiographic Findings

- Radiography
 - Cardiophrenic angle contour abnormality/mass
 - May occur elsewhere in mediastinum
 - In such cases, differentiation difficult from other congenital mediastinal cysts
 - May exhibit shape change with altered patient position or respiration
- PA chest radiography
 - Well-defined mass at right cardiophrenic angle or abnormal right cardiac contour
- Lateral chest radiography
 - Anterior inferior mediastinum
 - Superimposed over anterior cardiac silhouette

CT Findings

- NECT
 - Abuts pericardium
 - Usually at cardiophrenic angle
 - Right > left
 - Spherical, ovoid, tear drop-shaped
 - o Well-defined smoothly marginated; no local invasion
 - Thin or imperceptible wall
 - Simple fluid attenuation (0-20 HU) content
 - No mural nodules
 - Rarely internal septations
 - No calcification
 - No associated pericardial effusion
 - No associated lymphadenopathy
- CECT
 - Homogeneous simple fluid attenuation

- No internal enhancement or nodularity
- No mural enhancement

MR Findings

• T1WI

- Homogeneous signal
- Low or intermediate signal intensity
- Rarely contains proteinaceous fluid and exhibits high signal intensity
- T2WI
 - Homogeneous signal
 - High signal intensity (typically follows that of water, CSF)
 - Rarely, cyst wall and septa manifest as thin curvilinear low signal intensity structures
- T1WIC+
 - No internal enhancement
 - No enhancing mural nodules
 - No significant rim enhancement
- MR imaging findings are typically diagnostic

Ultrasonographic Findings

- Anechoic lesion content
- Evaluation of uniformly thin cyst wall
- Assessment of relationship to adjacent cardiac chambers/structures
 - Evaluation of hemodynamic impact on heart

Imaging Recommendations

- Best imaging tool
 - Echocardiography is primary imaging modality for evaluation of pericardium
 - Moderate to high sensitivity
 - Ability to differentiate solid from cystic masses
 - CT and MR
 - Allow evaluation of entire pericardium
 - Distinction of myocardial from pericardial disease
 - Further lesion characterization and differentiation from mediastinal mass
 - MR may be used for further assessment of indeterminate juxtacardiac lesions found on CT
- Protocol advice
 - Limited MR protocol sufficient for diagnosis
 - Axial and coronal T1WI and T1WI C+
 - Axial and coronal T2WI
 - Coronal imaging helpful for demonstration of relationship to heart and pericardium
 - Short-axis and 4-chamber imaging planes not necessary

DIFFERENTIAL DIAGNOSIS

Mediastinal Fat

- May mimic pericardial cyst on radiography
- Characteristic fat attenuation on CT
- May manifest as echo-free space on echocardiography

Morgagni Hernia

- Typically right cardiophrenic angle mass on radiography
 May be indistinguishable from mediastinal fat or pericardial cyst
- Characteristic fat attenuation on CT
 Contiguity of herniated fat with intraabdominal fat

• May contain bowel ± abdominal viscera

Bronchogenic Cyst

- Shared imaging characteristics with pericardial cyst
- Cyst wall may exhibit enhancement ± calcification
- Unilocular cyst
- Fluid content may exhibit water or soft tissue attenuation on CT
 - o May exhibit fluid-fluid or fluid-milk of calcium levels
- Characteristically located in middle/visceral mediastinum abutting trachea or carina
- Rarely occurs in pericardium, pleura, diaphragm

Thymic Cyst

- Anterior/prevascular mediastinal cyst in thymic bed
 Unilocular or multilocular
- Water attenuation on CT
- Fluid signal intensity on MR

Esophageal Duplication Cyst

- Shared imaging characteristics with bronchogenic cyst
- Typically paraesophageal or within esophageal wall

Loculated Pleural Effusion

- Evaluation of ipsilateral pleural space
- Pertinent history; more common postoperatively

Hematoma

- MR particularly useful
- Acute: High signal intensity on T1WI and T2WI
- Subacute: Heterogeneous signal, areas of high signal intensity on T1WI and T2WI
- Chronic: Dark peripheral rim and low signal intensity on T1WI: Calcification, fibrosis, hemosiderin
- High signal intensity areas on T1WI or T2WI may correspond to hemorrhagic fluid
- No enhancement on T1WI C+

Juxtacardiac Lymphadenopathy

- Pertinent history of known lymphoma or other malignancy
- Mantle radiation therapy: Cardiac blockers used to protect heart, may result in undertreated cardiophrenic angle region
- Recurrent lymphoma may manifest as cardiophrenic angle mass corresponding to lymphadenopathy

Pancreatic Pseudocyst

- Pertinent history of prior pancreatitis
- Usually extends through esophageal hiatus
- Associated peripancreatic inflammatory changes and fluid collections

Hydatidosis

- Cystic mass with well-defined borders ± calcifications
- Internal trabeculations due to daughter membranes
- May be pericardial or intramyocardial

PATHOLOGY

General Features

- Etiology
 - Benign congenital mesothelial cyst
 - Anomalous outpouching of parietal pericardium

- Occurs by 4th week of gestation
- o Coalescing vacuoles form intraembryonic body cavity

Gross Pathologic & Surgical Features

- Uni- or multilocular fluid-filled cyst, smooth internal surface
- No communication with pericardial space

Microscopic Features

- Fibrous wall lined by single mesothelial layer, mimics pericardium
- Differentiation from bronchogenic cyst and esophageal duplication cyst
 - Based on microscopic composition of cyst wall

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Typically asymptomatic; incidental finding
- Other signs/symptoms
 Rarely chest pain, odynophagia, or pericardial tamponade

Demographics

- Age
 - Mean age: 50 years
- Sex
 - Slight female predominance

Natural History & Prognosis

Benign course

Treatment

• No treatment required

- Surgical excision indicated if
 - o Chest pain
 - Tamponade/hemorrhage
 - Suspicion of malignancy
- No literature to support percutaneous drainage or fluid analysis

DIAGNOSTIC CHECKLIST

Consider

 Pericardial cyst in asymptomatic patient with homogeneous fluid-filled cardiophrenic angle lesion

Image Interpretation Pearls

• Consider cystic neoplasm if internal enhancement, heterogeneous content, or mural nodules

Reporting Tips

• Pericardial cyst is typically an imaging diagnosis based on location, morphology, and CT/MR characteristics

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- 1. Fadl SA et al: Comprehensive review of pericardial diseases using different imaging modalities. Int J Cardiovasc Imaging. 36(5):947-69, 2020
- Khayata M et al: Pericardial cysts: a contemporary comprehensive review. Curr Cardiol Rep. 21(7):64, 2019
- 3. Ünal E et al: The imaging appearances of various pericardial disorders. Insights Imaging. 10(1):42, 2019

Pericardial Cyst









(Left) Coronal T1WI + C MR of the same patient shows that the mass exhibits homogeneous intermediate signal intensity ≥ . (Right) Coronal T2WI MR of the same patient shows uniform high signal intensity within the lesion ≥, confirming its unilocular cystic character. Location, morphology, and simple internal characteristics are diagnostic imaging features of a pericardial cyst.





(Left) Coronal CECT of an asymptomatic patient shows an incidental multilocular pericardial cyst \blacksquare in the right cardiophrenic angle. While the vast majority of pericardial cysts are typically unilocular lesions, multilocular cysts may occur. (Right) Axial CECT of a patient with a pericardial cyst shows a water attenuation lesion in the right cardiophrenic angle. Although the cyst wall is imperceptible, there is a thin internal septation 🛃 within the mid portion of the cyst.

Thymic Cyst

KEY FACTS

TERMINOLOGY

- Congenital: Unilocular; thymopharyngeal duct remnant
- Acquired: Multilocular; inflammation, treatment, neoplasia

IMAGING

• Radiography

- o Anterior superior mediastinal mass
- NECT
 - Homogeneous water-attenuation cyst
 - Heterogeneous soft tissue-attenuation content:
 - Hemorrhage/infection/proteinaceous debris
- CECT
 - o Unilocular: Thin wall, water attenuation
 - o Multilocular: Thick wall, ± soft tissue component
- MR
 - T1WI: Homogeneous low signal intensity content
 - Intermediate/high signal if hemorrhage or infection
 - T2WI: Homogeneous high signal intensity content (variable signal in multilocular thymic cysts)

TOP DIFFERENTIAL DIAGNOSES

- Cystic anterior/prevascular mediastinal neoplasm
 - Cystic thymoma or thymic carcinoma
 - o Mature cystic teratoma
 - Lymphoma (especially Hodgkin)
- Lymphangioma/lymphatic malformation
- Pericardial cyst

CLINICAL ISSUES

- Uncommon: 1-3% of mediastinal masses
- 50% of congenital thymic cysts: 1st and 2nd decades
- Asymptomatic, incidental finding on radiography or CT
- Treatment: Observation, drainage, excision

DIAGNOSTIC CHECKLIST

- MR evaluation of suspected thymic cysts to exclude mural nodules, invasive features, lymphadenopathy
- Mural nodules in cystic anterior/prevascular mediastinal mass should suggest cystic neoplasm

(Left) Lateral chest radiograph of an asymptomatic patient shows an incidentally found soft tissue density 🔁 filling the anterior superior mediastinum. PA chest radiograph (not shown) demonstrated normal mediastinal contours. (Right) Axial CECT of the same patient demonstrates an unilocular thymic cyst that manifests as a wellcircumscribed noninvasive prevascular mediastinal cystic lesion 🛃 of homogeneous water attenuation that extends to both sides of midline.









Definitions

- Congenital thymic cyst: Embryonic remnants of thymopharyngeal duct
- Acquired thymic cyst
 - Inflammatory: Infection, autoimmune disorders
 - Association with malignant neoplasia
 - Multilocular thymic cyst: 1% of children with HIV

IMAGING

General Features

- Best diagnostic clue
 - Well-defined fluid-filled unilocular anterior/prevascular mediastinal cyst (congenital)
 - Multiloculated, variable wall thickness, soft tissue septa, ± nodularity (acquired)
- Location
 - Typically in anterior/prevascular mediastinum
- Size
- Variable: 2-17 cm; may fluctuate (benign feature)
- Morphology
 - o Spherical or ovoid, well-marginated

Radiographic Findings

- Anterior mediastinal mass
 - Abnormal mediastinal contour on PA radiography
 - Anterior mediastinal/retrosternal opacity on lateral radiography

CT Findings

- NECT
 - Prevascular mediastinal cyst, thin/imperceptible wall
 Spherical, ovoid, lobulated, saccular
 - ± soft tissue components (acquired cysts)
 - Homogeneous water attenuation or higher due to proteinaceous contents; high attenuation from hemorrhage/infection
- CECT
 - Unilocular thymic cyst
 - Simple water-attenuation prevascular mediastinal cyst
 - Imperceptible wall or uniform mural enhancementMultilocular thymic cyst
 - Enhancement of arct wall + is
 - Enhancement of cyst wall ± internal septa
 Enhancement of nodular soft tissue components

MR Findings

- T1WI
 - \circ Well-marginated thin-walled cyst \pm enhancement
 - Homogeneous low signal intensity content
 - Multilocular cyst: Enhancement of thick wall, septa, mural nodules
- T2WI
 - Homogeneous high signal intensity content
 - Visualization of low signal intensity cyst wall (thin or thick > 3 mm)
 - Consider MR follow-up of small equivocal prevascular mediastinal cysts
- T1WIC+FS
 - Critical sequence; lack of enhancement

DIFFERENTIAL DIAGNOSIS

Cystic Anterior/Prevascular Mediastinal Neoplasm

- Thymoma
- Solid mass; cystic mass with mural nodule(s),Cystic teratoma
- Multilocular cyst; foci of fat attenuation in 75%
- Lymphoma (especially Hodgkin)
 Mediastinal soft tissue mass ± cystic components
- Lymphangioma/Lymphatic Malformation
- Extrathoracic extension into neck, axilla, chest wall

Pericardial Cyst

• Cardiophrenic angle, water attenuation, imperceptible wall

PATHOLOGY

General Features

- Etiology
 - Congenital thymic cyst: Thymopharyngeal duct embryonic remnants
 - Acquired thymic cyst: Acute &/or chronic inflammation

Gross Pathologic & Surgical Features

- Congenital: Unilocular, thin wall, clear fluid
- Acquired: Fibrous walls, internal septa, turbid fluid

Complication of underlying neoplasia

Microscopic Features

- Variable epithelial lining: Squamous, columnar, cuboidal
- Thymic tissue remnants in cyst wall
- Multilocular thymic cyst: Chronic inflammation, necrosis, granulation tissue, lymphoid follicular hyperplasia

CLINICAL ISSUES

Presentation

Most common signs/symptoms
 Asymptomatic, incidental finding

Demographics

- Age
- 50% of congenital thymic cysts: 1st and 2nd decades
- Epidemiology
 - o Uncommon: 3% anterior/prevascular mediastinal masses

Treatment

• Observation, drainage, excision

DIAGNOSTIC CHECKLIST

Consider

• MR of suspected thymic cyst to exclude mural nodules &/or cystic neoplasm, invasive features, lymphadenopathy

Image Interpretation Pearls

 Mural nodules &/or soft tissue component in a cystic mediastinal mass should suggest cystic neoplasm

SELECTED REFERENCES

 Lee SH et al: Distinguishing between thymic epithelial tumors and benign cysts via computed tomography. Korean J Radiol. 20(4):671-82, 2019

KEY FACTS

TERMINOLOGY

Lesions of systemic and pulmonary arteries and veins
 10% of mediastinal masses on radiography

IMAGING

- Mediastinal mass that opacifies on CECT or CTA
- Radiography
 - o Wide mediastinum; mediastinal contour abnormality
 - Middle mediastinal, paratracheal, paracardiac mass
- CT
 - Hypoattenuating mass on NECT
 - Opacifies after contrast administration
 - Identification of parent or branch vessels
- MR: May be used as alternative to CT

Protocol advice

- Multiplanar reformations for lesion localization and assessment
- Cardiac gating for evaluation of vascular lesions of cardiac origin

TOP DIFFERENTIAL DIAGNOSES

- Hemangioma
- Lymphangioma
- Metastatic disease
- Extracardiac mediastinal angiosarcoma
- Hemangiopericytoma

CLINICAL ISSUES

- Surgical resection or endovascular therapy
 - o Lesions involving aorta and pulmonary arteries
 - Ascending aorta dissections and thoracic aortic aneurysms of certain sizes
 - Bypass graft aneurysms > 2 cm
 - o Significant symptoms, mass effect, rupture

DIAGNOSTIC CHECKLIST

• Consider mediastinal vascular lesion when mediastinal mass is detected on chest radiography

(Left) PA chest radiograph demonstrates a left superior mediastinal mass ➡ that projects above the left clavicle, indicating its middle or posterior mediastinal location. (Right) Sagittal CECT of the same patient shows aneurysmal dilation of the left subclavian artery 🔁 at its origin from the aortic arch. Approximately 10% of mediastinal masses and contour abnormalities identified on chest radiography represent vascular lesions.





(Left) Axial CECT shows a large hematoma in the visceral mediastinum with active extravasation \supseteq due to a bronchial artery pseudoaneurysm. (Right) Axial CECT shows contrast \blacksquare that partially opacifies an aneurysmal aberrant right subclavian artery. A large amount of low-attenuation thrombus is present within the large aneurysm. Curvilinear high-attenuation foci 🛃 represent displaced calcifications. Note aneurysmal dilatation of the diverticulum of Kommerell 🚬





Definitions

Lesions of systemic and pulmonary arteries/veins
 10% of mediastinal masses on radiography

IMAGING

General Features

- Best diagnostic clue
 Mediastinal mass that opacifies on CECT and CTA
- Location
 - Mediastinal compartment: Middle/posterior > anterior
- Size
 - o Variable
 - o Small lesions may not be visible on radiography
 - o Large lesions may mimic mediastinal neoplasms

Radiographic Findings

- Radiography
 - Systemic arteries
 - Thoracic aorta: Aneurysm and pseudoaneurysm
 Ascending aorta: Convexity of right
 - cardiomediastinal silhouette
 - Descending aorta: Focal mass that obscures left paraaortic interface or diffuse descending aorta enlargement and lateral displacement of left paraaortic interface
 - Aortic dissection
 - Most specific sign: Displacement of intimal calcification from aortic wall by > 1 cm
 - Nonspecific signs: Wide superior mediastinum, double aortic knob sign, progressive aortic enlargement, mass effect on mediastinum, apical cap, size disparity between ascending and descending aorta, cardiomegaly
 - Coronary artery aneurysm
 - Left or right paracardiac mass
 - Brachiocephalic artery: Tortuosity or aneurysm
 Left or right superior mediastinal mass
 - Saphenous vein graft aneurysm
 - Paracardiac mass
 Sinus of Valsalva aneurvsm
 - May not be visible when small
 Paracardiac mass when large
 - Left ventricular aneurysm
 - Paracardiac mass; may exhibit calcification

• Systemic veins

- Superior vena cava aneurysmal dilatation
 Wide right superior mediastinum
- Persistent left superior vena cava
- □ Wide left superior mediastinum
- Brachiocephalic vein aneurysm
 - Appears as double aortic knob
 - May mimic aortic coarctation
- Azygos vein
 - Enlargement: > 10 mm on upright radiography, > 15 mm on supine radiography
 - Appears as right paratracheal soft tissue
- Hemiazygos vein
 - Wide left paravertebral stripe

- Left superior intercostal vein
 "Aortic nipple"
- Pulmonary arteries
 - Enlargement
 - Middle mediastinal or hilar mass
 - Aberrant left pulmonary artery (pulmonary artery sling)
 - Opacity between trachea anteriorly and esophagus posteriorly
 - Ductus arteriosus aneurysm
 Middle mediastinal mass
 - Aneurysm and pseudoaneurysm
 Enlarged pulmonary trunk
- Pulmonary veins
 - Partial anomalous pulmonary venous return (PAPVR)
 Wide left superior mediastinum
 - Pulmonary venous varix
 - Perihilar or middle mediastinal mass
 - Pulmonary venous confluence
 - Retrocardiac mediastinal mass
- Aortic arch anomalies
 - Aneurysms and pseudoaneurysms
 - □ Enlargement or obscuration of aortic arch
 - □ Hilum overlay sign
 - Rightward tracheal deviation
 - Right aortic arch
 - □ Right paratracheal or superior mediastinal mass
 - Double aortic arch
 - Right arch appears as right paratracheal mass
 Cervical arch
 - Superior mediastinal mass extending above superior clavicular margin
 - Coarctation
 - Figure 3 sign: Mediastinal contour abnormality formed by dilated left subclavian artery and aorta distal to coarctation

CT Findings

- NECT
 - Vascular lesions may appear as low-attenuation masses; continuity with adjacent vasculature
- CECT
 - Venous lesions best seen on routine CECT
 - Often of same attenuation as parent or branch vessels
 - Communication with parent or branch vessels
- CTA
 - Opacification of vascular lesions depends on contrast bolus timing
 - Systemic artery lesions best seen on CTA performed for detection of aortic abnormalities
 - Pulmonary artery lesions best seen on CTA performed for detection of pulmonary embolism
 - Vascular masses exhibit similar attenuation to that of parent or branch vessels

MR Findings

- Can be used as alternative to CT
- Evaluation of lesion morphology
- Evaluation of cardiac valves and function

Imaging Recommendations

- Best imaging tool
 - CECT and CTA: Optimal assessment of lesion size, location, relationship to adjacent structures, complications
- Protocol advice
 - Multiplanar reformatted images useful for lesion localization
 - Cardiac gating may be helpful for evaluation of vascular masses of cardiac origin

DIFFERENTIAL DIAGNOSIS

Hemangioma

- Rare, benign vascular tumor
- Anterior/prevascular mediastinal location most common
- Well-circumscribed mass: Phleboliths, enhancement, fat

Lymphangioma

- Rare, benign tumor of lymphatic vessels
- Most commonly in anterior/prevascular mediastinum
- Uniform cystic mass, no contrast enhancement

Metastatic Disease

- Intense enhancement of enlarged lymph nodes
- Renal and thyroid cancers, melanoma, sarcoma

Extracardiac Mediastinal Angiosarcoma

- Anterior/prevascular mediastinal location most common
- Heterogeneous on CECT: Hemorrhage, necrosis, cysts

Hemangiopericytoma

- Accounts for 1% of vascular tumors
- Intense enhancement on CECT
- Heterogeneous if hemorrhage and necrosis

PATHOLOGY

General Features

- Etiology
 - Systemic arteries
 - Thoracic aorta: Aneurysm and pseudoaneurysm; atherosclerosis, cystic medial necrosis, trauma
 - Aortic dissection
 Congenital: Marfan and Ehlers-Danlos syndromes
 Acquired: Hypertension
 - Coronary arteries
 - Aneurysm: Atherosclerosis, infection, inflammation
 Fistula: Congenital
 - Brachiocephalic artery
 - Atherosclerosis and hypertension
 - Bypass graft aneurysm: Degeneration
 - Sinus of Valsalva aneurysm: Congenital
 - Left ventricular aneurysm: Congenital and acquired (myocardial infarction)
 - Systemic veins
 - Aneurysmal superior vena cava dilatation
 - Tricuspid valve disease and heart failure
 - □ Superior vena cava obstruction: Neoplasm, mediastinal fibrosis, lymphadenopathy
 - PAPVR and idiopathic (rare)
 - Left superior vena cava: Congenital

- Brachiocephalic vein aneurysm: Congenital, trauma, infection, inflammation, degeneration
- Azygos and hemiazygos vein enlargement
 - Portal hypertension, vena cava and hepatic vein obstruction, cardiac disease, azygos continuation of inferior vena cava
- Left superior intercostal vein enlargement
 - □ Increased flow or pressure in thoracic veins
- Pulmonary arteries
 - Enlargement
 - Pulmonary artery hypertension: Pre-capillary and post-capillary etiologies
 - □ Congenital: Valve absence or stenosis
 - Idiopathic aneurysm: Collagen vascular disease
 - □ Pseudoaneurysm: Infection and trauma
 - □ Aberrant left pulmonary artery: Congenital
 - □ Aneurysm of ductus arteriosus
- o Pulmonary veins
 - Pulmonary venous varix
 - □ Congenital and acquired (mitral valve disease)
 - Pulmonary venous confluence and PAPVR
- Aortic arch
 - Aneurysm and pseudoaneurysm: Atherosclerosis, cystic medial necrosis, trauma
 - Congenital: Right aortic arch, double aortic arch, cervical arch, coarctation
- Associated abnormalities
 - Superior vena cava aneurysm associated with lymphangioma (cystic hygroma)
 - PAPVR associated with atrial septal defect
 - o Congenital left ventricular aneurysm
 - Component of pentalogy of Cantrell
 - Sinus of Valsalva aneurysm associated with congenital heart defects

CLINICAL ISSUES

Treatment

- Surgical resection or endovascular therapy
 - More common for vascular lesions involving aorta and pulmonary arteries: Dissection involving ascending aorta, aneurysms of certain sizes
 - Bypass graft aneurysm > 2 cm
 - Vascular lesions involving other vessels that result in significant symptoms, mass effect, or rupture

DIAGNOSTIC CHECKLIST

Consider

• Mediastinal vascular lesion when mediastinal mass is detected on chest radiography

Image Interpretation Pearls

• CECT and CTA provide optimal assessment of vascular mass morphology, location, size, relationship to adjacent structures, and complications

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- Bai Y et al: CT and MRI manifestations of mediastinal cavernous hemangioma and a review of the literature. World J Surg Oncol. 17(1):205, 2019

Mediastinal Vascular Masses





(Left) PA chest radiograph shows a contour abnormality and increased convexity of the left cardiac border 🛃 (Right) Axial CECT of the same patient demonstrates that the radiographic abnormality corresponds to aneurysmal dilatation of the left atrial appendage \blacksquare . CECT and CTA are the optimal imaging modalities for the evaluation of mediastinal vascular masses and determination of their morphology, location, size, relationship to adjacent structures, and complications.





(Left) Axial NECT of a patient who presented with chest pain shows ill-defined soft tissue ⇒ in the right mediastinum adjacent to the esophagus. (Right) Axial CECT of the same patient shows a rounded focus of enhancement in the same location, which represented a pseudoaneurysm ⇒. Contrast enhancement of mediastinal vascular masses is affected by the presence or absence of intravenous contrast and the timing of the contrast bolus.





(Left) Axial cardiac CTA of a patient with Kawasaki disease demonstrates aneurysmal dilatation of the left anterior descending coronary artery →. (Right) Axial CECT of the same patient shows marked aneurysmal dilatation of the circumflex coronary artery \supseteq and portions of the left anterior descending $\stackrel{\frown}{>}$ and right 🔁 coronary arteries. The most common cause of coronary artery aneurysms is atherosclerosis. Other etiologies include genetic conditions, vasculitides, connective tissue diseases, infections, and drug use.

Coronary Artery Aneurysm

KEY FACTS

TERMINOLOGY

- Coronary artery diameter > 1.5x normal adjacent segments, involves < 50% of vessel
- Coronary artery ectasia: Diffuse coronary dilatation

IMAGING

- Coronary CTA
 - Evaluation of coronary aneurysm morphology, thrombosis, dissection
 - Calcification frequently present in atherosclerosis
- Size underestimation with mural thrombus or dissectionMR
 - Preferred modality when surveillance required
 - Calcification difficult to detect
 - Stents and clips may degrade image quality
- Angiography: May underestimate size if mural thrombus or dissection present

TOP DIFFERENTIAL DIAGNOSES

- Coronary fistula
- Coronary pseudoaneurysm

PATHOLOGY

- Atherosclerosis most common cause in USA
 Right coronary artery typically affected
- Kawasaki disease most common cause worldwide
 Left main coronary artery most commonly affected

CLINICAL ISSUES

- Most patients asymptomatic
- Acute coronary syndrome and heart failure
- Treatment: Anticoagulants, antiplatelets, surgery

DIAGNOSTIC CHECKLIST

• Consider coronary artery aneurysm in patients < 20 years with angina or acute myocardial infarction

(Left) Graphic illustrates the differences between saccular and fusiform aneurysms. While this is a morphologic characterization, and both aneurysms result most commonly from atherosclerosis, saccular aneurysms are more common and develop from a penetrating ulcer. (Right) Coronal CECT of a 61-year-old woman with chronic chest pain shows a calcified and thrombosed proximal right coronary aneurysm 🔁 adjacent to the right coronary artery 🔁.





(Left) Coronal coronary CTA of a 1-year-old-boy with Kawasaki disease shows a proximal right coronary aneurysm 🔁, a partially thrombosed right coronary aneurysm 🔁, and a left anterior descending coronary artery aneurysm 🔁. Note mild hemopericardium 🔁 from aneurysm leakage/rupture and a pericardial drainage catheter 🛃. (Right) Volume rendered coronary CTA of the same patient shows a right coronary aneurysm \square and a left anterior descending coronary artery aneurysm 🖂.





Definitions

 Coronary artery diameter > 1.5x normal adjacent segments; involves < 50% of vessel

IMAGING

General Features

- Best diagnostic clue
 Dilatation of coronary artery
- Morphology
 - Fusiform or saccular dilatation
 - May exhibit thrombus or dissection
 - Coronary artery ectasia: Diffuse dilatation

CT Findings

- Cardiac gated CTA
 - Evaluation of coronary aneurysm morphology, thrombosis, dissection
 - Calcification frequently present in atherosclerosis

MR Findings

- Available coronary angiography sequences
 Lumen dark on double IR FSE
 - Lumen bright on GRE or b-SSFP in absence of thrombus
- May be preferred modality when surveillance required
- Calcification difficult to detect
- Stents and clips may degrade image quality

Echocardiographic Findings

Echocardiogram
 Aneurysm detection in proximal coronary arteries

Angiographic Findings

- Fusiform and saccular coronary artery dilatation
- Size underestimation with mural thrombus or dissection

Imaging Recommendations

Best imaging tool
 Gated coronary CTA is imaging modality of choice

DIFFERENTIAL DIAGNOSIS

Coronary Fistula

- Dilated vessel associated with fistula
- Coronary ectasia proximal to fistula if large shunt or steal physiology present

Coronary Pseudoaneurysm

• Frequently secondary to chest trauma or catheter-based intervention

PATHOLOGY

General Features

- Etiology
 - Atherosclerosis is most common cause in USA
 - Right coronary artery most commonly affected (40%), followed by left anterior descending, left circumflex, and left main
 - Inflammatory: Kawasaki disease most common cause worldwide
 - Develops in 15-25% of untreated affected children

- May regress with treatment
- Left main coronary artery most commonly involved
- Takayasu arteritis (coronary involvement in 12%)
 Noninflammatory
- Connective tissue disease (systemic lupus erythematosus, Marfan, Behçet)
- Congenital, trauma, catheter-based intervention, mycotic emboli, cocaine use

Staging, Grading, & Classification

- True aneurysms have 3 intact vessel wall layers
- Pseudoaneurysms have 2 or fewer intact wall layers
- > 20 mm diameter in adults, considered "giant"

Gross Pathologic & Surgical Features

• Dilatation of coronary artery; may contain thrombus

Microscopic Features

• Atherosclerotic coronary aneurysms may exhibit media thinning or destruction

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Most patients asymptomatic
 - Acute coronary syndrome and heart failure may be caused by aneurysm or concurrent disease
- Clinical profile
 May result in thrombosis and myocardial infarction

Demographics

- Sex
- More common in males (2.2%) than females (0.5%)
 Epidemiology
- o Present in 4.9% of angiograms, 1.5% of necropsies

Natural History & Prognosis

- Related to severity of concomitant obstructive disease in patients with atherosclerosis
- Rupture reported but rare

Treatment

- Anticoagulants, antiplatelet therapy
- Surgical intervention if enlargement, embolization, or obstruction
 - Bypass and exclusion of aneurysm
 - Covered stent graft
- Kawasaki disease typically treated with high-dose intravenous γ-globulin and aspirin

DIAGNOSTIC CHECKLIST

Consider

• Coronary artery aneurysm in patients < 20 years who present with angina or acute myocardial infarction

SELECTED REFERENCES

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Paraesophageal Varices

KEY FACTS

TERMINOLOGY

- Dilated vessels within (esophageal) or adjacent to (paraesophageal) esophageal wall
- Uphill varices: Lower mediastinum, usually from portal hypertension
- Downhill varices: Upper mediastinum, usually from superior vena cava obstruction

IMAGING

- Radiography
 - Lateral displacement or obscuration of inferior azygoesophageal recess
 - o Visible in ~ 50% of patients with known varices
- **Esophagram**: Serpiginous filling defects
- CT
 - o Asymmetric apparent esophageal wall thickening
 - o Dilated vessels adjacent to or in esophageal wall
 - o May be unopacified on arterial phase imaging

TOP DIFFERENTIAL DIAGNOSES

- Hiatal hernia
- Esophageal carcinoma
- Mediastinal neoplasm

PATHOLOGY

- Uphill varices: Presinusoidal (portal vein thrombosis), sinusoidal (cirrhosis), postsinusoidal (Budd-Chiari syndrome)
- Downhill varices: Superior vena cava obstruction

CLINICAL ISSUES

- Alcoholic cirrhosis most frequent cause in USA
- Infectious cirrhosis most frequent cause worldwide
- Treatment: Transjugular intrahepatic portosystemic shunt, sclerotherapy, variceal ligation

DIAGNOSTIC CHECKLIST

- Evaluate for treatable underlying cause of varices
- Endoscopy: First-line test for esophageal varices

(Left) PA chest radiograph of a patient with alcoholic cirrhosis and paraesophageal varices shows lobulated masses near the gastroesophageal junction with lateral displacement of the azygoesophageal recess ► Contour abnormality of the lower azygoesophageal recess is the most common radiographic finding of paraesophageal varices, present in approximately 50% of cases. (Right) Graphic shows the morphologic features of varices in the esophageal wall ➡ and paraesophageal varices surrounding the lower 1/3 of the esophagus ₽.









Definitions

- Dilated vessels within (**esophageal**) or adjacent to (**paraesophageal**) esophageal wall
- **Uphill varices**: Lower mediastinum, usually from portal hypertension
- **Downhill varices**: Upper mediastinum usually from superior vena cava obstruction

IMAGING

General Features

- Best diagnostic clue
 - Lobular contour abnormality or mass of lower azygoesophageal recess
 - Serpiginous vessels in or about esophageal wall
- Location
 - Most commonly at lower 1/3 of esophagus

Radiographic Findings

- Radiography
 - Lateral displacement/obscuration of inferior azygoesophageal recess; visible in ~ 50%

Fluoroscopic Findings

- Esophagram
 - Tortuous, longitudinal filling defects projecting into esophageal lumen
 - Detection may be enhanced by Valsalva maneuver and Trendelenburg position

CT Findings

- Asymmetric apparent esophageal wall thickening
- Dilated vessels adjacent to or in esophageal wall; may be unopacified on arterial-phase imaging
- Increased number or tortuosity of mediastinal veins

MR Findings

- T1WI
 - Serpiginous flow voids on T1WI
 - Signal voids may be absent if slow flow
- MRV

• Optimally visualized on portal venous phase

Ultrasonographic Findings

• Hypo-/anechoic tubular structures on endoscopic US

Angiographic Findings

- **Downhill varices**: Multiple small collateral thoracic vessels on upper extremity venography
- **Uphill varices**: May be detected during transjugular intrahepatic portosystemic shunt placement

Imaging Recommendations

- Best imaging tool
- CECT optimal for detection and characterizationProtocol advice
- Imaging during portal venous phase

DIFFERENTIAL DIAGNOSIS

Hiatal Hernia

• Intrathoracic stomach, bowel, omentum

Esophageal Carcinoma

• Irregular or asymmetric esophageal wall thickening

Mediastinal Neoplasm

• Lymphadenopathy, gastrointestinal stromal tumor, paravertebral neurogenic tumors

PATHOLOGY

General Features

- Etiology
 - Uphill varices due to portal hypertension (hepatic venous pressure gradient > 12 mm Hg)
 - Reversal of flow diverts blood through left gastric vein to esophageal venous plexus
 - Uphill varices: Presinusoidal (portal vein thrombosis), sinusoidal (cirrhosis), or postsinusoidal (Budd-Chiari syndrome)
 - o Downhill varices from superior vena cava obstruction
 - Obstructing mass, central venous catheter, mediastinal fibrosis
- Associated abnormalities
 - Cirrhosis, splenomegaly, recanalized umbilical vein, spleno-renal shunt

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Hematemesis or gastrointestinal bleeding
- Other signs/symptoms
 - Signs of cirrhosis
 - Facial or upper extremity edema due to venous obstruction in superior mediastinum
 - Arm claudication (rare) due to venous regurgitation

Demographics

- Epidemiology
 - USA: Alcoholic cirrhosis most frequent cause
 - Worldwide: Cirrhosis due to hepatitis B, hepatitis C, and schistosomiasis are most frequent causes

Natural History & Prognosis

- Hemorrhage in up to 1/3 of affected patients
 Mortality for bleeding episode approximately 30%
- Downhill varices: Prognosis based on underlying cause
 Poor prognosis when due to obstructing neoplasm

Treatment

- Transjugular intrahepatic portosystemic shunt
- Sclerotherapy or variceal ligation

DIAGNOSTIC CHECKLIST

Consider

• Endoscopy: First-line test for esophageal varices

Image Interpretation Pearls

• Evaluate for treatable underlying cause of varices

SELECTED REFERENCES

 Manchec B et al: Contrast-enhanced CT may identify high-risk esophageal varices in patients with cirrhosis. AJR Am J Roentgenol. 215(3):617-23, 2020

Mediastinal Lymphangioma

KEY FACTS

TERMINOLOGY

- Synonym: Lymphatic malformation
- Rare, benign tumor of lymphatic vessels
- Often recurrent lymphangioma excised in childhood

IMAGING

- Radiography
 - o Well-defined smooth or lobular mediastinal mass
 - Superior anterior mediastinum in adults
 - Cervical region in children
- CT
 - Homogeneous or multicystic mediastinal mass
 - May surround or displace vessels/adjacent structures
- MR
 - o T1WI: Hyperintense relative to muscle
 - o T2WI: Typically high signal intensity
 - Visualization of cystic and infiltrative components

TOP DIFFERENTIAL DIAGNOSES

- Necrotic neoplasm
- Mature teratoma
- Thymic cyst
- Other mediastinal cyst
- Hematoma, seroma, abscess

PATHOLOGY

• Dilated vascular spaces lined by endothelium

CLINICAL ISSUES

- Asymptomatic or chest pain, dyspnea, stridor
- Treatment: Complete surgical excision; percutaneous drainage ± sclerotherapy for larger cysts

DIAGNOSTIC CHECKLIST

• Suspect lymphangioma in adult with cystic mediastinal mass and history of childhood resection

(Left) Coronal CECT of an asymptomatic patient with a mediastinal mass shows a well-circumscribed, mildly enhancing homogeneous mass \mathbf{E} in the prevascular mediastinum without evidence of local invasion. (Right) Sagittal CECT of the same patient confirms the superior mediastinal location and lobulated contours \blacksquare of the mass. There is mass effect on adjacent vessels. There are no calcifications evident within the mass.





(Left) Composite image with axial CECT (left) and axial T2WI MR (right) shows a mediastinal lymphangioma with multiple nodular components \square that are cystic \blacksquare with high to intermediate signal intensity content and fluid-fluid levels on MR. (Right) Composite image with axial SSFP (top) and T2W HASTE (bottom) MR shows a complex mass \blacksquare in the visceral mediastinum that exhibits infiltration and encasement of vascular structures 🔁 and heterogeneous predominant high signal intensity 🔁.





Synonyms

• Lymphatic malformation

Definitions

• Rare, benign tumor of lymphatic channels

IMAGING

General Features

- Location
 - o Cervical or axillary region in children
 - Mediastinal extension in 10%
 - o Upper anterior/prevascular mediastinum in adults
 - Also right paratracheal region, posterior/paravertebral mediastinum
 - May be recurrent lymphangioma excised in childhood

Radiographic Findings

- Well-defined smooth or lobulated mediastinal mass
- Pleural effusion may be evident

CT Findings

- Faintly enhanced homogeneous or cystic mediastinal mass
- Surrounds or displaces vessels/adjacent structures
- Occasionally infiltrative, may mimic malignancy
- Macrocystic components are often higher attenuation than water due to proteinaceous/chylous fluid
- Nodular components reflect meshwork of smaller cysts
- Calcification rare (unlike mediastinal hemangioma)
- Pleural effusion (often chylous)

MR Findings

- T1WI
 - o Overall hyperintense relative to chest muscle
 - o Macrocysts: Variable intensity depending on content
 - o Microcystic lesions may appear as solid tissue
- T2WI
 - Overall high signal intensity in multilocular lesions
 Occasional fluid-fluid levels: Layering blood products
- MR optimally depicts macrocystic and infiltrative components

Imaging Recommendations

- Protocol advice
 - Percutaneous needle biopsy often nondiagnostic

DIFFERENTIAL DIAGNOSIS

Necrotic Neoplasm

- Metastases, thymoma, lymphoma, germ cell neoplasm
- Necrosis more likely after treatment

Mature Teratoma

- Majority in anterior/prevascular mediastinum
- May contain soft tissue, calcium, fat, fluid

Thymic Cyst

- Unilocular or multilocular
- Well-defined cystic mass ± septations

Other Mediastinal Cysts

• Solitary spherical lesion of homogeneous attenuation

Hematoma, Seroma, Abscess

- Usually distinguished by clinical features
- Tissue sampling may be required for diagnosis

PATHOLOGY

General Features

- Etiology
 - Abnormal lymphatic budding vs. lymphatic sac sequestration during embryogenesis

Staging, Grading, & Classification

- Lymphangiomas classified based on size of lymphatics: Capillary, cavernous, cystic (hygromas)
- Lymphatic malformation classified based on size of cystic spaces (for treatment purposes)
 - Macrocystic: > 1-cm cystic spaces
 - o Microcystic: 0.5- to 10-mm cystic spaces
- Mixed cystic

Gross Pathologic & Surgical Features

- Unilocular or multicystic mass filled with milky fluid
- May be encapsulated
- May encase or infiltrate local structures

Microscopic Features

- Mass of thin-walled, dilated lymphatic vessels
- Lined by bland flattened endothelium, no atypia
- Benign lymphoid aggregates, stromal fibrosis
- No malignant transformation but local recurrence in 35%

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o 90% of patients present by age 2 years
 - Often asymptomatic in adults
 - o Chest pain, dyspnea, dysphagia
 - o Vascular or tracheal compression, stridor

Demographics

- Sex
 - Children, more common in males
 - Adults, more common in women
- Epidemiology
 - Up to 4.5% of mediastinal tumors

Treatment

- Complete surgical excision difficult if local encasement or infiltration; 20% may enlarge/recur
- Percutaneous drainage ± sclerotherapy for macrocystic lesions

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Consider lymphangioma in patient with cystic mediastinal mass and history of childhood resection

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- Itkin M et al: Nonmalignant adult thoracic lymphatic disorders. Clin Chest Med. 37(3):409-20, 2016

KEY FACTS

TERMINOLOGY

• Rare, benign vascular neoplasm

IMAGING

• Radiography

- Round or lobulated mediastinal soft tissue mass
- Typically located in anterior mediastinum
- Discrete round calcifications (phleboliths) in 10%
- CT
 - Mediastinal soft tissue mass with central, peripheral, or mixed enhancement
 - May surround &/or exert mass effect on adjacent structures
 - Discrete or ring-like calcifications (phleboliths) up to 30%
 - Feeding vessel, intratumoral vascularity, aberrant venous drainage may be evident on sequential scans
- MR
 - Heterogeneous signal intensity on T1WI
 - o High signal intensity on both T2WI and T2WI FS

TOP DIFFERENTIAL DIAGNOSES

- Lymphoma
- Germ cell neoplasms
- Thymoma
- Lymphangioma/lymphatic malformation

PATHOLOGY

- Interconnecting vascular spaces ± hemorrhage, cysts
- Areas of organized thrombus may calcify

CLINICAL ISSUES

- Asymptomatic in almost 1/2 of cases
- Typically young patients, most < 35 years
- Surgical excision usually required for diagnosis
- Excellent prognosis without documented recurrence

DIAGNOSTIC CHECKLIST

• Heterogeneously enhancing mediastinal soft tissue mass with phleboliths is virtually diagnostic of hemangioma

(Left) PA chest radiograph of an adult woman shows a large left-sided mediastinal mass 🔁 that obscures the aortic contour and extends superiorly through the thoracic inlet into the neck with mass effect on the trachea 🛃. (Right) Axial CECT of the same patient shows a left prevascular mediastinal mass \blacksquare with heterogeneous enhancement and a rounded calcification compatible with a phlebolith **E≥**. Some hemangiomas demonstrate a sequential enhancement pattern of "centripetal fill-in."





(Left) Coronal CECT of the same patient demonstrates the heterogeneously enhancing mediastinal mass \mathbf{E} , which extends into the neck and multiple intrinsic round and punctate calcifications \triangleright that represent phleboliths. Note multiple cysts and heterogeneous enhancement of the spleen 🖂. (Right) Axial CECT of the upper abdomen confirms areas of hypervascularity \square and cysts \blacksquare throughout the spleen compatible with additional hemangiomas.





Definitions

• Rare, benign vascular neoplasm

IMAGING

General Features

- Best diagnostic clue
 - Round or lobulated anterior/prevascular mediastinal mass with heterogeneous contrast enhancement and phleboliths
- Location
 - Majority in anterior/prevascular mediastinum (up to 75%)
 - Extrathoracic extension rare; usually to neck
- Morphology
 - o Well-circumscribed soft tissue mass, usually solitary

Radiographic Findings

- Well-defined mediastinal soft tissue mass
- Discrete round calcifications/phleboliths in 10%

CT Findings

- NECT
 - Rounded or lobulated mediastinal mass
 - Heterogeneous attenuation from intratumoral thrombus, dense vasculature, nodular soft tissue
 - High sensitivity for discrete rounded and ring-like calcifications/phleboliths (up to 30%)
 - o Intralesional fat (-40 to -120 HU) may be present
- CECT
 - Central, peripheral, and heterogeneous enhancement on sequential imaging
 - Nodular or tortuous tubular enhancing structures
 - Feeding arteries may be identified in early phase, aberrant dilated draining veins in delayed phase

MR Findings

- T1WI
 - Mixed high and intermediate signal intensity: Nodular tumor, vessels ± thrombus, fat
- T2WI
 - Predominant high signal related to protein/hemorrhage in vascular spaces ± myxoid and fat components
- T2WIFS
 - Persistent high signal on fat suppression sequences

Imaging Recommendations

- Best imaging tool
 - CT optimally demonstrates phleboliths, complex vascularity, and extent of mediastinal neoplasm
- Protocol advice
 - Image-guided needle biopsy rarely diagnostic; hemorrhage risk

DIFFERENTIAL DIAGNOSIS

Lymphoma

- Multiple lymph node compartments often affected
- Limited homogeneous enhancement on CECT
- Calcifications rare before treatment

Germ Cell Neoplasms

Teratoma: Ca++, soft tissue, fat, cysts ± fluid-fluid levels
 Ca++: Amorphous, curvilinear, punctate

Thymoma

- Lobulated mass, variable attenuation post-contrast
- Calcification (punctate, amorphous) in 10-40%; no fat

Lymphangioma/Lymphatic Malformation

- Cystic spaces common
- Contrast enhancement and calcifications rare

PATHOLOGY

General Features

- Associated abnormalities
 - Peripheral hemangiomas of skin, spleen, liver, kidney

Hereditary hemorrhagic telangiectasia

Staging, Grading, & Classification

• Capillary or cavernous (depending on vessel size); most lesions mixed

Gross Pathologic & Surgical Features

- Spongy lesion with nodular and dilated vascular spaces
- Foci of hemorrhage, cystic change, aneurysm, thrombus
- May encase or infiltrate adjacent structures

Microscopic Features

- Anastomosing dilated vascular channels without atypia
- Vascular spaces lined by bland flattened endothelium
- Foci of dystrophic calcification, myxoid, and fatty material

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic in ~ 50%
 - o Cough, chest pain, dyspnea, dysphagia, stridor
- Other signs/symptoms
 - Rarely dysphagia, superior vena cava syndrome, neurologic symptoms, back pain, hemorrhagic effusion
- Demographics

• Age

- Typically young patients: ~ 75% by age 35 (range: 2 months to 76 years)
- Epidemiology
- o < 0.5% of all mediastinal masses; no sex predilection

Treatment

• Surgical excision (open or thoracoscopic) for diagnosis and treatment

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Enhancing mediastinal soft tissue mass with phleboliths is virtually diagnostic of hemangioma

SELECTED REFERENCES

 Li JL et al: Mediastinal hemangiomas: spectrum of CT and MRI findings retrospective case series study and systematic review of the literature. Eur J Radiol. 126:108905, 2020

Thymic Hyperplasia

KEY FACTS

TERMINOLOGY

• Thymic enlargement due to thymic or lymphoid hyperplasia

IMAGING

- Radiography
 - Normal chest radiograph
 - Mediastinal widening or enlargement
- CT
 - True thymic hyperplasia: Diffuse, symmetric thymic enlargement, typically following chemotherapy
 - Lymphoid hyperplasia: Normal thymus, enlarged thymus, focal thymic mass
 - Enhancement similar to that of normal thymus
 - Heterogeneous enhancement suggests thymic neoplasm
- MR: ↓ signal on opposed-phase gradient-echo T1WI
 - Determination of chemical shift ratio &/or signal intensity index
- FDG PET/CT: Standardized uptake value (SUV) = 2.0-2.8

TOP DIFFERENTIAL DIAGNOSES

- Thymoma
- Recurrent or metastatic malignancy
- Lymphoma

PATHOLOGY

- True thymic hyperplasia: Secondary to recent stress, microscopically normal thymus
- Lymphoid hyperplasia: Association with myasthenia gravis, thymic lymphoid follicles

CLINICAL ISSUES

• Asymptomatic; typically no treatment required

DIAGNOSTIC CHECKLIST

- Consider thymic hyperplasia in patient on chemotherapy with enlarging thymus
- Consider lymphoid hyperplasia in patients with myasthenia gravis

(Left) Graphic shows the axial anatomy of the anterior/prevascular mediastinum. The thymus is surrounded by fat, bound posteriorly by the superior vena cava and ascending aorta and anteriorly by the sternum. (Right) Graphic illustrates the method for measuring the thymus on CT. The AP diameter (W) and thickness of each lobe (T) are measured as shown. Thymic thickness is the most frequently used measurement and should be correlated with the patient's age.





(Left) Composite image with axial CECT of a patient with thymic hyperplasia shows prevascular mediastinal soft tissue in the thymic bed that conforms to adjacent structures \bowtie with nodular areas \square that suggest neoplasia. (Right) Composite image with in- (left) and outof-phase (right) GRE MR of the same patient shows a prevascular mediastinal nodule \supseteq with marked signal drop on out-of-phase imaging \square , a typical feature of thymic hyperplasia that allows exclusion of thymic neoplasia.





Thymic Hyperplasia

TERMINOLOGY

Synonyms

• Thymic rebound

Definitions

• Thymic enlargement due to thymic or lymphoid hyperplasia

IMAGING

General Features

- Best diagnostic clue
 - Diffuse, nonlobulated symmetric thymic enlargement
 - Homogeneously decreased signal on opposed-phase gradient-echo T1WI MR
- Location
 - Anterior/prevascular mediastinum: Anterior to ascending aorta, right ventricular outflow tract, and superior vena cava
- Size
 - Measurement: Anteroposterior, transverse, thickness
 - Normal thymic thickness on CT
 - 6-19 years
 - □ Right lobe 1.0 cm ± 0.39; left lobe 1.1 cm ± 0.4 - 20-29 years
 - □ Right lobe 0.7 cm ± 0.24; left lobe 0.8 cm ± 0.14 - 30-39 years
 - □ Right lobe 0.5 cm ± 0.14; left lobe 0.7 cm ± 0.21
 - 40-49 years
 - □ Right lobe 0.6 cm ± 0.23; left lobe 0.6 cm ± 0.2 - > 50 years
 - Right lobe 0.5 cm ± 0.15; left lobe 0.5 cm ± 0.27
 Normal thymic thickness on MR
 - Thymus 30-50% larger than on CT
- Normal thymus on CT
 - Age < 10 years: Extremely variable, quadrilateral shape
 - Puberty: Triangular, bilobed, or arrowhead morphology
 - After puberty: Triangular or bilobed
 - Normal margins: Straight or concave
 - Multilobulated morphology at any age suggests neoplastic involvement
 - CT attenuation
 - Age < 20 years: Soft tissue (100%), homogeneous
 - 20-50 years: Homogeneous or heterogeneous from progressive fatty infiltration
 - > 50 years: Fat attenuation (90%)
 - Variable but homogeneous contrast enhancement
- Normal thymus on MR
 - Homogeneous signal intensity
 - o T1WI: Higher signal intensity than that of muscle
 - o T2WI: Signal intensity approaches that of fat
- Normal thymus on PET
 - Physiologic FDG uptake
 - Typically low: SUV = 1.0-1.8
 - Children, young adults, sporadically in older adults
- Normal thymus on ultrasound
 - Visible in > 90% at age 2-8 years
 - Approach: Intercostal parasternal imaging
 - Well-defined smooth borders, conforms to adjacent structures

- Echogenicity: Similar to that of liver, linear/branching echogenic foci
- Pliable, no mass effect on adjacent structures
- Longitudinal and AP dimensions
 - Right lobe (longitudinal): 1.54-4.02 cm (mean: 2.5 cm)
 - □ Right lobe (AP): 0.81-2.35 cm (mean: 1.4 cm)
 - □ Left lobe (longitudinal): 1.79-4.1 cm (mean: 2.9 cm)
 - □ Left lobe (AP): 0.78-2.47 cm (mean: 1.4 cm)

Radiographic Findings

- Typically normal chest radiograph
- May produce mediastinal widening

CT Findings

- NECT
 - True thymic hyperplasia
 - Diffuse, nonlobulated symmetric thymic enlargement
 - Same attenuation as normal thymus (according to age)
 - Calcification exceedingly rare
 - Thymic enlargement following chemotherapy
 - Follow-up imaging to document stability or resolution
 - Progressive enlargement suggests neoplasia; may require biopsy

• Lymphoid hyperplasia

- Normal thymic size (45%)
- Enlarged thymus (35%)
- Focal thymic mass (20%)
- CECT
 - Enhancement similar to that of normal thymus
 - Heterogeneous enhancement suggests thymic neoplasm

MR Findings

- Chemical-shift MR imaging
 - **Thymic hyperplasia**: Homogeneously decreased signal on opposed-phase gradient-echo T1WI
 - **Thymic malignancy**: No drop in signal on opposed-phase gradient-echo T1WI
 - Chemical shift ratio (CSR)
 - (Thymus signal out-of-phase/paraspinal muscle signal out-of-phase)/(thymus signal in-phase/paraspinal muscle signal in-phase)
 - Thymic hyperplasia and normal thymus CSRs of 0.5 to 0.6
 - Thymic epithelial neoplasms, lymphoma, and other lesions CSRs of 0.8 to 1.0
 - o Signal intensity index (SII)
 - SII = [(thymus signal in-phase thymus signal out-ofphase)/thymus signal in-phase] x 100
 - SII > 8.92% consistent with thymic hyperplasia
 - 100% sensitivity and specificity

Nuclear Medicine Findings

- PET
 - o Thymic hyperplasia: SUV = 2.0-2.8
 - o SUV > 4.0 suggests malignancy
 - Benign thymic uptake significantly overlaps with malignancy

- Octreoscan (indium-111-DTPA-octreotide scintigraphy) • Thymic hyperplasia: No radiotracer uptake
 - o Uptake in primary &/or metastatic thymic neoplasms

Imaging Recommendations

- Best imaging tool
 - CT: Most frequently used modality to detect thymic hyperplasia
 - MR with determination of CSR and SII: Optimal methods for differentiating thymic hyperplasia from neoplasia
- Protocol advice
 - In- and out-of-phase MR

DIFFERENTIAL DIAGNOSIS

Normal Thymus

- Borderline thymic enlargement in young subjects
- Correlation of thymic size with patient age

Thymoma

- Focal mass
- No signal decrease on opposed-phase gradient-echo T1WI MR

Recurrent or Metastatic Malignancy

- Nodular contour, necrosis, calcification, heterogeneous enhancement
- No signal decrease on opposed-phase gradient-echo imaging T1WI MR

Lymphoma

- Hodgkin more common than non-Hodgkin
- Homogeneous thymic enlargement, mediastinal &/or hilar lymphadenopathy

Thymic Cyst

- Thin wall, unilocular or multilocular
- No solid component
- No contrast enhancement

Ectopic Thyroid

- Heterogeneous lesion: Cysts and calcifications
- Uptake on thyroid scintigraphy

PATHOLOGY

General Features

- Etiology
 - True thymic hyperplasia
 - Usually acquired
 - Recent stress
 - e.g., chemotherapy, corticosteroid therapy, radiotherapy, Cushing syndrome treatment, bone marrow transplantation, thermal burns
 - Other causes: Hyperthyroidism, sarcoidosis, red blood cell aplasia
 - Initial thymic atrophy (~ 40% of original size)
 - After chemotherapy
 - Thymic atrophy in 90%; minimal volume coincides with maximal myelosuppression
 - □ Rebound thymic hyperplasia in 10-25%
 - Lymphoid hyperplasia
 - Most commonly associated with myasthenia gravis

 Other autoimmune diseases: Systemic lupus erythematosus, rheumatoid arthritis, scleroderma, vasculitis, thyrotoxicosis, Graves disease, Addison disease, polyarteritis nodosa, Behçet disease

Gross Pathologic & Surgical Features

- Weight
 - Under 30 years: > 50 g
 - o 30-60 years: > 30 g

Microscopic Features

- True thymic hyperplasia
 - Microscopically normal thymus
 - Size &/or weight exceed upper limits of normal for age
- Lymphoid hyperplasia
 - Abundant medullary secondary lymphoid follicles with germinal centers; expansion of thymic medulla
 - Compression atrophy of thymic cortex
 - Independent of size and weight (often normal)
 - Few or no germinal centers correlates with rapid remission; many germinal centers favor slow remission

CLINICAL ISSUES

Presentation

Most common signs/symptoms

 Usually asymptomatic

Demographics

- Epidemiology
 - True thymic hyperplasia post chemotherapy
 - Initial thymic atrophy
 - Thymic growth to original size (within 9 months) after cessation of stress
 - Thymic growth to 50% larger than original size (rebound phenomenon)
 - Thymic rebound occurs within 2 years of chemotherapy initiation
 - Lymphoid hyperplasia
 - Found in ~ 65% of patients with myasthenia gravis

Treatment

• Generally not required

DIAGNOSTIC CHECKLIST

Consider

 Thymic hyperplasia in patient with enlarging nonlobulated thymus undergoing chemotherapy or in patient with myasthenia gravis

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Thymic Hyperplasia





(Left) Composite image with axial CECT of a patient who developed thymic hyperplasia after chemotherapy for lymphoma shows thymic enlargement 🔁 that manifests as prevascular mediastinal soft tissue with preserved lobar anatomy surrounded by fat. (Right) Composite image with axial fused FDG PET/CT of the same patient shows mild thymic , FDG uptake 🛃. Thymic hyperplasia often exhibits little to mild FDG uptake, typically below 3.0 standardized uptake value (SUV).





(Left) Composite image with axial CECT (left) and FDG PET/CT (right) of a patient treated with chemotherapy for Hodgkin lymphoma shows thymic hyperplasia that manifests as thymic enlargement 🖻 with mild FDG uptake. (Right) Composite image with axial CECT (left), in- (center), and out-of-phase (right) MR of a patient with pharyngeal carcinoma treated with chemotherapy shows a prevascular mediastinal soft tissue mass \blacksquare that exhibits characteristic signal dropout ➡ on out-of-phase MR imaging.





(Left) Composite image with axial (left) and coronal (right) NECT of a patient with thyrotoxicosis and lymphoid thymic hyperplasia shows an enlarged heterogeneous thyroid \bowtie with mass effect on the upper trachea 🛃. (Right) Axial NECT of the same patient shows a diffusely enlarged homogeneous thymus \blacksquare with slightly convex borders. While most cases of thymic lymphoid hyperplasia relate to myasthenia gravis, other autoimmune processes, such as thyrotoxicosis, can be associated with it.

Mediastinal Goiter

KEY FACTS

TERMINOLOGY

- Goiter: Enlarged thyroid
- Cervical goiter: Completely within neck
- Retrosternal/substernal goiter: Extension into anterior (prevascular) mediastinum
- Mediastinal goiter: Extension into retroesophageal (middle, visceral) mediastinum
- Coexisting thyroid cancer in up to 5-15% of goiters

IMAGING

- **Radiography**: Tracheal displacement, often beginning at laryngeal level, may extend below thoracic inlet
- CT
 - Sharply demarcated heterogeneous mass in continuity with cervical goiter
 - High attenuation given intrinsic iodine content
 - Intense sustained contrast enhancement
 - o Calcification: Punctate, coarse (> 3 mm), ring-like
 - o Cystic change

TOP DIFFERENTIAL DIAGNOSES

- Thymoma
- Germ cell neoplasm
- Lymphoma
- Lymphangioma
- Congenital cysts

PATHOLOGY

Etiology: Multinodular goiter, follicular adenoma
 Rarely carcinoma or lymphoma

CLINICAL ISSUES

- Symptoms/signs: Asymptomatic, dyspnea, wheezing
- Treatment: Surgery is only definitive treatment

DIAGNOSTIC CHECKLIST

- Consider goiter in differential diagnosis of asymptomatic tracheal deviation
- Thyroid goiter should be surveilled with ultrasound

(Left) Graphic shows the characteristic morphologic features of mediastinal multinodular goiter with internal calcifications, cystic ⇒, and solid ≥ areas. Goiters may extend into the prevascular and visceral mediastinal compartments and often displace and compress adjacent structures, including the trachea, esophagus, and great vessels. (Right) PA chest radiograph of a patient with thyroid goiter shows marked compression and rightward displacement of the trachea \supseteq as well as mediastinal extension.





(Left) Lateral chest radiograph of a patient with a large intrathoracic goiter shows marked anterior displacement and bowing \supseteq of the trachea by the mediastinal mass 🔁. Few mediastinal lesions produce such tracheal abnormalities and include achalasia and goiter, but goiter is the most common. (Right) Coronal oblique CECT of the same patient shows a large heterogeneous soft tissue mass contiguous with the cervical thyroid with intrinsic low attenuation and coarse calcification, typical of benign thyroid goiter.





Mediastinal Goiter

TERMINOLOGY

Definitions

- Goiter: Enlarged thyroid gland
- Cervical goiter: Completely within neck
- **Retrosternal/substernal goiter**: Extension into anterior (prevascular) mediastinum
- Mediastinal goiter: Extension into
 retrotracheal/retroesophageal mediastinum
 - **Primary goiter**: Origin in ectopic thyroid tissue; supplied by intrathoracic vessels
 - **Secondary goiter**: Origin in cervical thyroid; supplied by neck vessels
- Coexisting thyroid cancer in up to 5-15% of all goiters

IMAGING

General Features

- Best diagnostic clue
 - Tracheal deviation at thoracic inlet
 - Most common cause of tracheal deviation
- Location
 - Thyroid bed (~ 55%)
 - o Mediastinal extension (~ 35%)
 - In or partially in anterior (prevascular) mediastinum
 Retrosternal or substernal goiter: Exclusively in anterior (prevascular) mediastinum
 - Mediastinal goiter (10-15%): Visceral mediastinum with retrotracheal/retroesophageal extension
 - Posterior or lateral to pharynx (10%)
- Size
 - o Variable: Few cm to > 10 cm

Radiographic Findings

- Radiography
 - Anterior or middle mediastinal mass
 - Cervicothoracic sign: Inferior goiter outlined by lung (i.e., border well-defined); cervical goiter borders obscured by surrounding neck soft tissues (i.e., border obscured)
 - May exhibit intrinsic calcification
 - Tracheal displacement typically present, often beginning at larynx
 - Tracheal narrowing
 - Radiography does not allow accurate assessment of degree of narrowing
 - o Lateral radiography
 - Anterior goiters fill retrosternal clear space
 - Retrotracheal goiters obscure Raider triangle; mass effect on posterior trachea

Fluoroscopic Findings

- Esophagram
 - Extrinsic compression of upper esophagus
 - Upward goiter displacement on deglutition (84%)

CT Findings

- NECT
 - Sharply demarcated heterogeneous mass in continuity with cervical goiter
 - Prevascular mediastinal goiter: Left side predominant, rightward tracheal deviation/compression

- Retroesophageal goiter: Right side predominant, leftward tracheal and esophageal deviation/compression
- **High-attenuation (70- to 85-HU)**, intrinsic iodine content
- **Calcification**: Amorphous, irregular, ring-like, punctate, coarse (> 3 mm)
- **Cystic changes**: Low attenuation, high attenuation due to hemorrhage
- Goiter descends 1.0-3.0 cm when patient imaged with arms overhead
- Ancillary findings
 - Pericardial effusion from severe hypothyroidism and myxedema
 - Tracheomalacia from tracheal compression
 - Lymphadenopathy with calcification, central necrosis, and cyst formation suggests coexistent thyroid malignancy
- Origin in ectopic mediastinal thyroid tissue; similar morphology, may mimic other lesions (e.g., thymic epithelial neoplasm, germ cell neoplasm, parathyroid adenoma)

CECT

- Prolonged and sustained contrast enhancement (> 25 HU)
- o Cystic areas do not enhance
- Avoid contrast in hyperthyroidism to prevent thyrotoxicosis and in candidates for radioiodine therapy
- Enhancing lymphadenopathy suggests coexistent metastatic thyroid carcinoma

MR Findings

- T1WI
 - o Intermediate signal, slightly higher than muscle
 - Heterogeneous signal
 - Cysts may exhibit high signal due to hemorrhage or proteinaceous material
- T2WI
 - Slightly higher signal than surrounding structures
 - Heterogeneous signal
 - Variable signal in cysts depending on contents and age of hemorrhage
- Optimal estimation of thyroid volume, better accuracy in substernal goiter

Ultrasonographic Findings

- Useful for evaluation of cervical goiter
- Ultrasound is indicated in most thyroid goiters to identify suspicious nodule(s) that may require tissue sampling
- Substernal component often difficult to assess
- Heterogeneous echotexture often with multiple nodules of varying sizes
 - Uniformly hypoechoic cysts
 - Echogenic foci with posterior shadowing due to calcifications
- Image-guided biopsy of suspicious lesions

Nuclear Medicine Findings

- I-123 and I-131 diagnostic but often unnecessary
 ↑ uptake in hyperthyroid patients
 - Absence of uptake does not exclude goiter
- Technetium pertechnetate not used due to high blood pool mediastinal activity
Imaging Recommendations

- Best imaging tool
 - Chest radiographic findings often characteristic
 - CT for definitive diagnosis and surgical planning
- Protocol advice
 - Include CT imaging of neck in patients with suspected mediastinal goiter to document connection to thyroid
 - Thyroid goiter should be assessed with ultrasound to identify suspicious nodule(s) that may require tissue sampling

DIFFERENTIAL DIAGNOSIS

Thymoma

- May exhibit solid and cystic areas and calcification
- No continuity with cervical thyroid

Germ Cell Neoplasm

- May exhibit solid and cystic areas, fat, and calcification
- No continuity with cervical thyroid

Lymphoma

- Rarely calcifies before treatment
- Multicentric lymphadenopathy, nodal coalescence

Lymphangioma

- Conforms to or envelops rather than displaces structures
- Cystic spaces
- Rare calcification

Congenital Cyst

- May be hyperdense due to protein and calcium content
- No continuity with cervical thyroid

PATHOLOGY

General Features

- Etiology
 - Multinodular goiter (51%): Hyperplasia from ↑ thyrotrophin-stimulating hormone (TSH) and ↓ thyroid hormone
 - Follicular adenoma (44%)
 - Chronic autoimmune thyroiditis (5%)
 - Other (rare): Carcinoma, amyloid, lymphoma

Gross Pathologic & Surgical Features

- Enlarged, heterogeneous thyroid
- Cystic degeneration
- Areas or hemorrhage
- Calcification

Microscopic Features

- Irregularly enlarged follicles with flat epithelium and abundant colloid
- Microscopic cancer foci in 5-15%
- Psammomatous calcification: Punctate calcifications 5-100 μm, associated with malignancy

CLINICAL ISSUES

Presentation

Most common signs/symptoms
 Asymptomatic mass (most common)

- o Dyspnea, wheezing, cough
- Other signs/symptoms
 - Dysphagia, hoarseness, phrenic nerve paralysis, Horner syndrome, jugular vein compression/thrombosis, cerebrovascular steal syndrome, superior vena cava syndrome, hyperthyroidism
 - Pemberton sign: Neck vein distention with upper extremity elevation due to venous obstruction
 - Thyrotoxicity due to autonomous functioning nodule, iodide ingestion, or iodinated contrast material
 - Plummer disease (toxic multinodular goiter): Autonomous functioning nodule and resultant hyperthyroidism

Demographics

- Age
 - o Increased frequency with advancing age
- Sex
- o M:F = 1:3
- Epidemiology
 - Affects 5% of people worldwide
 - Up to 20% descend into mediastinum
 - 2-21% of patients undergoing thyroidectomy have substernal thyroid component
 - Represents up to 7% of mediastinal tumors
 - o 5-15% of all goiters with coexistent thyroid cancer
 - Frequency of large goiters in decline

Natural History & Prognosis

- Patients with goiter should undergo thyroid function tests
- Slow growth unless underlying cause is corrected

Treatment

- Surgery is only definitive treatment
 - Considered when patient condition allows
 - 25% of asymptomatic patients develop acute respiratory distress
 - Cervicotomy for retrosternal/substernal goiter
 - Combined cervicotomy and transthoracic approach for mediastinal goiter
 - Imaging findings that suggest need for combined approach: Inferior displacement of left brachiocephalic vein, 70% of mass below thoracic inlet, inferior border below aortic arch
- Observation considered in small lesions and older patients

DIAGNOSTIC CHECKLIST

Consider

• Goiter in differential diagnosis of asymptomatic tracheal deviation

Image Interpretation Pearls

• Mediastinal mass in continuity with cervical thyroid is likely to represent mediastinal goiter

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Mediastinal Goiter





(Left) PA chest radiograph of a patient with intrathoracic goiter shows a large mass 🄁 that displaces the trachea \supseteq to the left and exhibits the cervicothoracic sign (note the fading contour 🔁 of the upper aspect of the lesion). Retroesophageal mediastinal goiters typically displace both the trachea and the esophagus. (Right) Lateral chest radiograph of the same patient shows a large mass 🛃 that displaces and and bows the posterior tracheal wall \blacksquare . Mass effect on the posterior trachea is a typical feature of goiters in this location.





(Left) Axial CECT of the same patient shows a large, heterogeneously enhancing visceral mediastinal mass 🛃 with intrinsic calcification in the right paratracheal and retrotracheal/retroesophageal regions and marked compression of the trachea \square and esophagus. (Right) Curved MPR CECT of the same patient shows continuity 🔁 between the mediastinal mass \square and the cervical goiter \square , a feature that allows localization of the mass in the cervicothoracic region, a finding highly suggestive of a lesion of thyroid in origin.





(Left) Composite image with axial CECT of a patient with an mediastinal goiter D that contained a small focus of papillary carcinoma shows a large mass in the visceral and prevascular 🔁 mediastinum that produces tracheal compression \supseteq . Occult malignancy occurs in up to 15% of goiters and is often not evident on CT. (Right) Axial NECT of a patient with a mediastinal goiter originating in ectopic prevascular mediastinal thyroid tissue shows a heterogeneous mass \blacksquare with cystic change and calcification.

Achalasia

KEY FACTS

TERMINOLOGY

- Achalasia: Esophageal dilatation due to primary motility disorder
- **Pseudoachalasia**: Esophageal dilatation due to other abnormalities

IMAGING

Radiography

- Markedly dilated esophagus
- Retrotracheal air-fluid level
- Small or absent gastric air bubble

• Esophagography

- o Markedly dilated esophagus, heterogeneous content
- Absence of primary peristalsis
- Delayed contrast emptying
- o "Bird-beak" deformity of distal esophagus
- CT
 - o Markedly dilated esophagus ± intrinsic air-fluid levelo Abrupt, smooth narrowing of distal esophagus

TOP DIFFERENTIAL DIAGNOSES

- Scleroderma
- Esophageal carcinoma

PATHOLOGY

• Myenteric plexus neuropathy of unknown etiology with incomplete relaxation of lower esophageal sphincter

CLINICAL ISSUES

- Dysphagia (98%), halitosis, recurrent aspiration, weight loss
- Complications
 - Aspiration bronchiolitis/aspiration pneumonia
 - o latrogenic perforation
- Treatment: Smooth muscle relaxants, pneumatic dilatation, Heller myotomy

DIAGNOSTIC CHECKLIST

• Consider importance of differentiating of achalasia from pseudoachalasia

(Left) Graphic shows the morphologic features of achalasia characterized by marked esophageal dilatation with intrinsic fluid, air, an airfluid level, retained food particles, and distal esophageal "bird-beak" deformity 🔁. (Right) Anterior oblique esophagram shows achalasia manifesting with a markedly dilated contrastfilled esophagus \square and birdbeak morphology of the distal esophagus 🖂. The possibility of distal esophageal cancer should always be considered as a potential etiology of distal esophageal obstruction.





(Left) PA chest radiograph of a patient with achalasia shows a large elongate right mediastinal mass 🔁 with an intrinsic air-fluid level 🛃 and lateralization of the azygoesophageal recess \square , consistent with a middle mediastinal mass produced by a massively dilated esophagus. Note absence of a gastric bubble. (Right) Axial CECT of the same patient shows a markedly dilated esophagus \square by abundant debris and anterior tracheal displacement ∠, which was also visible on lateral chest radiography (not shown).





Definitions

- Achalasia: Esophageal dilatation due to primary motility disorder
 - o Failure of relaxation of lower esophageal sphincter
- **Pseudoachalasia**: Esophageal dilatation due to other abnormalities
 - Reflux esophagitis
 - Chagas disease (trypanosomiasis)
 - Esophageal cancer, metastases

IMAGING

Radiographic Findings

• Radiography

- Abnormal elongate mediastinal contour, typically on the right
- o Markedly dilated esophagus ± intrinsic air-fluid level
- Lateralization of azygoesophageal recess
- Small or absent gastric air bubble
- o Lateral chest radiograph
 - Thick tracheoesophageal stripe
 - Anterior tracheal bowing
- Retrotracheal air-fluid level, debris
- **Esophagography** (timed barium swallow)
 - o Markedly dilated esophagus, heterogeneous content
 - Absence of primary peristalsis
 - Delayed contrast emptying: Complete barium clearance by 1 minute in most normal subjects and by 5 minutes in all normal subjects
 - o "Bird-beak" deformity of distal esophagus

CT Findings

- Esophageal dilatation with intrinsic fluid, air, air-fluid level, debris
- Normal esophageal wall thickness
- Abrupt, smooth narrowing of distal esophagus
- Assessment of complications
 - Aspiration bronchiolitis: Centrilobular micronodules/treein-bud opacities, ± bronchiectasis, bronchial wall thickening
 - Aspiration pneumonia
 - latrogenic perforation
 - Esophageal cancer (squamous > adenocarcinoma)

Imaging Recommendations

- Best imaging tool
 - Esophagography is imaging study of choice: Assessment of esophageal motility, reflux, aspiration
 - CT: Assessment of other abnormalities, including benign or malignant neoplasms

DIFFERENTIAL DIAGNOSIS

Scleroderma

- Esophageal dilatation and dysmotility
- Visible gastric bubble

Esophageal Carcinoma

- ± minimal esophageal dilatation
- Focal mass/mural thickening at site of tumor

PATHOLOGY

General Features

- Etiology
 - Myenteric plexus neuropathy of unknown etiology with resultant incomplete relaxation of lower esophageal sphincter

Microscopic Features

• Decreased number of ganglion cells in myenteric esophageal plexus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dysphagia (98%), halitosis, recurrent aspiration pneumonia, weight loss

Demographics

- Age
 - o Achalasia: Younger patients (30-50 years)
 - Pseudoachalasia: Older patients
- Epidemiology
 - o 1 case/100,000 persons
- Sex
 M = F

Natural History & Prognosis

- Esophageal carcinoma (2-7%)
- Recurrent aspiration pneumonia &/or aspiration bronchiolitis
- Diagnosis
 - Endoscopy, barium esophagram, and esophageal manometry are complementary tests for diagnosis of achalasia
 - o Esophageal manometry: Gold standard

Treatment

- Smooth muscle relaxants
- Pneumatic dilatation (risk of perforation)
- Heller myotomy (longitudinal incision of lower esophageal sphincter)

DIAGNOSTIC CHECKLIST

Consider

 Importance of differentiating achalasia from pseudoachalasia

Image Interpretation Pearls

- Suspect achalasia in patients with esophageal dilatation and small or absent gastric bubble on radiography
- CT used for exclusion of other diseases &/or complications

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Esophageal Diverticula

KEY FACTS

TERMINOLOGY

- Esophageal saccular protrusion or outpouching
- Pulsion diverticulum: Mucosa and submucosa without muscular layer
- Traction diverticulum: All esophageal wall layers

IMAGING

- Air-fluid level in superior mediastinum (Zenker) or mid esophagus (traction)
- Barium esophagram
 - o Pulsion diverticulum: Barium-filled sac; rounded
 - Traction diverticulum: Barium-filled tented or triangular outpouching
- Radiography
- Mediastinal air-fluid level in region of esophagus
- CT
 - Incidental finding
 - Air-, water-, or contrast-filled esophageal outpouch

TOP DIFFERENTIAL DIAGNOSES

- Pseudodiverticulosis
- Esophageal ulcer
- Phrenic ampulla
- Esophageal perforation

PATHOLOGY

- Zenker: Mucosal herniation through anatomic weakness in region of cricopharyngeal muscle
- Traction: Common in areas of endemic tuberculosis and histoplasmosis

CLINICAL ISSUES

- Pulsion diverticulum (Zenker)
 - o Upper esophageal dysphagia
 - Regurgitation and aspiration of undigested foodHalitosis; hoarseness; neck mass
- Traction diverticulum: Erosion, perforation

(Left) Graphic shows the different types of esophageal diverticula: Zenker (left), traction (middle), and epiphrenic (right). (Right) Axial NECT shows a large posterior hypopharyngeal pulsion (Zenker) diverticulum \blacksquare that contains retained food and an air-fluid level. Note healed tuberculosis ₽ in the left lung apex. Zenker diverticulum predisposes patients to aspiration pneumonia or aspiration bronchiolitis, complications that should be actively searched for in the lungs.





(Left) Axial CECT of a patient with a traction diverticulum shows a large outpouching \Rightarrow from the upper esophagus and calcified right pleural plaques ► Traction diverticula are associated with previous tuberculosis, sarcoidosis, and histoplasmosis. (Right) Sagittal CECT shows a large air-distended mid esophageal saccular outpouching 🔁 that fills the aortopulmonary window. Differentiation of pulsion diverticula from traction diverticula is sometimes difficult; however, any esophageal diverticulum may predispose to aspiration.





Definitions

- Esophageal saccular protrusion or outpouching
- Pulsion diverticulum
 - Mucosa and submucosa without muscular layer (Zenker, epiphrenic)
- Traction diverticulum
 - o All esophageal wall layers
 - Fibrosis in adjacent periesophageal tissues and granulomatous inflammation

IMAGING

General Features

- Best diagnostic clue
 - Air-fluid level in superior mediastinum (Zenker) or mid esophagus (traction)
 - Barium esophagram
 - **Pulsion diverticulum**: Barium-filled sac, rounded contour
 - **Traction diverticulum**: Barium-filled tented or triangular outpouching
- Location
 - Pharyngoesophageal junction: Pulsion (Zenker)
 - Mid esophagus: **Traction**

• Distal esophagus: **Epiphrenic**

- Size
 - Variable: Zenker size range (0.5-8 cm)
- Morphology
 - Pulsion: Rounded or saccular
 - Traction: Triangular

Radiographic Findings

• Mediastinal air-fluid level in region of esophagus

CT Findings

- Incidental finding
 - Air-, water-, or contrast-filled esophageal outpouching
- Centrilobular nodules should suggest associated aspiration bronchiolitis

Imaging Recommendations

Best imaging tool
 Esophagram: Visualization of esophageal diverticula

DIFFERENTIAL DIAGNOSIS

Pseudodiverticulosis

• Diffuse (50%) or segmental tiny outpouchings in long rows parallel to esophageal long axis

Esophageal Ulcer

• Solitary ring-like/stellate ulcer with edema halo

Phrenic Ampulla

• 2-4 cm luminal dilatation between "A" and "B" rings

Esophageal Perforation

- latrogenic
- Boerhaave syndrome

PATHOLOGY

General Features

- Etiology
 - **Zenker**: Mucosal herniation through anatomic weakness in region of cricopharyngeal muscle (Killian triangle)
 - Traction
 - Common in tuberculosis and histoplasmosis

Gross Pathologic & Surgical Features

• Posterior hypopharyngeal saccular outpouching with broad or narrow neck (Zenker)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Pulsion diverticulum
 - Zenker diverticulum
 - □ Upper esophageal dysphagia
 - □ Regurgitation and aspiration of undigested food
 - Halitosis, hoarseness, neck mass

Traction diverticulum

– Dysphagia

Demographics

- Age
 - Zenker diverticulum: 50% of patients in 7th-8th decades
 - Traction diverticulum: Usually seen in elderly patients
- Sex
 - Zenker diverticulum: M > F
 - Traction diverticulum: M = F
- Epidemiology
 - Traction diverticulum
 - Previous history of granulomatous disease

Natural History & Prognosis

- Complications
 - o Pulsion (Zenker)
 - Aspiration pneumonia
 - Bronchitis, bronchiectasis
 - Risk of perforation after endoscopy or enteric tube placement
 - o Traction
 - Erosion, inflammation
 - Perforation, fistula

Treatment

- Asymptomatic: No treatment
- Large or symptomatic: Surgical diverticulectomy or endoscopic repair

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

 Traction diverticula tend to empty when esophagus is collapsed

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KEY FACTS

TERMINOLOGY

• Acquired narrowing of esophageal lumen

IMAGING

• Radiography

- Identification of radiopaque foreign bodies
- o Initial assessment of indirect findings and complications
- CT
 - o Assessment of esophageal perforation/mediastinitis
 - Assessment of aspiration: Bronchiolitis, pneumonia
 - Prediction of stricture risk after caustic ingestion

• Esophagram

- Single-contrast: Optimal esophageal distention and stricture detection
- o Double-contrast: Optimal mucosal evaluation
- Barium is preferred contrast medium
- Water-soluble contrast for suspected perforation
- Assessment of stricture location and morphology

TOP DIFFERENTIAL DIAGNOSES

- Achalasia
- Vascular anomalies (rings)
- Esophageal carcinoma

PATHOLOGY

- Gastroesophageal reflux-induced (75%)
- Unrelated to gastroesophageal reflux (25%)
 - Radiation, sclerotherapy, caustic ingestion, surgical anastomosis, dermatologic disease, extrinsic compression, esophagitis, foreign bodies, infection

CLINICAL ISSUES

- Dysphagia
 - Benign: Longstanding, intermittent
 - o Malignant: Recent onset, rapid progression
- Aspiration: Productive cough, wheezing, dyspnea
- Treatment: Balloon dilatation

(Left) Composite image with axial (left) and sagittal (right) CECT of a 65-year-old woman with dysphagia and a left hilar lung cancer with mediastinal invasion shows significant stenosis of the left mainstem bronchus ➡. Note absence of a tissue plane surrounding the esophagus. (Right) Left anterior oblique barium esophagram obtained after tracheal and bronchial stent placement shows an esophageal stricture that exhibits an abrupt transition and cup-shaped suprastenotic dilatation 🔁.





(Left) Left anterior oblique barium esophagram of a 25year-old patient with epidermolysis bullosa shows a stricture on the upper esophagus 乏. This condition is typically managed with periodic balloon dilatation due to recurrences. (Right) Composite image with axial CECT (left) and esophagram (right) of a patient who ingested alkaline declogger shows diffuse esophageal wall thickening \blacksquare typical of the acute phase of the disease. A long-segment esophageal stricture 🛃 developed after several weeks.





Definitions

• Acquired narrowing of esophageal lumen

IMAGING

Radiographic Findings

- Identification of radiopaque foreign bodies
- Assessment of indirect findings and complications: Pneumothorax, pleural effusion, mediastinal widening, pneumomediastinum, tracheal displacement/compression, subcutaneous gas

CT Findings

- CECT
 - Assessment of complications
 - Mediastinitis, esophageal perforation
 - **Abscess formation** from primary or iatrogenic perforation (esophageal dilatation)
 - Evaluation of **aspiration**: Bronchiolitis (tree-in-bud opacities), pneumonia (consolidation)

• Caustic ingestion

- Informs management algorithm in acute setting
 Grade 1: Normal appearance
 - Grade 2: Fine rim of mucosal and external esophageal wall enhancement with mid wall edema (target sign); may allow non-operative management
 - □ Grade 3: Transmural necrosis with absent wall enhancement; associated with perforation, requires emergency surgery
- Prediction of stricture formation in non-operative cases
 - Mucosal and external esophageal wall enhancement, with mid wall edema (target sign): 17% risk of stricture
 - □ Fine rim of external wall enhancement (lack of mucosal enhancement): 83% risk for stricture
- Malignant stricture features
 - Eccentric mural thickening with irregular or nodular margins
 - Disrupted mucosal surface enhancement
 - Abrupt transition with cup-shaped suprastenotic dilatation

Fluoroscopic Findings

• Distal esophageal stricture

- Gastroesophageal reflux-induced ("peptic" stricture) - Classic: 1-4 cm, distal esophagus, smooth tapered
 - concentric narrowing, associated hiatal hernia – **Atypical**: Sacculations, step-ladder appearance, ring-
 - like narrowing
- Scleroderma: Distal esophagus, patulous esophagus, long segment stricture

• Upper and midesophagus strictures

- Barrett esophagus: Peptic stricture, most are distal, some affect mid esophagus; ring-like stricture, reticular appearance distal to stricture
- Caustic ingestion: 1-3 months after ingestion, ≥ 1 segment, may be diffuse, increased risk of malignancy

 Skin diseases: Upper or mid esophagus, concentric or asymmetric narrowing, ≥ 1 segment

Imaging Recommendations

- Best imaging tool
 - Esophagram
 - Single-contrast: Optimizes esophagus distention and stricture detection
 - Biphasic esophagram (double-contrast): Use of effervescent and barium, optimizes mucosal evaluation
 - Barium is preferred contrast medium
 - Water-soluble contrast used for suspected perforation or leak (e.g., caustic ingestion)

DIFFERENTIAL DIAGNOSIS

Achalasia

- Failure of relaxation of lower esophageal sphincter
- Dilated esophagus, air-fluid level on upright radiography

Vascular Anomalies (Rings)

- Extrinsic compression by anomalous vessels
- Classic esophagram findings

Esophageal Carcinoma

- Asymmetric esophageal narrowing, mass
- Local invasion, lymphadenopathy

PATHOLOGY

General Features

- Etiology
 - Gastroesophageal reflux-induced (75%)
 - Primary
 - Secondary: Scleroderma, Zollinger-Ellison syndrome, nasogastric intubation, alkaline reflux esophagitis

Unrelated to gastroesophageal reflux (25%)

 Radiation, esophageal sclerotherapy, caustic ingestion, surgical anastomosis, dermatologic disease (e.g., epidermolysis bullosa dystrophica), extrinsic compression (e.g., mediastinal fibrosis), eosinophilic esophagitis, foreign bodies, infection

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dysphagia
 - Benign: Longstanding, intermittent, nonprogressive
 - Malignant: Recent onset, fast progression, weight loss
 - Aspiration: Productive cough, wheezing, dyspnea

Natural History & Prognosis

• Strictures may recur after treatment

Treatment

• Balloon dilatation: May be complicated by perforation and mediastinitis

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Esophageal Carcinoma

KEY FACTS

TERMINOLOGY

• Primary esophageal neoplasm (adenocarcinoma or squamous cell carcinoma)

IMAGING

• Radiography

- Focal mediastinal mass
- o Displacement of azygoesophageal recess
- Dilatation of esophagus ± air-fluid level

• CT

- Asymmetric or circumferential esophageal mural thickening
- Focal esophageal mass

• Endoscopic ultrasound

- Optimal for determining depth of wall invasion
- PET/CT
 - Staging and restaging
 - Detection of synchronous malignancy

TOP DIFFERENTIAL DIAGNOSES

- Esophageal stromal tumor
- Esophageal metastases
- Esophagitis

PATHOLOGY

- Squamous cell carcinoma: Proximal 2/3 of esophagus
 Risk factors: Smoking, alcohol
- Adenocarcinoma: Distal 1/3 of esophagus
 Risk factors: Reflux, obesity, smoking

CLINICAL ISSUES

Symptoms

- o Dysphagia, weight loss
- Average age: 65-70 years; M > F
- Treatment

•

- Endoscopic therapy or surgery
- Neoadjuvant chemoradiation followed by surgery
- M1: Chemotherapy ± radiation

(Left) Graphic shows the morphologic features of esophageal carcinoma with asymmetric mural thickening of the distal esophagus. Adenocarcinoma is the most common histologic type in the USA and typically involves the mid and distal esophagus. (Right) Esophagram of a 55year-old patient shows an esophageal cancer that manifests as irregular distal esophageal stenosis 🔁 with an apple core appearance by a lobulated ulcerated mass $\overline{\rightarrow}$ Benign stenosis is typically smooth without ulceration.





(Left) Axial endoscopic ultrasound of a patient with esophageal cancer shows the muscularis as a hypoechoic layer \blacksquare and a mass \blacksquare that extends beyond the muscularis into the adventitia, consistent with T3 disease. Endoscopic ultrasound is the modality of choice to determine the T status of esophageal carcinoma. (Right) Axial CECT of a patient with esophageal carcinoma shows irregular mural thickening of the distal esophagus \blacksquare and preserved fat planes with mediastinal structures indicating no extraesophageal involvement.





Abbreviations

- Squamous cell carcinoma (SCC)
- Esophageal adenocarcinoma (EAC)

IMAGING

General Features

- Location: Based on main mass location; American Joint Commission on Cancer (AJCC) 8th edition
 - **Upper**: Cervical esophagus to lower border of azygos vein
 - **Middle**: Lower border of azygos vein to lower border of inferior pulmonary vein
 - **Lower**: Lower border of inferior pulmonary vein to stomach, including esophagogastric junction
 - Tumor at gastroesophageal junction classified as esophageal if tumor center < 2 cm into gastric cardia

Radiographic Findings

- Dilatation of esophagus ± air-fluid level
- Displacement or abnormal convex contour of azygoesophageal recess
- Thick posterior tracheal stripe on lateral radiograph
- Double-contrast esophagram
 - Focal mucosal irregularity, nodularity, ulceration
 - o Localized area of wall flattening and stiffening
 - Irregular luminal narrowing with abrupt borders
 - Large lobulated intraluminal mass

CT Findings

- Normal esophagus: Thin wall (< 5 mm), enhances homogeneously around small amount of luminal air; surrounding fat plane usually evident
- Esophageal wall thickening > 5 mm (asymmetric or circumferential)
 - Preserved fat planes between esophageal cancer and adjacent mediastinal structures excludes T4 disease
- Unable to differentiate between T1 and T2 disease
- Important role in excluding T3 and T4 disease by excluding local invasion
 - T3: Periesophageal fat infiltration
 - T4: Loss of fat planes between tumor and adjacent mediastinal structures
 - Displacement, indentation or fistula
 - ≥ 90° contact of aortic wall circumference
 - Sensitivity/specificity for T3 and T4 disease: 75%/78% and 75%/86%, respectively
- Focal esophageal mass
- Complications: Aspiration bronchiolitis (centrilobular nodules), tracheoesophageal fistula
- Malignant stricture
 - o Eccentric wall thickening, irregular or nodular margins
 - Disrupted mucosal surface enhancement
 - Abrupt transition with cup-shaped suprastenotic dilatation
- Lymphadenopathy
 - Thoracic and abdominal lymph nodes > 1 cm in short axis
 - Supraclavicular lymph nodes > 5 mm in short axis
- Metastatic disease: Intra- or extrathoracic metastases

MR Findings

• High-resolution T2WI with cardiorespiratory gating shows layers of esophageal wall

Ultrasonographic Findings

- Endoscopic ultrasound (EUS)
 - Optimal for determining T staging (esophagus wall penetration depth), especially initial stages
 - Differentiation of T1/T2/T3 tumors from T4 tumors
 - T1/T2 tumors (sensitivity/specificity; 82% and 99%) treated with surgical resection
 - T3/T4 tumors (sensitivity/specificity; 92% and 97%) preoperative chemoradiotherapy (CRT)
 - o Limitations: Suboptimal evaluation of stenotic tumors

Nuclear Medicine Findings

- PET/CT
 - Limited role in T staging other than determining mediastinal organ invasion
 - Detection of occult primary in patients with metastatic disease
 - Low sensitivity and specificity (51% and 84%, respectively) in regional lymph node (N) assessment
 - Lymph nodes often obscured by metabolic activity of primary tumor
 - High sensitivity and specificity (71% / 93%) for detecting distant metastases (M)
 - Additional metastatic sites in 41% cases
 - Identification of synchronous primary malignancies: 1.5-8% of patients at initial staging

Imaging Recommendations

- Best imaging tool
 - TNM staging of esophageal carcinoma includes EUS, MDCT, and FDG-PET/CT
 - EUS is modality of choice to determine T status and regional lymph node involvement
 - CT after initial diagnosis to evaluate for unresectable T4 or metastatic disease
 - PET/CT for staging, restaging, follow-up and detection of synchronous malignancy
 - Helps prevent unnecessary surgery by identifying occult metastases

DIFFERENTIAL DIAGNOSIS

Esophageal Stromal Tumor: Leiomyoma, Leiomyosarcoma

- Intramural extramucosal mass; may reach large sizes without proximal esophageal dilatation
- Leiomyoma: Smooth, homogeneous CT attenuation
- Leiomyosarcoma: Heterogeneous CT attenuation

Esophageal Metastases

Typically in patients with known primary cancer
 Breast, lung, gastric cancers

Esophagitis

- Inflammation caused by chemotherapy, radiation treatment, gastroesophageal reflux, infection
- Linear FDG uptake &/or wall thickening with long craniocaudal extension

Esophageal Carcinoma

Staging of Esophageal Carcinoma (TNM AJCC 8th Edition)

ТММ	Definitions
Tumor (T) Status: Depth of Esophageal Invasion	
Тх	Primary tumor cannot be assessed
ТО	No evidence of primary tumor
Tis	High-grade dysplasia (confined to epithelium by basement membrane)
T1	Invasion of muscularis mucosae, lamina propria, or submucosa
T1a	Invasion of lamina propria or muscularis mucosae
T1b	Invasion of submucosa
T2	Invasion of muscularis propria
Т3	Invasion of adventitia
T4a	Resectable invasion of adjacent structure (pleura, pericardium, azygos vein, diaphragm
T4b	Unresectable invasion of adjacent structure(s) (aorta, vertebral body, trachea)
Nodal (N) Status: Regional Lymph Nodes, Any Paraesophageal Lymph Node From Upper Esophageal Sphincter to Celiac Axis	
NO	No regional lymph node metastases
N1	1-2 positive regional lymph nodes
N2	3-6 positive regional lymph nodes
N3	≥ 7 positive regional lymph nodes
Metastasis (M) status	
MO	No distant metastases
M1	Distant metastases

PATHOLOGY

General Features

- Etiology
 - SCC: Typically in proximal esophagus
 - Risk factors: Tobacco use, alcohol consumption, human papilloma virus (HPV), achalasia
 - Incidence declining in Western countries; becoming less common than adenocarcinoma in USA
 - Adenocarcinoma: Typically in distal 1/3 of esophagus
 - Risk factors: Gastroesophageal reflux and Barrett metaplasia, smoking, obesity
 - Incidence increasing rapidly in Western countries

Staging, Grading, & Classification

- Histologic grade (G)
 - **G1**: Well differentiated
 - **G2**: Moderately differentiated
 - G3: Poorly differentiated or undifferentiated
- Separate stage grouping based on T, N, M, G for SCC and adenocarcinoma
 - **SCC**: Tumor location (upper, mid, lower thoracic) also included in stage grouping

Gross Pathologic & Surgical Features

- SCC
 - o Small, plaque-like mucosal thickening in early stage
 - Polypoid fungating intraluminal mass
 - Necrotizing ulcerations ± erosion into airway, aorta
 - Diffuse esophageal wall thickening and rigidity
- Adenocarcinoma: Early flat or raised patches, nodular mass

CLINICAL ISSUES

Presentation

Most common signs/symptoms
 Dysphagia, weight loss

Demographics

- Average age: 50-70 years
- M > F

Natural History & Prognosis

- 24% confined to esophagus at diagnosis
- 30% with distant metastases at diagnosis
- Overall 5-year survival for adenocarcinoma < 15%, worse for SCC

Treatment

- T1 N0 M0 disease: Endoscopic therapy or surgery (esophagectomy)
- M0 disease with deeper extent of tumor or regional lymph nodes: Neoadjuvant chemoradiation followed by surgery
- M1: Palliative treatment: Chemotherapy ± radiation
- Endoscopic procedures: Laser therapy, photodynamic therapy, radiofrequency ablation, brachytherapy, esophageal stent

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Esophageal Carcinoma





(Left) Sagittal CECT of a patient with distal esophageal carcinoma shows the craniocaudal extent of the esophageal mass \supseteq . CT is useful for detecting mediastinal invasion and tumor extent when luminal narrowing prevents endoscopy. (Right) Sagittal FDG PET/CT of the same patient shows the distal esophageal mass \supseteq and a regional upper mediastinal FDG-avid lymph node 🖂. Any lymph nodes adjacent to the esophagus from upper esophageal sphincter to celiac axis is considered regional.





(Left) Coronal FDG PET of 59year-old patient with esophageal carcinoma shows the FDG-avid primary malignancy in the middle third of the esophagus ∋ and FDG uptake in the left supraclavicular region ≥. (Right) Axial FDG PET/CT of the same patient shows an FDG-avid right supraclavicular lymph node ∋ that is not adjacent to the esophagus, and is therefore considered metastatic disease.





(Left) Coronal FDG PET of a patient with esophageal carcinoma 🖾 shows a focal area of FDG uptake in the pelvis 🖂 suspicious for metastasis. (Right) Axial FDG PET/CT of the same patient shows FDG uptake within the left aluteus maximus muscle Biopsy showed metastatic disease. PET/CT has high sensitivity and specificity for detecting distant metastases and should be part of the initial staging in patients considered for surgical treatment. The presence of metastases precludes surgical resection.

Mediastinal Lipomatosis

KEY FACTS

TERMINOLOGY

• Excessive unencapsulated fat deposition in mediastinum

IMAGING

• Radiography

- Smooth symmetric mediastinal widening
- Increased subepicardial/mediastinal fat
- Increased extrapleural fat deposits: Well-marginated, mimics pleural thickening

• CT

• Prevascular mediastinal fat deposition

• Fat attenuation (-60 to -120 HU)

- No soft-tissue nodules within fatty tissue
- No mass effect on or compression of adjacent structures
- MR
 - o Hyperintense on T1WI and T2WI
 - o Isointense to subcutaneous fat

TOP DIFFERENTIAL DIAGNOSES

- Fat-containing mediastinal mass
 e.g., liposarcoma, teratoma
- Mediastinal lymphadenopathy
- Mediastinitis

PATHOLOGY

- Etiology: Obesity, Cushing syndrome
- Mature adipocytes and cellular hyperplasia

CLINICAL ISSUES

- Asymptomatic; incidental imaging finding
- Rarely: Chest pain, dyspnea, cough

DIAGNOSTIC CHECKLIST

- Homogenous mediastinal fat on CT
- Presence of soft tissue nodules or mass effect should suggest neoplasia

(Left) Graphic demonstrates the morphologic features of mediastinal lipomatosis. Unencapsulated mediastinal adipose tissue ➡ surrounds the normal mediastinal structures without obstruction or mass effect. (Right) Axial CECT of a asymptomatic patient with mediastinal lipomatosis shows markedly increased homogeneous fat \square predominantly in the prevascular mediastinum without significant mass effect on or compression of adjacent structures or intrinsic soft tissue components.





(Left) PA chest radiograph of a patient with mediastinal lipomatosis shows smooth superior mediastinal widening \supseteq without mass effect on the mediastinal structures. (Right) Coronal NECT of a patient with mediastinal lipomatosis shows fat attenuation tissue \square that preferentially affects the prevascular mediastinum but also the left cardiophrenic region 🔁. CT allows confident diagnosis of mediastinal lipomatosis and exclusion of underlying lymphadenopathy or mass.





Definitions

• Fat deposition in mediastinum

IMAGING

General Features

- Best diagnostic clue
- Widened mediastinum by adipose tissue
 Location
 - Most frequent in prevascular mediastinum
 - May be associated with increased subepicardial and extrapleural fat
- Morphology
 - No mass effect on mediastinal structures

Radiographic Findings

- Smooth symmetric mediastinal widening
- Increased mediastinal and subepicardial fat may be visible on lateral radiography
- Increased extrapleural fat deposition: Well-marginated, mimics pleural thickening

CT Findings

- Mediastinal fat deposition; predilection for prevascular mediastinum
- Fat attenuation (-60 to -120 HU)
- No soft-tissue nodules within fatty tissue
- No mass effect on or compression of adjacent mediastinal structures

MR Findings

- Hyperintense on T1WI and T2WI
- Isointense to subcutaneous fat
- Signal dropout on fat suppression sequences

Imaging Recommendations

- Best imaging tool
 - CT allows confirmation of mediastinal fat attenuation

DIFFERENTIAL DIAGNOSIS

Fat-Containing Mediastinal Mass

- Distinction from lipomatosis: Identification of dominant soft tissue elements and mass effect
- Mature teratoma: Prevascular mediastinal cystic mass; may exhibit calcification &/or fat attenuation
- Thymolipoma: Conforms to shape of adjacent structures (heart, hemidiaphragm)
- Liposarcoma: Soft tissue components; mass effect
- Lipoblastoma: Chest wall lesion; infants < 3 years
- Hibernoma: Rare benign tumor of brown fat

Mediastinal Lymphadenopathy

- Lobular or laterally convex contours; correspond to mediastinal lymph node stations
- Lipomatosis may mimic lymphadenopathy on radiography

Mediastinitis

- May produce mediastinal widening on radiography
- Hazy infiltration of fat, discrete fluid collections, ± intrinsic gas

PATHOLOGY

General Features

- Etiology
 - Obesity
 Cushing syndrome: Hypercortisolism
 - Exogenous steroids: Treatment of asthma, chronic obstructive pulmonary disease (COPD), connective tissue disease, immune suppression after organ transplantation
 - Excessive corticosteroid production by adrenal neoplasm
 - **Cushing disease**: Excessive adrenocorticotrophic hormone (ACTH) secreted by pituitary neoplasm
 - Ectopic production of ACTH as paraneoplastic syndrome: Small cell lung cancer, thymic carcinoid, islet cell tumor of pancreas

Gross Pathologic & Surgical Features

• Diffuse adipose tissue; unencapsulated fat

Microscopic Features

• Mature adipocytes and cellular hyperplasia

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Asymptomatic; incidental imaging finding
- Other signs/symptoms
 - Chest pain
 - o Dyspnea
 - o Cough

Natural History & Prognosis

• Incidentally detected lipomatosis often follows an benign indolent course

Treatment

- None necessary
- Treatment of underlying condition may cause regression

DIAGNOSTIC CHECKLIST

Consider

- Mediastinal lipomatosis as cause of mediastinal widening in patients on corticosteroids
- Exclusion of adrenal neoplasm in affected patients

Image Interpretation Pearls

- When mediastinal lipomatosis is suspected radiographically, look for other clues of excess adipose tissue
- Mediastinal fat should be homogeneous on CT; dominant soft tissue components or mass effect should suggest neoplasia

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Mediastinitis

KEY FACTS

TERMINOLOGY

- Acute mediastinitis: Potentially life-threatening focal or diffuse mediastinal inflammation usually caused by infection
- Acute descending necrotizing mediastinitis (ADNM)

IMAGING

• Radiography

- o Mediastinal widening
- Pneumomediastinum
- o Mediastinal air/air-fluid level
- CT
 - Increased attenuation of mediastinal fat
 - Localized fluid collection ± peripheral enhancement
 - Free gas bubbles, pneumomediastinum
 - Pericardial effusion
 - Pleural effusion
 - CT esophagogram: localization of esophageal perforation

TOP DIFFERENTIAL DIAGNOSES

- Postoperative seroma
- Mediastinal hematoma/hemorrhage
- Fibrosing mediastinitis

PATHOLOGY

- 90% of acute mediastinitis secondary to esophageal perforation or rupture
- ADNM has highest mortality rate among mediastinitis causes

CLINICAL ISSUES

- Symptoms: Fever, chills, retrosternal pain
- High mortality: 5-50%

DIAGNOSTIC CHECKLIST

- Careful evaluation of entire thorax for exclusion of associated aspiration pneumonia, empyema, osteomyelitis
- Search for mediastinal extension of head and neck infections

(Left) PA chest radiograph of a patient who presented with neck and chest pain 3 days after a dental procedure shows abnormal soft tissue in the right paratracheal \blacksquare and aortopulmonary window 🔁 regions. (Right) Axial CECT of a patient status post subtotal esophagectomy and esophagogastric anastomosis, who presented with fever on postoperative day 10, shows stranding of the mediastinal fat, extensive mediastinal air pockets 🛃, and left greater than right bilateral pleural effusions 🔁.





(Left) Axial CECT of a patient who sustained a hypopharyngeal perforation during intubation shows increased attenuation of the mediastinal fat, a right paratracheal fluid collection \blacksquare , bilateral pleural effusions, and a mediastinal drainage tube 🖾. Acute descending necrotizing mediastinitis is an uncommon, but potentially life-threatening condition. (Right) Sagittal CECT of a patient with mediastinitis shows direct extension of extraluminal air $ar{ arrow}$ from the neck into the retroesophageal mediastinum.





Abbreviations

• Acute descending necrotizing mediastinitis (ADNM)

Definitions

• Acute mediastinitis: Potentially life-threatening focal or diffuse mediastinal inflammation usually caused by infection

IMAGING

General Features

- Best diagnostic clue • Wide mediastinum
 - Fluid collections, air-fluid levels
- Location
- o Mediastinum
- Size
 - o Variable

Radiographic Findings

- Mediastinal widening
- Pneumomediastinum
- Mediastinal air/air-fluid level
- Pleural effusion
- Displaced or changed alignment of sternal wires in poststernotomy mediastinitis

Fluoroscopic Findings

- Esophagram
 - Use of water-soluble contrast in patients with suspected esophageal perforation
 - False-negative in 10% of patients
 - May follow with barium esophagram

CT Findings

- Increased attenuation of mediastinal fat
- Pneumomediastinum: Free gas, air bubbles
- Localized fluid collection ± peripheral enhancement
- Lymphadenopathy
- Pleural effusion
 - Empyema: Loculated pleural effusion
 - Bronchopleural fistula: Intrinsic air or air-fluid levels
- Pericardial effusion
- Pulmonary opacities
- Pleuromediastinal fistula
- Post-cardiac surgery
 - CT appearance of postsurgical mediastinum similar to mediastinitis after first 2-3 weeks post surgery
 - Increased attenuation of mediastinal fat
 - Nonspecific finding
 - May relate to postsurgical hemorrhage or edema
 - Diagnostic yield of CT improves after postoperative day 14
 - New or increased mediastinal air &/or fluid highly suspicious for mediastinitis
 - o Cortical erosion of sternum suggests osteomyelitis
 - Dehiscence of sternotomy site
- Esophageal perforation
 - Leak of ingested contrast into mediastinum &/or pleural space

- **CT esophagogram** has shown similar yield compared to conventional esophagogram
 - Negative CT esophagogram may preclude upper gastrointestinal studies
- Extraluminal air
- Pneumothorax
- Hydropneumothorax
- Subcutaneous gas
- Esophageal wall thickening
- Pleural effusion
 - Right-sided with iatrogenic, mid esophageal perforation
 - Left-sided with spontaneous, distal esophageal perforation
- ADNM
 - Direct extension of cervical infection into mediastinum
 - Jugular vein thrombosis (Lemierre syndrome)
 - Demonstration of contiguity of mediastinal and neck fluid collections

• Direct extension from chest wall infection

- Destruction of articular surface (usually at sternoclavicular joint)
- Joint space widening
- Adjacent chest wall air and fluid collections
- o Obliteration of fat planes around brachiocephalic vessels

MR Findings

- T1 hypointensity and T2 hyperintensity within mediastinal fat
- Enhancement of mediastinal fat
- Peripheral enhancement surrounding fluid collection

Imaging Recommendations

- Best imaging tool
 - CT for evaluation of site and extent of mediastinitis and identification of drainable fluid collection
 - High sensitivity
 - Allows prompt diagnosis and treatment
 - Useful for monitoring treatment response
 - CT esophagogram has shown similar yield as conventional esophagogram
 - Negative CT esophagogram may preclude upper gastrointestinal studies
- Protocol advice
 - Contrast-enhanced chest CT for optimal visualization of loculated fluid collections

DIFFERENTIAL DIAGNOSIS

Postoperative Seroma

- Difficult to distinguish from mediastinitis within 2-3 weeks post surgery
- Must correlate imaging findings with clinical scenario
- Needle aspiration of fluid collections may be necessary to distinguish seroma from abscess

Fibrosing Mediastinitis

- Subacute or chronic (instead of acute) presentation
- Mediastinal soft tissue or calcification without pneumomediastinum or fluid collection

- Typically history of trauma, surgery, central line placement
- Hyperattenuating hematoma helpful for diagnosis when present
- Exclusion of findings of vascular injury
 - Pseudoaneurysm, dissection, contrast extravasation

PATHOLOGY

General Features

- Etiology
 - o 90% of acute mediastinitis related to iatrogenic or spontaneous esophageal perforation
 - Dilatation of stricture or achalasia
 - Endoscopy
 - Esophageal tube/stent placement
 - Necrotic esophageal tumor
 - Ulceration of hiatal hernia
 - Esophagitis
 - Boerhaave syndrome
 - □ Spontaneous esophageal perforation associated with forceful vomiting
 - Ingestion of sharp foreign body or erosive chemical
 - **Postoperative acute mediastinitis** (median sternotomy)
 - 0.5-5% of cardiac surgery patients
 - Mortality rate ranges from 7-80%
 - Risk factors: Obesity, insulin-dependent diabetes mellitus, internal mammary artery graft (especially if bilateral)
 - Direct spread from osteomyelitis or septic joint (sternoclavicular joint)
 - Risk factors
 - □ Intravenous drug use
 - Diabetes
 - □ Rheumatoid arthritis

• ADNM (extension from head and neck infection)

- Anatomic continuity of fascial spaces allows spread of infection from neck to mediastinum
 - □ Contributing factors: Gravity and negative intrathoracic pressure during inspiration
 - □ Routes of spread: Carotid space (skull base to aortic arch), prevertebral space (skull base to T3)
 - Danger space: Retropharyngeal/retroesophageal space from skull base to diaphragm
- Common causes
 - Odontogenic infection
 - □ Suppurative tonsillitis
 - □ Retropharyngeal abscess
- Airway perforation
 - Penetrating or blunt trauma
 - Intubation
 - Bronchoscopic procedures
 - Bronchogenic carcinoma
- Hematogenous spread of infection

Gross Pathologic & Surgical Features

• Mediastinal inflammation/infection ± abscess formation

Microscopic Features

• ADNM and esophageal perforation • Mixed aerobic and anaerobic organisms

- Post-sternotomy and septic joint-related mediastinitis
 - Gram-positive cocci (S. aureus) and gram-negative bacilli (Pseudomonas)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Fever, chills
 - Retrosternal pain
- Other signs/symptoms
 - o Tachycardia
 - Dyspnea
 - o Dysphagia, odynophagia
 - o Subcutaneous air
 - o Sepsis
 - o Neck swelling in patients with ADNM
 - Purulent discharge from sternal wound in patients with post-sternotomy mediastinitis

Demographics

- Age
 - Any age group can be affected

Natural History & Prognosis

- 5-50% mortality
- Highest mortality rate for ADNM: 30-50%
- Mortality increases with delay in diagnosis

Treatment

- Intravenous broad-spectrum antibiotics as soon as possible in all cases
- CT-guided percutaneous aspiration or drainage of fluid collections
- Surgical irrigation and drain placement often needed
 - Esophageal perforation: Primary closure within 24 hours
 - Postoperative mediastinitis and chest wall infection
 - May require resection of involved skeletal structure(s)

DIAGNOSTIC CHECKLIST

Consider

• Acute mediastinitis in patients with fever and chest pain and wide mediastinum on radiography

Image Interpretation Pearls

- Careful evaluation of entire thorax for exclusion of associated aspiration pneumonia, empyema, osteomyelitis
- Difficult diagnosis of mediastinitis in immediate postoperative period

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Mediastinitis





(Left) Axial CECT of a patient with fever and anterior chest wall erythema that developed 8 weeks post cardiac surgery shows a dehiscence of the sternotomy 🔁 and increased attenuation of the mediastinal fat 🔁, consistent with mediastinitis. (Right) Axial CECT of the same patient shows dehiscence \supseteq and lysis at the sternotomy site, consistent with osteomyelitis. When evaluating patients for post-sternotomy mediastinitis, the sternum should be carefully inspected for evidence of osteomyelitis.





(Left) Axial CECT of the same patient shows a small thickwalled fluid collection 🖂 arising from the sternotomy and extending to the presternal subcutaneous fat. (Right) Sagittal CECT of the same patient shows a fluid collection with an enhancing rim adjacent to the manubrium 🔁 and extensive fat stranding along the entire prevascular (anterior) mediastinum 🖃. Evaluation of patients for poststernotomy mediastinitis should include careful assessment of the cranial and caudal extent of the process.





(Left) Axial CECT of a patient with fever and chest pain that developed 4 weeks after coronary artery bypass shows prevascular mediastinal air 🖂 and fluid, consistent with mediastinitis and abscess and moderate to large bilateral pleural effusions. (Right) Axial NECT of an IV drug user with a septic joint shows erosion of the left sternal cortex \boxtimes , soft tissue attenuation of the prevascular mediastinal fat ➡, and obliteration of presternal tissue planes 🚬 Direct extension of anterior chest wall infection is an unusual cause of mediastinitis.

KEY FACTS

TERMINOLOGY

• Mediastinal fat necrosis (MFN)

IMAGING

- Juxtapericardial ovoid fat attenuation nidus with surrounding inflammatory change
- Analogous to pericolonic epiploic appendagitis
- Small pericardial effusion; focal pericardial thickening (3-5 mm)
- Small unilateral pleural effusion ± adjacent atelectasis
- Temporal resolution of findings on follow-up imaging

TOP DIFFERENTIAL DIAGNOSES

- Acute myocardial infarction
- Acute pulmonary thromboembolic disease
- Fat-containing mediastinal mass
- Pericardial cyst
- Pericardial metastasis
- Metastatic lymphadenopathy

PATHOLOGY

• Necrosis of mediastinal fat; most frequently juxtapericardial

CLINICAL ISSUES

- Rare self-limiting cause of acute chest pain
- May mimic acute pulmonary thromboembolism and acute coronary and aortic syndromes
- More common in men; ages 40-50 years
- Self-limited fat necrosis; symptoms subside in 48-72 hours
- Conservative management now standard of care
 - o Self-limited process \rightarrow resolves on follow up imaging

DIAGNOSTIC CHECKLIST

- May affect any mediastinal or juxtapericardial location
- Confident prospective CT diagnosis is crucial
 Avoidance of invasive intervention
- Consider MFN in patients who present with pleuritic chest pain and exhibit focal mediastinal inflammatory changes surrounding fat attenuation/signal structure

(Left) Axial NECT of a 57-yearold man with suspected acute aortic syndrome shows a heterogeneous left prevascular mediastinal ovoid lesion \blacksquare that abuts the pericardium and contains tiny fat attenuation foci. Note adjacent fat stranding \blacksquare and lingular atelectasis 🔁. (Right) Sagittal NECT of the same patient shows pericardial thickening \blacksquare adjacent to the fat-containing 🔁 lesion. The ovoid morphology and pericardial thickening comprise 2 of the 3 components of the mediastinal fat necrosis triad.





(Left) Axial CECT of a 61-yearold man with acute left chest pain shows mediastinal fat necrosis manifesting as an ovoid fat attenuation lesion \square in the left cardiophrenic angle with thin central linear and peripheral rim-like soft tissue. Note left lower lobe subsegmental atelectasis 🔁 and left pleural effusion \square . (Right) Axial NECT of the same patient obtained 9 months later shows resolution of inflammatory changes around the lesion *≥*, which involves mediastinal fat distant or away from the heart and pericardium.





- Abbreviations
- Mediastinal fat necrosis (MFN)

Synonyms

- Epipericardial fat necrosis
- Pericardial fat necrosis
- Misnomer; there is no pericardial fat
- "Mediastinal fat necrosis"
 - Preferred over "epipericardial fat necrosis"; lesions do occur away from pericardium

Definitions

- Rare self-limiting cause of pleuritic chest pain
 Necrosis of mediastinal fat
- **Subepicardial** fat: Immediately adjacent to myocardium • Deep to serous visceral pericardium or epicardium
- **Epiperi**-cardial fat: Mediastinal fat **superficial** to pericardium

IMAGING

General Features

- Best diagnostic clue
 - Focal mediastinal inflammatory change in patient with angina or chest pain
 - Exclusion of other common causes of chest pain: Acute coronary syndrome (ACS), acute aortic syndrome, pulmonary thromboembolism
 - Triad
 - □ Acute pleuritic chest pain
 - Mediastinal fat attenuation lesion with adjacent soft tissue and stranding
 - Adjacent pericardial thickening
- Location
 - Most frequently juxtapericardial mediastinal fat
 - May involve mediastinal (cardiophrenic or paradiaphragmatic) fat away from heart
 Precordial

 - Paradiaphragmatic
 - \Box ± adhesions to chest wall
 - Mediastinal fat may invaginate between interlobar pleural surfaces
 - o Left hemithorax involvement most common
- Size
 - Variable; typically 1-3 cm
- Morphology
 - Ovoid fat attenuation structure + surrounding inflammatory fluid/stranding
 - Thin "soft tissue" rim common; inflammatory pseudocapsule along lesion periphery
 - Helps distinguish MFN from other fat-containing mediastinal lesions
 - Not to be confused with peripheral rim enhancement

Radiographic Findings

- Often normal
- Paracardiac opacity; often rounded
- Small unilateral pleural effusion ± atelectasis
- Unilateral volume loss and intercostal space crowding (respiratory splinting)

CT Findings

- Juxtapericardial **ovoid fat attenuation** structure with adjacent inflammation
 - Intrinsic and extrinsic strands of fluid &/or soft tissue attenuation
 - Ill-defined mediastinal fluid
 - Mediastinal fat infiltration
 - Focal **pericardial thickening** (3-5 mm)
 - Small pericardial effusion common
- Small unilateral pleural effusion **±** adjacent atelectasis
- Temporal resolution of findings on serial imaging; may calcify

MR Findings

- May be useful for further delineation of indeterminate or atypical lesions
 - Intermediate-signal fluid/hemorrhage may obscure classic ovoid fat signal lesion
 - Adjacent atelectasis may mimic lung parenchymal process
- Dual Echo GRE: Confirmation of intravoxel fat → opposedphase signal loss
- T1WI FS +C: Documentation of absence of central soft tissue component

Imaging Recommendations

- Best imaging tool
 - CT is modality of choice
 - CTA for exclusion of other more common vascular causes of chest pain
 - o MR may play role in troubleshooting and surveillance
- Protocol advice
- Intravenous contrast administration; may enable distinction of mediastinal lesion from adjacent enhancing atelectasis

DIFFERENTIAL DIAGNOSIS

- Acute Myocardial Infarction
- Typical chest pain
- EKG and biochemical abnormality
- Radiography: Normal or cardiogenic edema

Acute Pulmonary Thromboembolic Disease

- Pleuritic chest pain
- Pleural effusions common
- Intraluminal pulmonary artery filling defect

Acute Aortic Syndrome

- Acute tearing chest pain, radiating through back; hypertension
- Intramural hematoma, dissection, penetrating ulcer

Fat-Containing Mediastinal Mass

- Larger lesion; ± soft tissue, fluid, calcification
- Thin soft tissue rim around ovoid fat density helps distinguish MFN from other fat-containing mediastinal masses

Pericardial Cyst

- Cardiophrenic angle fluid attenuation lesion with imperceptible wall
- Adjacent inflammation uncommon

Pericardial Metastasis

- Nodular pericardial thickening in patient with known malignancy
 - Breast and lung cancers most common primary malignancies
- Associated pericardial effusion

Metastatic Lymphadenopathy

- Indolent or subacute presentation
- Absence of acute inflammatory change

Rib Fracture

- History of traumatic injury or aggressive coughing
- Pleuritic chest pain, pleural effusion common

PATHOLOGY

General Features

- Etiology
 - Unclear; postulated mechanisms
 - Acute rise in intrathoracic pressure during heavy lifting or Valsalva
 - □ Rapid ↑ in capillary pressure resulting in focal hemorrhage → incites fat necrosis
 - Acute torsion of vascular pedicle; only few pathologically confirmed cases published
 - Underlying pre-existing lesion (e.g., mediastinal lipomatosis, lipoma, hamartoma)
 - Local trauma from cardiac and diaphragmatic motion predisposes patient to development of fat necrosis
 - Herniation and resultant strangulation of epipericardial fat through small pericardial defect
 - Cardiophrenic or paradiaphragmatic location most common; possibly due to respiratory mobility

Gross Pathologic & Surgical Features

- Yellow fatty mass with tissue strands that extend into adjacent adipose tissue + local inflammation
- Often involves mediastinal fat pad

Microscopic Features

- Shares pathologic features of fat necrosis seen elsewhere
 Breast, subcutaneous, omental, epiploic appendagitis
- Appearance varies with lesion age (duration of symptoms)
- Early: Fat necrosis with acute inflammatory infiltrates (neutrophils) and lipid laden macrophages
- Late: Lesion surrounded by **fibrous pseudocapsule**; internal fibrous septa surrounding necrotic fat lobules
 - May correlate with soft tissue attenuation rim sometimes seen on imaging

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute excruciating, central or unilateral chest pain
 - Mimics other emergent acute vascular entities
 - Pulmonary thromboembolism
 - □ ACS
 - Acute aortic syndrome
 - o Stabbing unilateral pleuritic chest pain

- Pain typically ipsilateral to location of MFN
- Other signs/symptoms
 - Typically normal EKG and laboratory values
 Substantial pericardial involvement may result in EKG or biochemical (Troponin, ESR, CRP) abnormalities

Demographics

- Age
 - Any age; pediatric cases reported
 - o Most commonly 40-50 years of age
- Sex
 - Men more commonly affected

Natural History & Prognosis

- Self-limited fat necrosis; symptoms subside in 48-72 hours
- Recurrent or repeat instances infrequent
- May calcify as result of saponification
 - Presumed cause of intrapleural thoracolithiasis

Treatment

- Historically, many MFN lesions were surgically excised due to their mildly aggressive appearance
- Conservative management now standard of care
 - Relies on prospective imaging diagnosis based on characteristic findings
 - Similar to intra-abdominal epiploic appendagitis

• Do not touch lesion

- o Self-limited process \rightarrow will resolve on follow up imaging
- Conservative management of pain/inflammation
 - Non-steroidal anti-inflammatory drugs (NSAID)

DIAGNOSTIC CHECKLIST

Consider

• MFN in patients who present with pleuritic chest pain and exhibit focal mediastinal inflammatory changes surrounding fat attenuation/signal structure

Image Interpretation Pearls

- Ovoid fat attenuation/signal nidus most frequently occurs in juxtapericardial position; precordial, paradiaphragmatic, ± adherent to chest wall
- May involve mediastinal fat away from pericardium: May project into interlobar fissures between visceral pleural surfaces

Reporting Tips

- MFN: Easily diagnosable condition
- Confident prospective diagnosis based on CT findings is imperative for optimal patient management
 - Avoidance of **unnecessary** invasive interventionsConservative management is now standard of care
- Short-interval follow-up CT (4-6 weeks) or mediastinal MRI may be useful in diagnosing atypical or indeterminate lesions

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Mediastinal Fat Necrosis





(Left) Axial coronary CTA shows mediastinal fat necrosis manifesting as a heterogeneous left prevascular mediastinal lesion with fat attenuation and a thin peripheral soft tissue rim E. (Right) Composite image with axial CECT of a patient with chest pain and mediastinal fat necrosis shows an ovoid heterogeneous attenuation lesion 🔁 with intrinsic fat and calcification and a small left pleural effusion 🖾. Such calcifying lesions may evolve to become "thoracoliths."





(Left) Axial CTA of a 54-yearold woman with acute left chest pain shows an ovoid soft tissue lesion \blacksquare in the left cardiophrenic angle adjacent to the heart. Soft tissue attenuation is atypical, but the presentation and typical location prompted consideration of mediastinal fat necrosis. (Right) Coronal CTA image of the same patient shows the ovoid soft tissue lesion 🛃 in the left cardiophrenic angle. Note inflammatory soft tissue strands \implies that project cephalad to the lesion.





(Left) PA chest radiograph of a 68-year-old woman who presented with severe acute left chest pain shows a mediastinal contour abnormality \square that partially obscures the left cardiac border. (Right) Composite image with axial CECT of the same patient shows that the radiographic abnormality corresponds to fat necrosis manifesting as an ovoid fat attenuation lesion \supseteq with thin linear central soft tissue and a soft tissue attenuation rim 🛃 Note pericardial thickening &/or fluid ᠫ and a small left pleural effusion 🖂.

KEY FACTS

TERMINOLOGY

• Proliferation of hematopoietic cells outside bone marrow when marrow hematopoiesis fails

IMAGING

- Radiography
 - o Well-defined unilateral/bilateral paravertebral mass
 - Rib expansion, conspicuous trabeculation
 - No osseous erosion or calcification
- CT
 - Paravertebral, well-marginated soft tissue mass(es)
 - Typical location along costovertebral junctions
 - o Fatty degeneration indicates old burned-out lesions
- MR
 - Fat replacement: Hyperintense on T1WI and T2WI
 - Iron deposition: Hypointense on T1WI and T2WI
- Nuclear medicine
 - May exhibit uptake of Tc-99m sulfur colloid

TOP DIFFERENTIAL DIAGNOSES

- Neurogenic neoplasm
- Lymphadenopathy
- Paraesophageal varices

PATHOLOGY

• Associations: Myelofibrosis, β-thalassemia, hereditary spherocytosis, hemolytic anemia, sickle cell anemia

CLINICAL ISSUES

- Often asymptomatic, incidental finding
- Symptoms may relate to mass effect
- Rarely cord compression: Intraspinal involvement
- Treatment: None if asymptomatic; transfusion, hydroxyurea, splenectomy (hereditary spherocytosis), radiation (spinal cord compression)

DIAGNOSTIC CHECKLIST

• Consider extramedullary hematopoiesis in patients with chronic anemia and paravertebral mass(es)

(Left) PA chest radiograph of a patient with sickle cell anemia and extramedullary hematopoiesis shows bilateral lower thoracic paravertebral masses that exhibit lateral displacement of the right \boxtimes and left \supseteq paravertebral stripes. (Right) Axial CECT (bone window) of a patient with extramedullary hematopoiesis shows a heterogeneous right paravertebral mass 🔁 with intrinsic low attenuation and a left paravertebral soft tissue nodule **≥**. Note conspicuous vertebral body trabeculations and normal ribs.





(Left) Composite image with lateral chest radiograph (left) and sagittal CECT (right) of a patient with myelofibrosis and extramedullary hematopoiesis shows paravertebral masses on the lateral radiograph 🔁 that correspond to lowattenuation paravertebral masses 🔁 on CT. (Right) Axial CECT of the same patient shows a well-defined heterogeneous right paravertebral mass 🔁 with intrinsic low attenuation 🔁 that could represent fat attenuation, a finding typically seen in burned-out lesions.





Definitions

• Proliferation of hematopoietic cells outside bone marrow when marrow hematopoiesis fails

IMAGING

General Features

- Best diagnostic clue
 Paravertebral mass or masses with rib expansion
- Location
 - Paravertebral region caudal to 6th thoracic vertebra
- Size: 5 mm to > 5 cm

Radiographic Findings

- Radiography
 - Paravertebral mass
 - Well-defined borders
 - Unilateral or bilateral; single or multiple
 - Discrete or contiguous masses
 - No osseous erosion or calcifications
 - Very slow growth

o Ribs

- Rib expansion, conspicuous trabeculae
- Most evident at costovertebral articulations
- Adjacent ribs may be normal
- o Lung
 - Rare pulmonary involvement
 - Nodules, masses, reticular opacities, fibrosis

CT Findings

- NECT
 - o Paravertebral, well-marginated, soft tissue mass(es)
 - Typically along costovertebral junctions
 - Fatty degeneration indicates old burned-out lesions (akin to yellow marrow)
 - Rare lung involvement: Nodules, masses, reticular opacities, fibrosis
 - No calcification
- CECT
 - Mild heterogenous contrast enhancement (may indicate active hematopoietic activity)

MR Findings

- Fat replacement: Hyperintense on T1WI and T2WI
- Iron deposition: Hypointense on T1WI and T2WI
- Assessment of intraspinal extension in patients with neurologic symptoms

Nuclear Medicine Findings

• May exhibit uptake of Tc-99m sulfur colloid

DIFFERENTIAL DIAGNOSIS

Neurogenic Neoplasm

- Paravertebral neoplasms of peripheral nerve or sympathetic ganglion origin
- Benign pressure skeletal erosion; no osseous expansion

Lymphadenopathy

- Rarely limited to paravertebral regions
- Metastatic disease, lymphoma

Paraesophageal Varices

- Serpiginous-enhancing mediastinal vessels
- Ancillary findings of chronic liver disease
- No osseous expansion

PATHOLOGY

General Features

- Associated abnormalities
 - Common: Myelofibrosis, β-thalassemia, hereditary spherocytosis, congenital hemolytic anemia, sickle cell anemia
 - Less common: Lymphoma/leukemia, Gaucher disease, Paget disease, rickets, hyperparathyroidism, pernicious anemia

Gross Pathologic & Surgical Features

- Paravertebral masses of hematopoietic marrow
- Other sites of extramedullary hematopoiesis
 - Liver, spleen, lymph nodes, retroperitoneum, kidneys, adrenal glands, breast, thymus, prostate, spinal cord, pericardium, intracranial dura matter

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Often asymptomatic, incidental finding
 - Symptoms may relate to mass effect
 - Rarely cord compression: Intraspinal growth of paravertebral mass or intraspinal hematopoiesis

Demographics

- Age
 - Clinical presentation in **3rd-5th decades**
- Ethnicity
 - Thalassemia most common in Mediterranean countries
 Sickle cell disease most common in African Americans
- Epidemiology
 Splenectomy might predispose to extramedulla
 - Splenectomy might predispose to extramedullary hematopoiesis

Natural History & Prognosis

- Complications
 - Hemothorax, may be massive (uncommon)
 - Spinal compression (uncommon)

Treatment

- No treatment if asymptomatic
- Transfusion, hydroxyurea
- Splenectomy in hereditary spherocytosis
- Small doses of radiation in spinal cord compression

DIAGNOSTIC CHECKLIST

Consider

• Extramedullary hematopoiesis in patients with chronic anemia and unexplained paravertebral mass(es)

SELECTED REFERENCES

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Hiatal Hernia

KEY FACTS

TERMINOLOGY

- Hiatal hernia, hiatus hernia (HH)
- Herniation through esophageal hiatus
- Sliding HH: Intrathoracic herniation of gastroesophageal (GE) junction and gastric cardia
- Paraesophageal hernia (true): Normal position of GE junction and intrathoracic gastric herniation

IMAGING

- Radiography
 - Well-marginated retrocardiac soft tissue mass
 - May contain air &/or air-fluid level
 - Laterally displaced inferior azygoesophageal recess
- CT
 - Direct visualization of HH and its contents
 - Identification of GE junction in relation to herniated stomach
- Evaluation of lung for atelectasis, pneumonia, aspiration
- UGI/esophagram: Imaging study of choice

TOP DIFFERENTIAL DIAGNOSES

- Epiphrenic diverticulum
- Esophagectomy
- Achalasia

CLINICAL ISSUES

- Slidina HH > 90%
- Paraesophageal hernia < 10%
- Sliding HH
 - Asymptomatic; incidental finding on imaging
 - Symptoms of GE reflux disease (GERD)
 - Regurgitation, dysphagia, hoarseness
- Paraesophageal hernia
 - Ranges from asymptomatic to life-threatening emergency
- Treatment
 - o Medical treatment
 - Surgery for symptomatic hernia
 - Prophylactic surgery for paraesophageal hernia

(Left) Coned-down PA chest radiograph of a 77-year-old woman with an asymptomatic small sliding hiatal hernia 🗩 shows lateral displacement of the lower aspect of the azygoesophageal recess produced by a well-defined gas-containing soft tissue structure, the herniated stomach. (Right) Lateral chest radiograph of the same patient shows the small hiatal hernia with an intrinsic airfluid level 🛃. Hiatal hernias typically affect older adult patients. Small hernias may be subtle on radiography.





(Left) Composite image with coronal (left) and sagittal (right) NECT shows a type I sliding hiatus hernia 🔁. The upper stomach (note intrinsic gastric folds \ge and the gastroesophageal junction 🗁 herniate through the esophageal hiatus. (Right) Graphic illustrates the anatomy of sliding (type I) hiatal hernia in which both the gastroesophageal junction 🔿 and gastric cardia 🄁 herniate into the thorax through the esophageal hiatus. Sliding hiatal hernia is the most common type of hiatal hernia.





Abbreviations

• Hiatal hernia, hiatus hernia (HH)

Definitions

- Herniation through esophageal hiatus
- **Sliding HH**: Intrathoracic herniation of gastroesophageal (GE) junction and gastric cardia
- **Paraesophageal hernia (true)**: Normal position of GE junction and intrathoracic gastric herniation along distal esophagus

IMAGING

Radiographic Findings

- Well-marginated retrocardiac soft tissue mass
 May contain air &/or air-fluid level
- May extend to left, right, or bilaterally
- Laterally displaced inferior azygoesophageal recess
- Difficult diagnosis of paraesophageal hernia or gastric volvulus; requires high index of suspicion

Fluoroscopic Findings

- Esophagram
 - Lower esophageal mucosal "B" ring observed ≥ 2 cm above diaphragmatic hiatus
 - Gastric folds within herniated stomach
 - Sensitivity with single-contrast esophagram: 100%

CT Findings

- Wide esophageal hiatus
- Direct visualization of HH and contents
 Stomach, omentum, other abdominal organs
- Identification of GE junction in relation to herniated stomach for diagnosis of paraesophageal hernia
- Assessment for gastric volvulus
- Evaluation lung for atelectasis, consolidation, aspiration

Imaging Recommendations

- Best imaging tool
 - Upper gastrointestinal (UGI) series/esophagram initial study of choice: Optimal mucosal evaluation: Esophagitis, ulcer, stricture
 - CT with multiplanar reformations for exclusion of volvulus and identification of other herniated viscera

DIFFERENTIAL DIAGNOSIS

Epiphrenic Diverticulum

- Acquired distal esophageal diverticulum
- Associations: Motility disorder, esophagitis, stricture

Bochdalek Hernia

- Herniated abdominal contents through pleuroperitoneal canal remnant
- Fat; rarely bowel, spleen, kidney

Esophagectomy

- Protrusion of dilated neoesophagus to right of midline
- Appropriate history, surgical changes

Achalasia

• Failed relaxation of lower esophageal sphincter

• Markedly dilated esophagus; tapered distal esophagus "bird beak" sign

PATHOLOGY

General Features

- Etiology
 - Enlarged esophageal hiatus: ↑ intraabdominal pressure: Obesity, pregnancy, aging

Staging, Grading, & Classification

- Surgical classification
 - Type I: Intrathoracic GE junction and gastric cardia (sliding HH); > 90%
 - **Type II**: Normal GE junction, intrathoracic gastric fundus (paraesophageal hernia); very rare
 - **Type III**: Intrathoracic GE junction and fundus (fundus above GE junction); **2nd most common type**
 - Type IV: Herniated stomach + other organ
 - o Types II-IV: Risk of ischemia, obstruction, volvulus

Gross Pathologic & Surgical Features

• Sliding HH

- Weakening of phrenoesophageal membrane
- May spontaneously reduce in erect position

• Paraesophageal hernia

- Typically nonreducible
- May be complicated by gastric volvulus
 - Organoaxial or mesenteroaxial "position" may be present without obstruction or strangulation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Sliding HH
 - Asymptomatic; incidental finding
 - GE reflux disease (GERD), early satiety, regurgitation, dysphagia
 - Mass effect on tracheobronchial tree, aspiration
 - Hoarseness, chest pain
 - Paraesophageal hernia: Range from symptomatic to lifethreatening emergency

Demographics

- Age
 - Prevalence increases with age
- Sex
 o F > M

Natural History & Prognosis

• Acute gastric volvulus: Near 50% mortality

Treatment

- Medical treatment
- Surgery for symptomatic disease
- Prophylactic surgery for paraesophageal hernia

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Hiatal Hernia

(Left) Graphic illustrates a type II paraesophageal hernia. The gastroesophageal junction *▶* is in a normal location, and a portion of the stomach herniates into the thorax alongside the distal esophagus. (Right) Coronal CECT of a patient with a moderate type II paraesophageal hernia shows the normal position of the distal esophagus \supseteq and gastroesophageal junction. The gastric fundus 🛃 herniates into the thorax in a paraesophageal location. Note incidental hepatic hemangiomas 🖂.





(Left) PA chest radiograph of an asymptomatic older woman with a moderate-tolarge hiatal hernia shows a retrocardiac mass that produces lateral displacement of the inferior aspect of the azygoesophageal recess 🔁. Although the lesion does not contain gas, the morphologic features are characteristic of hiatal hernia. (Right) Lateral chest radiograph of the same patient shows a retrocardiac soft tissue mass with a small intrinsic air bubble 🄁 representing gas within the herniated stomach.





(Left) Coronal NECT of the same patient shows an enteric tube that demonstrates the intrathoracic location of the gastroesophageal junction 🔁 in this type III paraesophageal hernia. Intrathoracic omental fat produces lateral displacement of the inferior azygoesophageal recess \blacksquare . (Right) Graphic demonstrates the anatomy of the type III hernia in which both the gastroesophageal junction 🔁 and the gastric fundus 🔁 herniate into the thorax through the esophageal hiatus. The fundus is above the gastroesophageal junction.





Hiatal Hernia





(Left) Graphic demonstrates the morphologic features of a type IV hernia in which a structure other than the stomach, in this case a portion of the transverse colon \bowtie , herniates into the thorax. (Right) Coronal CECT of an asymptomatic older woman with a large type IV hernia shows a completely intrathoracic stomach with organoaxial orientation and cranial location of the greater curvature of the stomach 🔁. Portions of herniated bowel (not shown) were also present.





(Left) Coronal CECT of a patient with a large strangulated hiatus hernia shows a dilated fluid-filled proximal stomach \blacksquare and a . collapsed distal stomach 🛃 due to obstruction. (Right) Axial CECT of an asymptomatic patient with hiatal hernia shows herniation of omental fat \blacksquare through the esophageal hiatus. Hiatal hernia results from weakness of the phrenoesophageal membrane and may result in herniation of fat &/or bowel.





(Left) Axial CECT of a patient with a large intrathoracic stomach shows marked gastric distention that produces mass effect on the heart and relaxation atelectasis 🛃 of the basilar segments of the left lower lobe. (Right) Axial CECT of a patient with a small-to-moderate hiatal hernia → shows profuse right lower lobe tree-in-bud opacities , consistent withcellular bronchiolitis from chronic aspiration. Hiatal hernias may produce pulmonary abnormalities related to mass effect &/or aspiration.



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Introduction

Among the many complex organs and systems contained in the chest, the cardiovascular system is one of its most significant components and may exhibit a wide variety of disease processes. Among these, coronary artery disease carries the highest mortality in the USA. While many cardiothoracic pathologies are well understood by practitioners of cardiothoracic and general radiology, many cardiovascular diseases have been historically considered entities outside the realm of thoracic radiology and are often evaluated and managed by nonradiologists, specifically cardiologists.

Many factors contribute to the lack of understanding of cardiovascular disorders among radiologists. While chest radiography is an excellent first imaging study for the assessment of cardiovascular disease, it often lacks sufficient sensitivity for definitive diagnosis. For example, although chest radiography can provide indirect evidence of coronary artery disease, the findings are often nonspecific (e.g., cardiomegaly, pulmonary venous hypertension). Direct evidence of critical abnormalities, such as hemodynamically significant coronary artery atherosclerotic plaques, is not visible on radiography and requires advanced techniques for diagnosis.

Historically, assessment of a large number cardiovascular disorders was performed outside the radiology department at a time when other imaging techniques were more appropriate (e.g., coronary angiography). With the commercial introduction and wide availability of multidetector computed tomography (CT) in the late 1990s, radiologists became increasingly involved in the diagnosis of many cardiovascular disorders. This noninvasive technology provides exquisite anatomic detail superior to that provided by conventional angiography. Simultaneous with the development of multidetector CT, a tremendous evolution of magnetic resonance (MR) imaging technology took place, placing the comprehensive assessment of cardiovascular disorders within the realm of diagnostic radiology.

The boom of these technologies has had such an impact that today, cardiovascular imaging is an integral part of cardiothoracic radiology, and in some institutions it is even a separate subspecialty of radiology. Because the heart and great vessels are anatomically and functionally integrated to the rest of the organs and structures in the thorax, separate imaging assessment is not logical. The reintegration of cardiac and thoracic imaging and an increased understanding of cardiovascular disease can only have a positive impact on advancing and optimizing patient care.

Acute Aortic Syndrome (AAS) and Thoracic Aortic Aneurysms

The term **AAS** refers to a heterogeneous group of disorders that manifest with chest pain and share a common risk factor: Arterial hypertension. The AAS concept was introduced in an attempt to clarify the pathophysiology of **penetrating aortic ulcers** and **intramural hematomas** and their relationship with **aortic dissection** and **incomplete dissection**, as both lesions can result in dissection. However, although penetrating aortic ulcers can progress to intramural hematoma, the reverse is not the case. The various pathophysiologic pathways that form part of AAS and the various terms used to describe the component lesions of the syndrome often create confusion. Furthermore, **complicated thoracic aortic aneurysms** frequently manifest with chest pain and hypertension and can exhibit clinical presentations identical to those of AAS. Therefore, although complicated aortic aneurysms are not strictly included in the definition of AAS, they need to be considered when discussing AAS. It should be noted that statistically more patients who present with chest pain have **coronary syndrome** than either AAS or complicated aortic aneurysm. The differentiation can frequently be made based on clinical grounds and laboratory findings, but this may not be the case for every patient. Finally, and to complicate matters further, coronary syndrome may coexist with AAS and complicated aortic aneurysm.

The imaging evaluation of hypertensive patients with acute chest pain begins with chest radiography. Although chest radiography is considered insensitive as a negative chest radiograph does not exclude aortic pathology, radiographic abnormalities may suggest specific cardiovascular diseases, particularly when serial radiographs are available to help document important interval changes. Highly suggestive findings of aortic pathology include interval aortic enlargement, new aortic contour abnormality, and pathologic displacement of aortic intimal calcifications. In patients with contained aortic rupture of any etiology, chest radiography may demonstrate indirect signs of acute aortic bleeding, such as mediastinal widening, displacement of mediastinal structures, alteration of normal mediastinal interfaces, and pleural effusion.

CT and MR remain the cornerstones of definitive diagnosis of AAS. Both techniques are equivalent in their ability to demonstrate acute aortic pathology and its complications. CT is generally considered more widely available and is more practical than MR for imaging acutely-ill subjects since image acquisition takes only a few seconds. Optimal CT evaluation of AAS requires the performance of unenhanced CT (NECT) prior to performing a contrast-enhanced CT (CECT). For example, intramural hematoma can only be diagnosed with certainty on NECT, and there are pitfalls related to CECT that may mimic extravasation and can be easily verified only if NECT is available. Intramural hematoma manifests as a crescentic hyperdensity of the aortic wall. Penetrating aortic ulcer often manifests as a focal outpouching of contrast that extends beyond the expected aortic wall confines. Aortic dissection classically exhibits an endoluminal intimomedial flap. Finally, thoracic aortic aneurysms manifest with fusiform, saccular, irregular, or diffuse aortic dilatation. All these aortic disorders may be associated with aortic rupture, which often results in sudden death shortly after symptom onset. The few patients that reach the hospital often have a contained aortic rupture or slow aortic bleeding. CT often depicts the site of rupture and a variety of other important findings, including mediastinal hematoma, hemothorax, and contrast extravasation in the mediastinum, pericardium, &/or pleura.

Nonacute Aortic Pathology

Several chronic disorders may also affect the thoracic aorta. An understanding of the pathophysiology and imaging features of these entities is important as they may simulate acute aortic pathology or AAS. Nonacute aortic disorders include vasculitis and neoplasia. **Takayasu arteritis** and **giant cell arteritis** are the most common vasculitides that affect the aorta. Both CT and MR are equivalent in their ability to demonstrate imaging abnormalities, consistent with vasculitis, including vessel wall thickening and luminal stenosis or dilatation. Neoplastic processes of the aorta are rare, but when present are almost always malignant. The most common malignant neoplasm of the aorta is angiosarcoma. It should be noted that primary aortic malignancy may be difficult to differentiate from intraluminal thrombus. In these cases, contrast-enhanced MR can help distinguish between the two entities.

Pulmonary Thromboembolic Disease [Pulmonary Embolism (PE)]

It is difficult to summarize current concepts related to imaging of pulmonary thromboembolic disease since the amount of medical literature on this subject is overwhelming. Nevertheless, it is important to emphasize several generally accepted concepts. CTA of the pulmonary arteries remains the cornerstone for the diagnosis of PE. Ventilation-perfusion scintigraphy (VQ scan) is as good as CTA, but the latter provides the advantage of simultaneous evaluation of the entire thorax for other causes of chest pain. The Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II study showed that combining CTA with venous-phase imaging (CTA-CTV) (i.e., from the inferior vena cava confluence through the popliteal veins) results in a higher sensitivity for diagnosis with similar specificity. However, this is not a protocol used in general practice given the fact that compression Doppler lower extremity sonography is as effective as CTV in the diagnosis of venous thrombosis.

It is generally accepted that CTA is overused in the evaluation of thromboembolic disease since the positivity rate remains very low. In addition, CTA delivers a not negligible dose of ionizing radiation. The problem may relate to inconsistent or suboptimal use of clinical criteria for the diagnosis of PE and the subjective overestimation of the probability of PE. Future research on this subject will likely focus on establishing better patient selection criteria that will hopefully allow a more rational use of this excellent imaging technique.

During the last decade, concerns have been raised regarding the amount of ionizing radiation associated with CT scanning and its deleterious effects. An increased radiation dose is associated with an increased risk of carcinogenesis. Children and young women (particularly pregnant women) are among the groups at higher risk. One of the most serious concerns is the development of breast carcinoma in association with radiation delivered to the breast during CTA. Several measures have been adopted to decrease this risk. Bismuth breast shields, which decrease the radiation dose to the breast without qualitative or quantitative changes in image quality, have been previously employed. Many institutions opt to work with manufacturers toward developing state-of-the-art CT scanners and dose reduction protocols that can be applied to all patients imaged with CT. An important strategy is to perform a VQ scan in patients with suspected PE, whose chest radiograph is normal. While the amount of radiation may be similar with both techniques, the amount of radiation delivered to the breast during scintigraphy is likely much less than that associated with CTA.

Cardiac Valvular Disease

The accurate assessment of cardiac valvular disease is an excellent example of the impact of novel technology in cardiothoracic diagnosis. Although several radiographic abnormalities related to valvular disease are extensively described in the classic imaging literature, it was not until echocardiography and MR became widely available that objective information was extracted from imaging evaluations. These technologies provide quantitative and qualitative evaluation of cardiovascular disorders. Such quantitative information allows identification of disease progression and helps establish management strategies for patients with valvular disease. While color Doppler echocardiography continues to be the overall imaging modality of choice, several technical limitations are recognized (e.g., poor acoustic windows, complex anatomy), including its inability to fully quantify valvular regurgitation. For this reason, MR has emerged as an excellent noninvasive diagnostic tool capable of fully quantifying all parameters needed to monitor valvular disease and plan surgery when needed. While currently the role of MR is yet to be officially defined, it is well recognized as an invaluable tool when echocardiography is inconclusive. Finally, with the advent of coronary CTA, reports on its use for the assessment of valvular function have shown promise.

Cardiac and Pericardial Masses

In general, cardiac and pericardial masses are uncommon. **Metastatic disease** is the most common neoplastic process that affects the heart and pericardium. Less common pericardial tumors include benign neoplasms (e.g., teratoma, solitary fibrous tumor, hemangioma) and primary malignancies (e.g., mesothelioma). On the other hand, less common cardiac masses include benign lesions (e.g., myxoma, papillary fibroelastoma, cardiac rhabdomyoma, fibroma, lipoma, lipomatous hypertrophy of the interatrial septum, paraganglioma, hemangioma, lymphangioma) and malignancies (e.g., angiosarcoma, leiomyosarcoma, rhabdomyosarcoma, lymphoma).

Echocardiography and MR continue to be the mainstay of cardiac imaging diagnosis. Echocardiography is readily available, portable, fast, and inexpensive. However it has limitations such as poor acoustic windows in patients with large body habitus or in the presence of calcification. An important advantage of multidetector CT over other modalities is its consistent capability to demonstrate calcification. However, acquisition of cardiac images results in significant radiation to the chest and often requires the use of iodinated contrast. MR is considered the gold standard for the evaluation of pericardial and cardiac masses. Although the main advantage of MR is its superior tissue characterization, it provides additional advantages, that include no limitations regarding acoustic windows, absence of ionizing radiation, and the use of a safer contrast medium (i.e., gadolinium).

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Approach to Cardiovascular Disorders

(Left) Axial CECT of a patient with type A aortic dissection shows intimomedial flaps in both the ascending \square and the descending \implies aorta. (Right) Composite image with axial (left) and oblique coronal (right) CECT shows a contrast outpouching 🔁 that extends beyond the confines of the aortic wall, consistent with a penetrating aortic ulcer. Penetrating aortic ulcers may remain stable or grow and may be associated with intramural hematoma, aortic dissection, or aortic pseudoaneurysm (contained aortic rupture).

Aortic Dissection



Penetrating Aortic Ulcer



(Left) Composite image with axial NECT (left) and CECT (right) shows a type A intramural hematoma that manifests with crescentic high $attenuation \blacksquare$ that mimics mural thickening \boxtimes on CECT. A descending aorta penetrating ulcer 🔁 is also associated with extraluminal crescentic hyperdensity 🔁, which in this case represents a contained rupture. (Right) Composite image with axial NECT (left) and CECT (right) the pulmonary trunk. Central pulmonary emboli are rarely visible on NECT.

Intramural Hematoma



Pulmonary Thromboembolism and Right Heart Strain Pulmonary Thromboembolism



Pulmonary Artery Sarcoma

(Left) Axial CECT demonstrates bilateral pulmonary emboli 🔁 and marked right atrial and right ventricular enlargement. The right ventricle \mathbf{E} is at least twice as wide as the left ventricle, consistent with right ventricular strain. (Right) Composite image with axial CECT (left) and pulmonary artery DSA (right) shows a pulmonary artery angiosarcoma that manifests as a pulmonary artery filling defect 🖅 on CT and DSA with obliteration of the right lower lobe pulmonary artery lumen.





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Approach to Cardiovascular Disorders

Valve Stenosis







Cardiac/Pericardial Neoplasms

(Left) Composite image with coronal and axial cine MR of a patient with aortic stenosis shows (clockwise from bottom left) diastolic regurgitation \supseteq , the coapted aortic valve, a systolic ejection jet 🛃, and axial MR of the aortic valve that documents limited valve aperture due to partially fused leaflets. (Right) Composite image with PA chest radiograph (left) and cine MR (right) of a patient with pulmonic stenosis shows an enlarged pulmonary trunk 🛃 and a systolic pulmonic ejection jet ➡ on SSFP MR.

Cardiac/Pericardial Neoplasms



(Left) Axial CECT of a patient with metastatic lung cancer shows heterogeneously enhancing nodules and masses \blacksquare of the pericardium, consistent with pericardial solid metastases. (Right) Axial CECT of a patient with pericardial tamponade physiology secondary to malignant pericardial mesothelioma shows heterogeneously enhancing, likely necrotic, pericardial masses and necrotic juxtacardiac lymphadenopathy \blacksquare , which was biopsied percutaneously for histologic diagnosis.



Cardiac/Pericardial Neoplasms



(Left) Axial oblique SSFP MR of a patient with a right atrial angiosarcoma shows a heterogeneous mass \blacksquare that obliterates the right atrial lumen. (Right) Axial CECT of a patient with cardiac rhabdomyosarcoma shows nodular soft tissue that encases the heart and bilateral pleural effusions. While metastases are the most common cardiac and pericardial malignancies, mesothelioma and angiosarcoma are the most common primary malignancies of the pericardium and heart, respectively.

Atherosclerosis

KEY FACTS

TERMINOLOGY

• Lipid deposition on arterial walls leading to thickening, hardening, and occlusion

IMAGING

- Affects medium-sized and large arteries
- Most common in descending aorta
- Predilection for vessel branch points
- Radiography
 - Vessel wall calcification
- NECT
 - Calcified atherosclerotic plaques
 - Penetrating ulcer; soft tissue beyond aortic wall
 - Hyperattenuating crescentic wall thickening: Intramural hematoma
- CTA
 - Noncalcified (> 4-mm) and calcified plaques
 - Aneurysm: Often related to atherosclerosis
 - Penetrating ulcer vs. ulcerated plaque

- MR
 - Plaque characterization: Lipid hyperintense on T1WI, hypointense on T2WI
 - Equivalent to CECT for complication assessment

TOP DIFFERENTIAL DIAGNOSES

- Aortitis/arteritis (Takayasu arteritis, giant cell arteritis, post radiation, syphilis, etc.)
- Mönckeberg medial sclerosis
- Aortic sarcoma or metastases

CLINICAL ISSUES

- Asymptomatic
- Acute aortic syndrome: Chest pain from penetrating ulcer, intramural hematoma, aortic dissection
- Visceral/extremity ischemia; branch stenoses, emboli
- Porcelain aorta: Higher risk for embolic stroke during surgery; associated with severe symptomatic aortic valve stenosis (15-18%)

(Left) Graphic demonstrates the morphologic features of aortic atherosclerosis. Deposition of fat, cholesterol, and other substances produces *irregular plague on the aortic* intima, which may result in thrombus and ulceration with or without intramural hematoma. (Right) Macroscopic cut section of the thoracic aorta shows an irregular intimal surface. Lipid and cholesterol deposition result in irregular plaque and ulceration $\overline{\supseteq}$. In turn, ulceration may lead to intramural hematoma. (Courtesy A. Burke, MD.)





(Left) PA chest radiograph of a patient with atherosclerosis shows intimal calcification 🄁 of the aortic arch and descending aorta, which increases the risk of ischemic stroke. (Right) Lateral chest radiograph of the same patient shows extensive aortic intimal calcification 🔁 secondary to calcified atherosclerotic plaque. Calcified plaque is the most common manifestation of atherosclerosis on radiography and is often associated with atherosclerosis elsewhere, including the coronary arteries.





Synonyms

Arteriosclerosis

Definitions

• Lipid deposition on arterial walls leading to thickening, hardening, and occlusion

IMAGING

General Features

- Location
 - Affects medium-sized and large arteries
 - Most common in descending aorta
 - Predilection for vessel branch points
 - Ascending aorta more often involved in diabetes and familial hypercholesterolemia
 - Aortic root may be involved in familial hypercholesterolemia
 - Syphilis causes ascending aortic atherosclerosis
- Morphology
 - Porcelain aorta: Heavy circumferential calcification or severe atheromatous plaque that prevents safe aortic cross clamping or cannulation
 - Associated with higher risk for embolic stroke during surgery; commonly associated with severe symptomatic aortic valve stenosis (15-18%)

Radiographic Findings

- Radiography
 - Visualization of vessel wall calcification
 - Pseudoaneurysm from penetrating aortic ulcer (> 2-3 cm) may manifest as focal mass or focal aortic dilatation
 - Ascending aorta calcification is marker of disease severity
 - Coronary atherosclerosis
 - Calcified plaques occasionally visible
 - Coronary plaques imply higher risk of
 - hemodynamically significant stenosis
 - Calcified atherosclerotic plaques of central pulmonary arteries
 - Longstanding severe pulmonary hypertension
 - Eisenmenger syndrome
 - Chronic thromboembolic pulmonary hypertension

CT Findings

- NECT
 - Calcified atherosclerotic plaques
 - Coronary artery calcium (CAC)
 - Marker of atherosclerotic burden
 - □ CAC associated with ↑ risk of stroke, myocardial infarction, revascularization surgery, and death
 - Absence of CAC has excellent negative predictive value
 - Superior to noninvasive functional testing for detection of angiographically significant coronary stenosis in patient with CAC < 400
 - CAC of zero: < 1% annual mortality over 15-year period due to coronary event
 - CAC > 300: 10x increased risk of coronary event
 - Penetrating ulcer suggested by soft tissue extending beyond presumed aortic wall

- Hyperattenuating crescentic wall thickening indicates coexistent intramural hematoma (IMH)
- CTA
 - Noncalcified (> 4-mm) and calcified plaques
 - **Aneurysm**: Often related to atherosclerosis, dilatation of > 50% of normal vessel diameter
 - Penetrating aortic ulcer
 - Contrast extends beyond aortic wall confines
 - Adjacent soft tissue often related to contained rupture (pseudoaneurysm)
 - May be associated with IMH; crescentic or concentric aortic wall thickening
 - Ulcerated plaque: Contrast does not extend beyond aortic wall confines
- Cardiac gated CTA
 - Does not replace diagnostic coronary angiography but is as sensitive as conventional angiography
 - Exclusion of stenoses in patients with low pretest probability of significant disease
 - Presence and extent of coronary artery disease on coronary CTA; strong independent predictors of cardiovascular events
 - High-risk plaque features for acute coronary syndrome: Low-attenuation (< 30 HU), positive vessel remodeling (outward expansion), spotty calcification, and napkin-ring sign (low attenuation adjacent to vessel lumen and surrounding higher-attenuation ring)
 - High-risk plaque features > 3x more likely to occur in occlusive than non-occlusive lesions
 - Plaque consistency: Lipid rich (< 30 HU), fibrous (30-150 HU), calcified (> 220 HU)

MR Findings

Plaque characterization

Lipid component

- Hyperintense on T1WI, hypointense on T2WI
- Lipid-rich plaques tend to be more inflamed
- Fibrocellular components: Hyperintense on T1WI and T2WI
- Calcium deposits: Hypointense on T1WI and T2WI

Ultrasonographic Findings

- Intravascular ultrasonography
 High spatial secolution for accessment of at
 - High spatial resolution for assessment of atherosclerotic plaque, its components, and vascular remodeling
 - Supportive technique during conventional angiography
 - Used to follow plaque progression

Angiographic Findings

- Plaques: Filling defects or irregular luminal vessel surface
- Penetrating ulcer: Focal contrast collection outside aortic wall confines
- Angiography often required before therapeutic stenting or endarterectomy

Nuclear Medicine Findings

- PET/CT
 - Symptomatic and unstable plaques are more FDG avid
DIFFERENTIAL DIAGNOSIS

Acute Aortic Syndrome (AAS)

- Classic aortic dissection, incomplete dissection, penetrating aortic ulcer, IMH
- May lead to aortic rupture
- Aortic dissection
 - o Intimomedial flap separates true and false lumina
 - Intimal calcification displaced from aortic wall
- IMH
 - High-attenuation crescentic or circumferential aortic wall thickening on NECT
- Penetrating atherosclerotic ulcer may coexists with IMH

Thoracic Aortic Aneurysm

- Acute penetrating aortic ulcer with contained rupture (pseudoaneurysm) appears as focal peripheral crescentic hemorrhage on NECT
- Predisposing conditions: Atherosclerosis, trauma, infectious aortitis, cystic medial necrosis, bicuspid aortic valve, hypertension, smoking

Aortitis/Arteritis (Takayasu, Giant Cell Arteritis, Syphilis, etc.)

- Concentric or circumferential wall thickening ± aneurysm
- Scattered vascular stenoses
- May simulate IMH on CECT
- Aortic wall thickening not hyperattenuating on NECT

Aortic Sarcoma or Metastases

- Extremely rare; difficult to differentiate from exophytic atherosclerotic plaque
- Noncalcified discrete aortic wall soft tissue mass

Mönckeberg Medial Sclerosis

- Common medial arterial calcification seen in diabetes and chronic kidney disease
- Calcium and phosphate accumulate in intima and media with arterial wall ossification

PATHOLOGY

General Features

- Etiology
 - Plaque results from build up of lipid, cholesterol, and other substances on vessel walls
 - Plaques narrow and stiffen arteries, resulting in blood flow obstruction
 - Plaques may break off, embolize or develop clot and produce tissue damage (ischemia, infarction, death)
 - Plaques weaken vessel wall, may result in aneurysm formation
 - Complicated atherosclerotic plaque may lead to aortic ulceration ± IMH
- Genetics
 - Familial hypercholesteremia is major risk factor

Gross Pathologic & Surgical Features

• **Aneurysm**: Dilatation in setting of type IV, V, or VI lesions, layered luminal thrombi fill aneurysm to approximate original lumen diameter

Microscopic Features

- Lesions begin in intima and progressively affect entire arterial wall
- Atheroma: Accumulation of cells or cellular debris
 - o Contains lipids, calcium, and fibrous connective tissueo Located between endothelial lining and smooth muscle
- media
 Foam cells in atheroma: Monocyte macrophages containing numerous lipid inclusions rich in cholesteryl esters
- Vulnerable plaque: Plaque with thin fibrous cap that is prone to rupture and thrombosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic
- Other signs/symptoms
 - AAS: Chest pain from penetrating ulcer, IMH, incomplete dissection, classic dissection
 - Visceral or extremity ischemia from branch stenoses or emboli
- Clinical profile
 - Risk factors: Diabetes mellitus, heavy alcohol use, high blood pressure, hypercholesterolemia, high-fat diet, increasing age, obesity, personal or family history of heart disease, smoking

Demographics

- Age
 - Correlates with advancing age; very common in older adults
- Sex
- o Male > female
- Epidemiology
 - Common in Western cultures
 - Less common in Asia and Africa: Postulated role of dietary &/or genetic factors

Natural History & Prognosis

- Atherosclerosis progresses with age
- Natural history and prognosis related to onset of complications

Treatment

- Modification of risk factors and statins
- Medical or surgical therapy for complications

DIAGNOSTIC CHECKLIST

Consider

• Coronary artery disease in setting of substantial aortic atherosclerotic disease

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Atherosclerosis





(Left) Sagittal oblique reformatted CTA of a patient with aortic atherosclerosis demonstrates calcified \boxtimes and noncalcified \supseteq atherosclerotic plaques along the tortuous descending thoracic aorta. (Right) Axial CTA of a patient with atherosclerosis shows a large soft tissue atherosclerotic plaque of the descending aorta and a focal area of ulcerated plaque \blacksquare . Ulcerated plaque differs from a penetrating aortic ulcer in that the former does not extend beyond the confines of the aortic wall.





(Left) Oblique axial coronary CTA demonstrates a mixed plaque 🛃 along the proximal left anterior descending coronary artery that reduces the vessel lumen by more than 75% of the vessel diameter, corresponding to hemodynamically significant coronary artery obstruction. (Right) Right anterior oblique coronary angiography of the same patient demonstrates a 90% stenosis 🛃 of the proximal left anterior descending coronary artery. Coronary artery disease frequently coexists with aortic atherosclerosis.





(Left) Curved MPR coronary CTA of a 45-year-old man with diabetes mellitus and chronic renal failure on hemodialysis demonstrates extensive coronary artery calcification ⇒ of the left anterior descending coronary artery. (Right) Axial NECT of a 28year-old woman with Takayasu aortoarteritis shows abnormal aortic dilatation at the level of the aortic arch and an extensively calcified arterial wall (⊃).

KEY FACTS

TERMINOLOGY

• Aortic dilatation > 50% (or > 1.5x normal diameter)

IMAGING

• Radiography

- Ascending aorta aneurysm: Often not visible
- Aortic arch aneurysm: Enlarged/obscured aortic arch
- Descending aorta aneurysm: Focal or diffuse abnormality of left paraaortic interface
- Peripheral curvilinear calcification
- Rupture: Wide mediastinum, left pleural effusion
- CT
 - Aortic dilatation ± curvilinear mural calcification
 Saccular or fusiform morphology
 - Crescentic mural high attenuation indicates contained/impending rupture
 - Hematoma: Hemothorax, hemopericardium, hemomediastinum

TOP DIFFERENTIAL DIAGNOSES

- Tortuosity (aging) of aorta
- Mediastinal mass

PATHOLOGY

- Atherosclerotic aortic aneurysm
- Infectious (mycotic) aneurysm
- Cystic medial necrosis

CLINICAL ISSUES

- Atherosclerotic aneurysm: Most are asymptomatic
- Infectious (mycotic) aneurysm: Fever, leukocytosis

DIAGNOSTIC CHECKLIST

- Consider ruptured aneurysm in patient with acute chest pain, wide mediastinum, and pleural effusion on radiography
- Normal radiography does not exclude aneurysm or dissection; cross-sectional imaging required for diagnosis

(Left) Graphic shows the morphologic features of saccular and fusiform aortic aneurysms. Saccular aneurysms (left) are focal and mass-like. Fusiform aneurysms (right) are elongate. (Right) Axial CECT of a 70-year-old man with prior revascularization surgery who presented with acute chest pain shows an ascending aorta aneurysm with an associated intimomedial flap \square consistent with a Stanford type A aortic dissection. Note patent venous graft 🔁 anterior to the aorta and pulmonary trunk.





(Left) Composite image with axial NECT (left) and axial CECT (right) of 2 patients with ruptured aortic aneurysms shows signs of rupture that include the crescent sign \square , hemothorax 🛃, and mediastinal hematoma 🔁. (Right) Composite image with axial (left) and sagittal (right) CTA of a patient with mycotic aortic aneurysms secondary to S. aureus aortic valve endocarditis shows saccular aneurysms \blacksquare near the aortic isthmus. Infectious or mycotic aneurysms are typically secondary to S. aureus and Salmonella spp.





TERMINOLOGY

Abbreviations

- Thoracic aortic aneurysm (TAA)
- Abdominal aortic aneurysm (AAA)

Definitions

• Aortic dilatation > 50% (or > 1.5x normal diameter)

IMAGING

Radiographic Findings

- Ascending aorta aneurysm
 - Often not visible
 - o Convexity of right superior cardiomediastinal silhouette
- Aortic arch aneurysm
 - Enlargement or obscuration of aortic arch
 - o Hilum overlay sign
 - Rightward tracheal deviation
- Descending aorta aneurysm
 - o Focal mass that obscures left paraaortic interface
 - Diffusely enlarged descending aorta; lateral displacement of left paraaortic interface
- Peripheral curvilinear calcification
- Ruptured aneurysm
 - Mediastinal widening; obliterated normal interfacesLeft pleural effusion

CT Findings

- NECT
 - **Curvilinear mural calcification**: Common in atherosclerosis, absent in mycotic aneurysms
 - **Crescent sign**: Crescentic mural high attenuation indicates contained/impending rupture
 - **Hematoma**: Hemothorax, hemopericardium, hemomediastinum
- CTA
 - Blunt sinotubular junction (annuloaortic ectasia)
 - Crescent-shaped intraluminal thrombus
 - Intimomedial flap (dissection)
 - Rupture: Active extravasation (uncommon)
 - o Morphology
 - Fusiform: Atherosclerosis, connective tissue disorder
 - Saccular: Penetrating aortic ulcer or infection

MR Findings

• Similar sensitivity to CT but not used in acute setting

Imaging Recommendations

- Best imaging tool
 - CECT for optimal evaluation of location, size, relationship to major branch vessels, complications

DIFFERENTIAL DIAGNOSIS

Tortuosity (Aging) of Aorta

• Diffuse aortic dilatation

Mediastinal Mass

- Curvilinear calcification typical of vascular lesions
- CECT differentiates neoplasm from vascular lesion

PATHOLOGY

General Features

- True aneurysm: Contains all 3 aortic wall layers
- Atherosclerotic aortic aneurysm
 - Degenerative process, most common (75%)
 - Shape: Fusiform (most common), saccular
 - Location: Arch > descending > ascending
 - Diameter > 6 cm significantly increases risk of rupture
- Infectious (mycotic) aneurysm
 - Predisposing factors: IV drug use, adjacent pyogenic infection, immunodeficiency
 - Most common pathogens: *Salmonella* spp. and *Staphylococcus aureus*
 - Saccular > fusiform; any location

Cystic medial necrosis

- Hypertension (more common), bicuspid aortic valve, Marfan syndrome (more severe)
- Location: Ascending aorta, aortic annulus (annuloaortic ectasia); aortic regurgitation

Gross Pathologic & Surgical Features

- Saccular: Focal mass-like aortic dilatation
- Fusiform: Diffuse elongate aortic dilatation

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Atherosclerotic TAA: Asymptomatic (most common), chest pain, compression (hoarseness, dysphagia, atelectasis, superior vena cava syndrome)
 - Infectious (mycotic) aneurysm: Fever, leukocytosis
 - Acute chest pain: Rupture, dissection
 - Degenerative TAA less prone to rupture than AAA

Demographics

- Epidemiology
 - Prevalence of 3-4% in patients over 65 years
 - Relative risk increases with age

Treatment

- Risk reduction: Hypertension control, smoking cessation
- Indications for surgery
 - o Size criteria
 - Ascending aorta > 5.0 cm (4.5 cm for familial or Marfan syndrome and bicuspid aortic valve)
 - Descending aorta > 5.5 cm
 - $\circ~$ Growth rate > 5 mm per year (for an eurysm > 5 cm)
 - Symptomatic patients

DIAGNOSTIC CHECKLIST

Consider

- Ruptured aneurysm in patient with acute chest pain, wide mediastinum, and pleural effusion on radiography
- Normal radiography does not exclude aneurysm or dissection; cross-sectional imaging required for diagnosis

SELECTED REFERENCES

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Acute Aortic Syndromes

KEY FACTS

TERMINOLOGY

- Acute aortic syndrome (AAS): Aortic dissection, incomplete dissection, penetrating aortic ulcer, intramural hematoma
- Aortic dissection (AD) or class 1 dissection
 - Aortic media separated by intimomedial flap between false and true aortic lumina
 - Entrance and reentrance tears; may be multiple
- Intramural hematoma (IMH) or class 2 dissection
 - Aortic media hemorrhage from spontaneous rhexis (rupture) of vasa vasorum
 - o Absent or small entrance/re-entrance tear
- Penetrating aortic ulcer (PAU) or class 4 dissection
 - Ulceration of atherosclerotic lesion that penetrates internal elastic lamina
 - Variable amount of intramural hemorrhage

IMAGING

- AD: Aortic intimomedial flap on CTA
- IMH: Circular or crescentic aortic wall hyperdensity on NECT

- PAU: Contrast outpouching beyond aortic wall
- Focal aortic projection (FAP): Intramural blood pool (IBP), ulcer-like projection (ULP), PAU

PATHOLOGY

- Stanford classification for AD, ID, and IMH
 - Type A: Involves ascending aorta
 - Type B: Involves only descending aorta

CLINICAL ISSUES

- Treatment of AD and IMH
 - Stanford type A: Surgical reconstruction
 Stanford type B: Medical treatment
- Treatment of PAU: Close follow-up, medical treatment; endovascular therapy or surgery if progression or complications
- Treatment of FAP
 - IBP: Observation; treatment if progression
 - ULP or PAU: Emergent intervention

(Left) Graphic shows the relationship between acute aortic syndrome entities and progression patterns (arrows). Classic dissection does not evolve to penetrating aortic ulcer, but the opposite may occur. All entities may result in aortic rupture. (Right) Graphic shows the Svensson classification and the morphology of specific entities that likely represent aortic dissection subtypes. Class 1 is a classic dissection; class 2 is an intramural hematoma; class 3 is a focal intimal tear; and class 4 is a penetrating aortic ulcer.





(Left) Composite image with axial CTA of 2 patients with type A (left) and type B (right) aortic dissection shows the beak sign ₽, an acute angle between the flap and the false lumen 🔁. (Right) Composite image with axial CTA of 2 patients with type A (left) and type B (right) aortic dissections shows the cobweb sign \supseteq that manifests as subtle linear filling defects that represent strands of media in the false lumen. Both signs are important for differentiating the true from the false lumen.





TERMINOLOGY

Definitions

- Acute aortic syndrome (AAS): Aortic dissection (AD), incomplete dissection (ID), penetrating aortic ulcer (PAU), intramural hematoma (IMH)
 - AD or class 1 dissection
 - Aortic media separated by intimomedial flap between false and true aortic lumina
 - Entrance and re-entrance tears (occasionally several communications)
 - o IMH or class 2 dissection
 - Aortic media hemorrhage from spontaneous vasa vasorum rhexis (occasionally trauma)
 - Absent (or very small) entrance and re-entrance tears
 - PAU or class 4 dissection
 - Ulcerated atherosclerotic lesion that penetrates internal elastic lamina
 - Associated with variable amounts of intramural hemorrhage
- Rhexis: Rupture of vasa vasorum leading to IMH
- Focal aortic projection (FAP): Intrinsic contrast collection within intramural or subadventitial hematoma
 - Intramural blood pool (**IBP**) (branch pseudoaneurysm); benign, can be observed
 - o pau
 - Ulcer-like projection (ULP); treated as PAU

IMAGING

General Features

- Best diagnostic clue
 - AD: Aortic intimomedial flap on CTA
 - IMH: Crescentic aortic wall hyperdensity on NECT – Narrow window (width 200 HU, level 40 HU)
 - **PAU**: Contrast outpouching extending beyond aortic wall confines

Radiographic Findings

- Normal radiograph does not exclude diagnosis
- AD: Displaced intimal calcifications (rare)
- Contained aortic rupture: Mediastinal widening/mass, pleural effusion, mass effect

CT Findings

- NECT
 - **AD**: Aortic intimomedial flap can inferred if intimal calcification is present
 - IMH: Circular or crescentic hyperdensity of aortic wall with variable extension
 - **PAU**: Aortic outpouching + ulcerated atherosclerotic plaques
 - Contained aortic rupture: Focal crescent sign
- CTA
 - o AD
 - Aortic intimomedial flap and fenestrations
 - Differentiation of true from false lumen
 - False lumen: Larger, decreases in systole, may thrombose, swirling or turbulent flow in late systole, **beak sign** (acute angle between false lumen and aortic flap), **cobweb sign** (strand-like filling defects in false lumen)

- True lumen collapse: Slit-like, C-shaped true lumen configuration, dismal prognosis with high mortality due to organ or limb ischemia
- ECG-gated CTA: Useful for assessment of ascending aorta (degraded by pulsation artifact in nongated studies), relationship with coronary ostia
- IMH: Crescentic aortic wall thickening

• PAU

- Contrast-filled outpouching surrounded by IMH, pseudoaneurysm, or rupture

o ID

- No intimomedial flap
- **Aortic rupture**: Indirect signs (mediastinal hematoma, pleural effusion, pericardial effusion) more common than direct signs (frank contrast extravasation)
- FAP
 - Contrast collection within IMH ± PAU and ID (i.e., subadventitial hematoma)
 - IBP
 - Can be tracked to aortic branch (MIP reformation often helpful), often one or several intercostal arteries
 - Narrow neck at origin, difficult identification of communication with aortic lumen
 - Normal evolution to decreased size or resolution
 ULP
 - ULP
 - Broad neck, easily identified connection to aortic lumen
 - ULP vs. PAU: Differentiation often relies on visualization of atherosclerotic disease in PAU
 - Often progression to rupture, dissection, or saccular aneurysm; treated same as PAU (i.e., stenting or surgery)

MR Findings

- AD
 - o Sensitivity and specificity as good as CTA
 - Spin echo techniques demonstrate flap and fenestrations as well as periaortic hematoma and hemopericardium
 - Gradient echo (GRE): Thrombosed AD is hyperintense
 - ECG-gated steady-state free precession (SSFP): Useful for assessment of ascending aorta (degraded by pulsation artifact in nongated studies), relationship with coronary ostia
 - Cine-SSFP: Useful for assessment of aortic valve regurgitation seen as proximal signal dephasing; dephasing signal may be seen at entry and re-entry sites
 - Phase-contrast: Allows quantification of flow in false lumen and quantification of aortic valve regurgitation
 - 3D-MRA with gadolinium: Gold standard MR technique; determines flap extent and location and relationship to and patency of vital aortic branches
- IMH
 - T1WI: Acute IMH is isointense, subacute IMH is hyperintense
 - Phase-contrast MR very sensitive for differentiation of slow flow in dissection vs. no flow in IMH
 - o t2WI
 - Acute IMH is hyperintense
 - After 1 to 5 days, IMH has lower intensity

- GRE: IMH is hyperintense
- PAU
 - T1 spin echo techniques: Optimal to characterize ulceration
 - T1 and T2 spin echo: Show mural crater with adjacent isoor hyperintensity (blood products)
 - o 3D-MRA: Shows mural crater

Echocardiographic Findings

• TEE is equivalent to CT and MR imaging

Imaging Recommendations

- Best imaging tool
 - CT is more widely available and faster
- Protocol advice
 - NECT always necessary to identify and assess IMH

DIFFERENTIAL DIAGNOSIS

Acute Coronary Syndrome (ACS)

• Negative EKG and cardiac enzymes in AAS with definitive imaging findings; AAS and ACS may coexist

Aortitis (Takayasu and Giant Cell Arteritis)

- Concentric or circumferential wall thickening of large and medium-sized arteries ± aneurysm
- Scattered areas of vascular stenosis
- May simulate IMH on CTA, but thick wall is not hyperdense on NECT
- Mural enhancement on delayed C+ MR

Aortic Sarcoma

- Extremely rare, difficult to differentiate from exophytic atherosclerotic plaque
- Noncalcified discrete aortic wall mass

PATHOLOGY

General Features

- Etiology
 - AD:Cystic medial degeneration
 - o IMH: Vasa vasorum rhexis, rarely blunt chest trauma
 - **PAU**: Atherosclerotic lesion ulceration

Staging, Grading, & Classification

- AAS
 - Groups all 4 entities based on similar clinical presentation, risk factors, and shared pathophysiology
 - Useful concept for understanding PAU and IMH and their relationship with AD
- Stanford classification for AD, ID, and IMH
 - Type A: Involves ascending aorta ± descending aorta
 - Type B: Involves only descending aorta

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Chest (back) pain
- Chronic severe arterial hypertension
- Other signs/symptoms
 - D-dimer may be elevated; negative test helps exclude AAS

Natural History & Prognosis

- Patterns of evolution
- AD
 - False lumen thrombosis; smaller than true lumen with early thrombosis (rare); larger than true lumen when thrombosis occurs late
 - Early false lumen rupture; if in ascending aorta, hemopericardium and tamponade often result
 - Periaortic hematoma (crescent sign);
 - impending/contained rupture
- IMH
 - Aortic rupture with hemopericardium (tamponade), hemothorax, and mediastinal hemorrhage
 - Localized communicating dissection; IMH and AD may coexist at different aortic levels
 - Growth and progression of IMH
 - Spontaneous resolution; common in distal IMH
 - Stability over time; infrequent
 - Predictors of progression to complications: Ascending aorta involvement, maximum aortic diameter (> 5 cm), large intimal erosions (> 2 cm)

o pau

- Aneurysm formation; slow progression
- Pseudoaneurysm (contained rupture) contained by adventitia
- AD; entrance tear is ulcer crater

Treatment

- AD and IMH
 - Stanford type A: Surgical reconstruction
 - Stanford type B: Medical treatment; endovascular therapy &/or surgery if progression or complications
- **PAU**: Close follow-up, medical treatment; endovascular therapy or surgery if progression or complications

Essential Imaging Report Content

- Location of aortic abnormality
- Maximum diameter of any dilatation, measured from external aortic wall, perpendicular to axis of flow and length of aortic abnormality
- Patients with genetic syndromes at risk for aortic root disease: Measurements of aortic valve, sinuses of Valsalva, sinotubular junction, and ascending aorta
- Presence of internal filling defects consistent with thrombus or atheroma
- Presence of IMH, PAU, or calcification
- Extension of aortic abnormality to branch vessels, including dissection and aneurysm, and secondary evidence of end-organ injury.
- Evidence of aortic rupture: Periaortic and mediastinal hematoma, pericardial and pleural effusion, and contrast extravasation from aortic lumen
- If prior study available, direct image-to-image comparison to identify any increase in diameter

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Acute Aortic Syndromes





(Left) Composite image with axial CTA shows a fenestration ⇒ (left) and dynamic compression 🔁 (right) of the true lumen. Dynamic compression often implies a poor prognosis with higher mortality rates due to organ or limb ischemia. (Right) Composite image with axial NECT (left) and CTA (right) of a patient with a ruptured type B aortic dissection shows a high-attenuation aortic hematoma 🔁 that produces a . crescent sign, a left hemothorax ₽, and opacification of the true aortic lumen 🔁 on CTA.





(Left) Composite image with axial CECT of a patient with type A aortic dissection shows an intimomedial flap \supseteq and aortic rupture with hemopericardium 🔁, which often results in tamponade. (Right) Composite image with axial HASTE (left), SSFP (center), and 3D volumetric contrast-enhanced (CE) MRA (right) of a patient with type B dissection shows adequate flap visualization \square in all sequences. MR is equivalent to CTA for assessment of aortic dissection, and 3D volumetric CE MRA allows reformations in any plane.





(Left) Composite image with NECT (left) and CTA (right) shows a hyperdense crescentic intramural hematoma 🔁 that manifests as hyperdense aortic wall thickening \supseteq on CTA. (Right) Sagittal CTA shows intramural hematoma secondary to penetrating aortic ulcer. A large shallow ulceration 🔁 extends beyond the expected aortic margin and the aortic wall thickening \supseteq caused by the intramural hematoma. Penetrating aortic ulcer is a focal aortic projection that requires emergent endovascular or surgical treatment.

(Left) Composite image with axial NECT (left) and CTA (right) shows incomplete dissection that manifests with crescentic hyperdensity \blacksquare and thickening \square of the ascending aorta, identical to findings of intramural hematoma. Note bulging 🔁 along the posterior ascending thoracic aorta, a classic feature of incomplete aortic dissection. (Right) Composite image with axial CTA before (left) and after (right) treatment shows a descending thoracic aorta penetrating aortic ulcer 乏 excluded 🔁 with endovascular therapy.





(Left) Axial CTA MIP

reformatted image shows a type B intramural hematoma and an intramural blood pool \square , which does not communicate with the aortic lumen but communicates with an adjacent intercostal artery Image: Description: Contemporary Series (Right) Sagittal oblique CTA of the same patient shows multilevel intramural blood pools \supseteq related to contiguous intercostal arteries, an appearance is often referred to as the Chinese ring-sword sign. These findings can be closely observed on follow-up imaging and will typically resolve.





(Left) Composite image with axial CECT of a patient with an ulcer-like projection 크 (left) that enlarges ≥ on follow-up imaging obtained 10 days later (right) is shown. Ulcer-like projections and penetrating aortic ulcer often exhibit progression and thus require emergent intervention. (Right) Composite image with axial HASTE (left) and SSFP (right) of a patient with type B intramural hematoma shows a hyperintense crescent on HASTE 🛃 (T1WI) which is isoto slightly hyperintense on SSFP 🖾, consistent with a subacute lesion.



Acute Aortic Syndromes





(Left) Composite image with axial NECT (left) and CTA (right) of a patient with acute aortic syndrome shows an ascending aorta intramural hematoma 🔁 and a descending aorta dissection and intimomedial flap \supseteq . (Right) Composite image with axial (left) and sagittal (right) CTA of a patient with a descending aorta penetrating aortic ulcer shows a contrast outpouching \supseteq that extends beyond the expected aortic margin and adjacent retrocrural hemorrhage \square , consistent with a contained rupture.





(Left) Composite image with axial NECT (left) and CTA (right) shows a descending aorta penetrating aortic ulcer \supseteq complicated by retrocrural hemorrhage and contained rupture 🔁. Note that the penetrating aortic ulcer cannot be identified without contrast. (Right) Sagittal oblique SSFP MR shows an anterior ascending aorta penetrating aortic ulcer 乏 with extensive adjacent hematoma 🄁. MR is equivalent to CTA and is an excellent imaging technique to identify penetrating aortic ulcer and its complications.





(Left) Axial CTA of a patient with a normal descending aorta shows a frequent pitfall in the diagnosis of acute aortic syndrome. The aortic wall and the adjacent enhancing subsegmental atelectasis 🔁 mimic an intimomedial flap and a false lumen, respectively. (Right) Composite image with axial CTA (left) and gated CTA (right) shows an apparent ascending aortic intimomedial flap \Longrightarrow that does not persist on cardiac gated CTA. Such ascending aortic pseudoflaps are frequently seen due to pulsation artifacts.

Marfan Syndrome

KEY FACTS

TERMINOLOGY

• Congenital systemic connective tissue disorder; skeletal, cardiovascular, and ocular abnormalities

IMAGING

• Radiography

- Ascending aortic aneurysm
- o Cardiomegaly
- Pectus deformity, scoliosis, scalloped vertebrae
- Pneumothorax; apical bullae
- CT
 - o Annuloaortic ectasia, aneurysm
 - Aortic rupture: Crescent sign, hematoma
 - Dissection: Intimal flap, true/false lumen

• Echocardiography

- At diagnosis to assess ascending aorta and 6 months thereafter to determine rate of enlargement
- MR: Similar to CT in sensitivity

TOP DIFFERENTIAL DIAGNOSES

- Familial thoracic aortic aneurysm
- Ehlers-Danlos syndrome
- Bicuspid aortic valve

PATHOLOGY

- Mutation in FBN1 gene encoding for fibrillin 1
- Autosomal dominant; 25% de novo mutations
- Microscopy: Cystic medial necrosis

CLINICAL ISSUES

- Signs and symptoms: Cardiac/vascular, pulmonary, thoracic skeletal abnormalities
- Treatment: B-adrenergic receptor blockade, surgical reconstruction

DIAGNOSTIC CHECKLIST

• Consider Marfan syndrome in young patient with ascending aortic aneurysm &/or aortic dissection

(Left) Axial CECT of a young woman with Marfan syndrome shows a markedly dilated aortic root 🔁. Note the normal diameter of the descending thoracic aorta 🔁 for comparison. Early surgical intervention is endorsed in patients with Marfan syndrome given increased risk of complications. (Right) Coronal CECT of the same patient shows an onion bulb configuration of the proximal ascending thoracic aorta 🖂 due to dilatation of the sinuses of Valsalva and effacement of the sinotubular junction.





(Left) Coronal CECT of a patient with Marfan syndrome and acute chest pain due to aortic dissection shows an intimomedial flap \implies involving the ascending thoracic aorta. Note effacement of the sinotubular junction \bowtie (i.e., lack of transition along the sinotubular junction), a finding consistent with annuloaortic ectasia. (Right) Axial CECT of a patient with Marfan syndrome who underwent a Bentall reconstruction of the ascending aorta shows a $pseudoaneurysm \implies along the$ left coronary anastomosis 🔁.





Marfan Syndrome

TERMINOLOGY

Definitions

• Congenital connective tissue disorder characterized by skeletal, cardiovascular, and ocular abnormalities

IMAGING

Radiographic Findings

- Ascending aortic aneurysm: Mediastinal widening, right superior cardiomediastinal contour abnormality
- **Cardiomegaly**: Aortic/mitral regurgitation, cardiomyopathy
- Pectus deformity, scoliosis, scalloped vertebrae
- Pneumothorax; apical bullae

CT Findings

- NECT
 - Annuloaortic ectasia/aneurysm: Effacement of sinotubular junction (60-80% of patients); absent normal transition between aortic root and tubular ascending aorta
 - Aortic rupture, often contained
 - Crescent sign: Crescentic eccentric high attenuation
 - Hemomediastinum, hemothorax, hemopericardium
- CTA
 - More sensitive than radiography
 - Direct visualization
 - Dissection: Intimomedial flap, true/false lumen
 - Rupture: Active extravasation

MR Findings

- Similar to CT in sensitivity
- Direct visualization of aortic dissection
- Optimal valve assessment: Aortic &/or mitral regurgitation

Echocardiographic Findings

• Initial assessment of aortic size and 6 months thereafter to determine rate of enlargement

Imaging Recommendations

- Protocol advice
 Appual imaging after init
 - Annual imaging after initial echocardiography
 More frequently if aortic diameter ≥ 4.5 cm or growth

DIFFERENTIAL DIAGNOSIS

Familial Thoracic Aortic Aneurysm

• Sinus of Valsalva aortic aneurysm

Ehlers-Danlos Syndrome

- Aneurysm/rupture: Medium/large muscular arteries
- Systemic: Joint hypermobility, atrophic scars, easy bruising, hernias, hollow organ rupture

Bicuspid Aortic Valve

- Ascending aortic aneurysm
- Aortic stenosis, post stenotic dilatation

PATHOLOGY

General Features

- Etiology
 - Mutation in FBN1 gene encoding for fibrillin 1
 - Estimated prevalence: 1 in 5,000 to 10,000

- TGFBR mutations
 - TGG-beta receptor 1 or receptor 2 (*TGFBR1* and *TGFBR2*)
 - Responsible for 10% of cases of Marfan syndrome
- Genetics
 - o Autosomal dominant; 25% de novo mutations

Microscopic Features

• Cystic medial necrosis

CLINICAL ISSUES

Presentation

- Clinical profile
 - Cardiac abnormalities
 - Mitral valve regurgitation
 - > 50% auscultatory/echocardiographic evidence of mitral valve dysfunction, typically prolapse
 - Progression of mitral valve prolapse to mitral regurgitation by adulthood
 - Aortic valve regurgitation: Late occurrence from aortic annulus stretching
 - Vascular abnormalities
 - Annuloaortic ectasia and aortic aneurysm
 - Aortic dissection
 - □ Often **type A**; ± propagation to descending aorta
 - Acute-onset heart failure typically from severe aortic regurgitation
 - Involvement of coronary arteries; myocardial infarction or sudden cardiac death
 - Dilated pulmonary trunk
 - Pulmonary abnormalities
 - Bullae: Predisposition to spontaneous pneumothorax

Thoracic skeletal abnormalities

Pectus deformity; can contribute to restrictive lung disease

Demographics

- Sex
 - Males and females equally affected
- Epidemiology
 - Incidence: 2-3/10,000 individuals

Natural History & Prognosis

- Improved prognosis with annual imaging, medical/surgical intervention
- Higher aortic dissection risk in pregnancy

Treatment

- B-adrenergic receptor blockade: Standard of care
- Surgical reconstruction: Elective according to aortic diameter, dissection, rupture

Diagnostic Checklist

• Consider Marfan syndrome in young patients with ascending aortic aneurysm &/or aortic dissection

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KEY FACTS

TERMINOLOGY

- Takayasu arteritis (TA)
- Pulseless disease
- Chronic granulomatous vasculitis of large vessels

IMAGING

- Best diagnostic clue: Mural thickening of large vessels
 Thoracic aorta and branches
 - o Pulmonary artery involvement less common
- NECT: Aortic wall thickening
- **CECT**: Aortic wall thickening and enhancement
- MRA: Aortic narrowing, dilatation
- Angiography: 4 types classified by location
- FDG PET/CT: Treatment monitoring
- Complications
 - o Stenosis > occlusion
 - o Aneurysm
 - o Dissection

TOP DIFFERENTIAL DIAGNOSES

- Giant cell arteritis
- Aortic coarctation

PATHOLOGY

- Autoimmune etiology suspected
- Specific types of HLA common among patients

CLINICAL ISSUES

- Disease stages
 - Early or prepulseless phase
 - o Vascular inflammatory phase
 - Late quiescent occlusive or pulseless phase
 - o Triphasic disease in minority of patients
- F:M = 8:1
- Heart failure most common cause of death
- Treatment
 - o Corticosteroids, angioplasty, surgical bypass

(Left) Composite image with axial CECT (left) and fused axial FDG PET/CT (right) shows soft tissue thickening of the wall of the descending aorta 🛃 that exhibits mild FDG uptake \blacksquare , consistent with active Takayasu arteritis. FDG PET/CT can be used to identify regions of inflammation and monitor treatment response in affected patients. (Right) Coronal CECT of a patient with Takayasu arteritis shows marked mural thickening of the descending thoracic aorta ⇒, the most common abnormality identified on CT.





(Left) Axial CECT of a patient with Takayasu arteritis who presented with chest pain demonstrates wall thickening \supseteq and dilatation \supseteq of the ascending and descending thoracic aorta. (Right) Coronal CECT of the same patient shows marked mural thickening of the thoracic aorta \supseteq that involves the proximal aspect of the left common carotid artery 🔁 with resultant significant stenosis. Complications of Takayasu arteritis include vessel stenosis, occlusion, and aneurysm formation.





TERMINOLOGY

AbbreviationsTakayasu arteritis (TA)

Synonyms

• Pulseless disease

Definitions

• Chronic granulomatous vasculitis of large vessels

IMAGING

General Features

- Best diagnostic clue
- Wall thickening of large vesselsLocation
- Thoracic aorta and branches
- Left subclavian artery most commonly affected
- o Pulmonary artery involvement less common

Radiographic Findings

- Radiography
 - o Irregular or dilated descending thoracic aortao Diminished pulmonary vessels and rib notching

CT Findings

- NECT
 - Vessel wall thickening, iso-/hyperdense to muscle
- CECT
 - $\circ~$ Vessel wall thickening and enhancement
 - $\circ~$ Stenosis, occlusion, aneurysm

MR Findings

- T1WI
 - $\circ~$ Wall thickening: Aorta and branches
- T1WIC+
- Enhancement of thickened vessel wall
- MRA
 - Focal/diffuse narrowing of aorta and branches
 - Aortic dilatation (ascending > descending)
 - Stenosis > occlusion
 - Aortic regurgitation, dissection, aneurysm

Angiographic Findings

- Early: Aortic wall thickening, rarely stenosis
- Late: Stenosis, occlusion, aneurysm; 4 types
 Type I: Branches of aortic arch
 - Type II: Aorta and branch vessels
 - Type III: Aorta, coarctation may result
 - Type IV: Aortic dilation

Nuclear Medicine Findings

- PET
 - FDG uptake; may be low grade to intense
 - Treatment monitoring

Imaging Recommendations

- Protocol advice
 - Multiplanar reformatted images for evaluation of stenosis

DIFFERENTIAL DIAGNOSIS

Giant Cell Arteritis

Affects large vessels in older patients

Aortic Coarctation

- Aortic narrowing, rib notching
- More common in males

PATHOLOGY

General Features

- Etiology
 - Autoimmune etiology suspected
- Genetics
 Specific types of HLA common among patients

Gross Pathologic & Surgical Features

• Wall thickening of large vessels

Microscopic Features

• Granulomatous inflammation of arterial wall

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Early or prepulseless phase
 - Low-grade fever, malaise, weight loss, fatigue
- Vascular inflammatory phase
 - Vascular regurgitation
 - Symptoms minimized by collateral formation
- Late quiescent occlusive or pulseless phase
 - Diminished/absent pulses, vascular bruits
 - Hypertension, aortic regurgitation
 - Neurologic symptoms (dizziness, seizures)
- Triphasic pattern (seen in minority of patients)
 - Disease usually recurrent \rightarrow phases may coexist
 - Interval between early and late phases variable

Demographics

- Age
 - Most common in 2nd and 3rd decades of life

• Sex

- o F:M = 8:1
- Epidemiology
 - Most common in Asia
 - o Affects 6/1,000 persons worldwide

Natural History & Prognosis

- Congestive heart failure most common cause of death
- Hypertension is poor prognostic factor

Treatment

- Corticosteroids are first-line treatment
- Cyclophosphamide and methotrexate
- Angioplasty, surgical bypass, or stent placement for stenosis and occlusion

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KEY FACTS

TERMINOLOGY

- Superior vena cava (SVC) syndrome
- SVC obstruction by intraluminal or extrinsic disease
- Impaired venous return from head, neck, upper extremities, and trunk

IMAGING

- Radiography
 - May be normal
 - o Mediastinal widening
 - o Mediastinal/paramediastinal mass
- CT and MR
 - SVC nonopacification or intraluminal signal abnormality
 - Extrinsic compression by mass or lymphadenopathy
 - Intraluminal filling defect
 - o Multiple collateral vessels
- Nuclear medicine: Radionuclide uptake in liver: Hot quadrate sign

TOP DIFFERENTIAL DIAGNOSES

- Occlusion or stenosis of central or deep upper extremity veins
- Venous thoracic outlet (Paget-Schroetter) syndrome
- Persistent left SVC and absent right SVC
- Lipomatous hypertrophy of interatrial septum

PATHOLOGY

- Malignant etiologies (80-90%): Lung cancer, metastatic disease, lymphadenopathy, lymphoma
- Benign etiologies (10-20%): Granulomatous disease, iatrogenic, previous radiation therapy

CLINICAL ISSUES

• Face, neck, upper trunk, and upper extremity edema

DIAGNOSTIC CHECKLIST

• Consider SVC obstruction when patient with known malignancy develops typical signs and symptoms

(Left) Axial CECT of a 63-yearold woman with treated left breast cancer who presented with shortness of breath shows a right upper lobe adenocarcinoma contiguous with enlarged right prevascular mediastinal lymph nodes that produces near complete occlusion \supseteq of the superior vena cava (SVC). (Right) Sagittal CECT of the same patient shows the mass \bowtie invading the SVC, tortuous dilated varicosities \blacksquare in the upper visceral mediastinum, and a dilated opacified azygos vein 🔁





(Left) Graphic illustrates SVC obstruction
ightarrow secondary tomediastinal invasion by a lung tumor 🔁 with resultant brachiocephalic vein and right intercostal collateral vessel *A* distention. (Right) Coronal CECT of a 58-year-old man with a large small cell lung cancer and marked coalescent mediastinal lymphadenopathy shows densely opacified and dilated right upper extremity veins 🖂, dilated chest wall and intercostal venous collaterals ➡, and pleural/phrenic collaterals 🛃.





TERMINOLOGY

Synonyms

• Superior vena cava (SVC) syndrome

Definitions

- Obstruction of SVC due to intraluminal or extrinsic disease
 - Impaired venous return from head, neck, upper extremities, and trunk to right atrium

IMAGING

General Features

- Best diagnostic clue
 - $\circ~$ Nonopacification of SVC
 - Multiple collateral vessels

Radiographic Findings

- Radiography
 - May be **normal**
 - Most common in mediastinal fibrosis
 - latrogenic SVC obstruction
 - Wide mediastinum
 - Dilated SVC
 - Mediastinal mass or lymphadenopathy

• Right hilar or paramediastinal mass

- Lung cancer
- Metastatic disease
- Lymphadenopathy
- Enlarged azygos arch and azygos vein
- o Dilated left superior intercostal vein (aortic nipple)

CT Findings

- CECT
 - Nonopacification of SVC
 - Obstruction
 - Intraluminal thrombus
 - Extrinsic compression by mass or lymphadenopathy
 - $\circ~$ Multiple collateral vessels and varicosities
 - Neck, chest wall, mediastinum

$\circ \ {\rm Enlarged} \ {\rm mediastinal} \ {\rm vessels}$

- Azygos and hemiazygos veins
- Superior intercostal veins
- Brachiocephalic veins
- Inflow of contrast-enhanced blood into inferior vena cava (IVC)
- Hyper-enhancement of hepatic segment IV = **hot spot**, **hot quadrate sign**
 - Portosystemic shunt via internal thoracic vein → veins of Sappey → peripheral left portal veins
 - Not always present

MR Findings

- T1WIC+
 - Evaluation of adjacent structures and causes of external SVC compression
- MRV
 - $\circ~$ Signal loss in SVC as result of thrombus or occlusion
 - Enlarged azygos arch and azygos vein
 - Multiple collateral vessels
 - Neck, chest wall, mediastinum

Ultrasonographic Findings

Grayscale ultrasound

- Dilatation of visualized SVC
 - Direct visualization can be technically challenging given overlying bones and air-filled lungs
- Distended subclavian, brachiocephalic, and jugular veins
- Echogenic intraluminal thrombus
- Pulsed and Color Doppler
 - ↓ flow velocity or absent color Doppler signal
 - Altered waveforms of central subclavian, brachiocephalic, and jugular veins
 - Abnormal monophasic waveforms
 - Absence of normal phasicity in response to cardiac and respiratory cycles or provocative maneuvers

Angiographic Findings

- Digital subtraction angiography (DSA)
 - Performed superior or peripheral to obstruction
 - Stasis or retrograde flow in subclavian or brachiocephalic veins
 - May mimic subclavian or brachiocephalic vein occlusion
 - Intraluminal filling defect = thrombus
 - Nonopacification = occlusion
 - Multiple collateral vessels; azygos arch and vein enlargement
 - Extrinsic compression by mass or lymphadenopathy
 Effacement of SVC
 - o Indwelling catheters and pacemaker leads
 - Long, smooth eccentric narrowing

Nuclear Medicine Findings

- Radionuclide uptake in hepatic segment IV: Hot quadrate sign
- Radionuclide venography with Tc-99m-MAA
 - Generated time-activity curves can show evidence of SVC obstruction
 - o Multiple collateral vessels

Imaging Recommendations

- Best imaging tool
 - CT and MR for optimal demonstration of SVC thrombus or occlusion
 - Evaluation of adjacent mediastinal structures
 - DSA useful for endovascular or surgical planning
- Protocol advice
 - Coronal and sagittal reformations to visualize site and extent of obstruction
 - Diluted contrast (1:2) may help reduce streak artifacts due to dense contrast column in SVC
 - Delayed acquisition (60 seconds) may help reduce mixing artifacts from nonopacified IVC and azygos venous blood

DIFFERENTIAL DIAGNOSIS

Occlusion or Stenosis of Central or Deep Upper Extremity Veins

- Chronic occlusion or thrombus involving brachiocephalic or deep upper extremity veins
- Multiple neck and upper chest collaterals; SVC patent
- Typically from indwelling catheters or pacemaker leads

• Upper extremity swelling may mimic SVC obstruction

Venous Thoracic Outlet (Paget-Schroetter) Syndrome

- Fixed or dynamic axillosubclavian vein stenosis ± thrombus or occlusion
 - Venous compression in costoclavicular space between 1st rib, subclavius muscle, and clavicle
- Multiple neck and upper chest collaterals; SVC patent

Persistent Left Superior Vena Cava With Absent Right Superior Vena Cava

- No right SVC; collateral vessels absent
- Opacified venous structure in left visceral mediastinum
 Drains into dilated coronary sinus
- Aberrant course of catheters and pacemaker leads
 Course along left visceral mediastinum

Lipomatous Hypertrophy of Interatrial Septum

- Dumbbell-shaped area of fat attenuation in interatrial septum; spares fossa ovalis
- May extend superiorly along low SVC for variable length with resultant luminal narrowing; rarely obstruction

PATHOLOGY

General Features

- Etiology
 - Malignant
 - Lung cancer most common
 - Metastatic disease
 - Breast, renal, and testicular cancers most common
 - Mediastinal lymphadenopathy and lymphoma
 - Primary mediastinal mass
 - Benign
 - latrogenic
 - Indwelling catheters and pacemaker leads
 Prior mediastinal/paramediastinal radiation
 - Granulomatous disease
 - Tuberculosis, histoplasmosis, sarcoidosis
 - Silicosis
 - Pyogenic infection
 - Aortic aneurysm resulting in compression

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Edema and flushing
 - Face, neck, upper trunk, and upper extremities
 - Dyspnea and cough
 - o Palpable subcutaneous collateral vessels
 - Neck and chest wall
- Other signs/symptoms
 - o Headache
 - Stridor from epiglottic edema
 - o Syncope, seizures, visual changes
- Clinical profile

◦ SVC obstruction is clinical diagnosis

 Patients may be asymptomatic with chronic, wellcompensated stenosis or occlusion

Demographics

- Age
 - Age range: 18-76 years
 Mean: 54 years
 - Malignant etiologies: Older; 40-60 years
 - o Benign etiologies: Younger; 30-40 years
- Sex
 - Malignant etiologies: M > F
 - Benign etiologies: M = F
- Epidemiology
 - Malignancy: Etiology in 80-90%
 - Small cell lung cancer and lymphoma most common
 - Benign causes: Etiology in 10-20%
 - Fibrosing mediastinitis most common
 - Iatrogenic: indwelling central venous catheter (dialysis, intravenous port)
 - Most common benign cause in cancer patients

Natural History & Prognosis

- Gradual, progressive obstruction of SVC
- Insidious onset of symptoms
 SVC obstruction is rare cause of death in both benign and malignant etiologies
 - Survival dependent on underlying disease process and tumor histology

Treatment

- Anticoagulation
- Malignant etiologies
 - o Radiation therapy to reduce tumor bulk and mass effecto Chemotherapy targeted toward neoplasm
- Endovascular therapy
 - o Catheter-directed thrombolysis (acute thrombus)
 - Endovascular angioplasty ± stenting
 - Variable success and durability; may require repeat intervention to maintain patency
- Surgical therapy
 - Open debulking and decompression
 - Venous reconstruction or grafting
 - Spiral vein graft: Favorable (> 90%) long-term patency in benign SVC obstruction
 - Polytetrafluoroethylene (PTFE) grafts

DIAGNOSTIC CHECKLIST

Consider

• SVC obstruction in patient with known malignancy with new flushing and edema in neck and upper trunk

Image Interpretation Pearls

- Nonopacification of SVC
- Multiple collateral vessels in neck, chest wall, and mediastinum

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(Left) Coronal CECT of a 28year-old-woman undergoing treatment for lymphoma who presented acutely with swelling and erythema in the face, neck, and upper extremities shows a nearly occlusive thrombus in the SVC associated with the tip \blacksquare of an indwelling port catheter. (Right) Concurrent coronal neck CECT of the same patient shows extensive bilateral subcutaneous neck edema \Longrightarrow ; an ancillary finding often seen in patients with acute SVC obstruction.





(Left) Axial CECT of a 53-yearold man with a previously removed indwelling dialysis catheter that produced SVC obstruction ➡ shows opacification of mediastinal varicosities 🔁 resulting from collateral venous drainage. (Right) Coronal CECT of the same patient shows a hypoattenuating filling defect in the SVC 🛃 and dilated upper mediastinal veins 🛃. Chronic indwelling central venous catheters are a common iatrogenic cause of SVC obstruction.





(Left) Composite image with axial CECT (left) and digital subtraction angiography (right) of a patient with SVC obstruction due to an indwelling central catheter shows a vascular stent 🔁 that restored flow through the SVC. (Right) Axial CECT of a 76-year-old man shows hyperenhancement of hepatic segment 4 (hot quadrate sign) \blacksquare and dilated subcutaneous vessels 🗈 secondary to altered venous drainage and collateral vessel recruitment in the setting of chronic SVC obstruction.

Pulmonary Edema

KEY FACTS

TERMINOLOGY

- Pulmonary edema: Abnormal accumulation of extravascular lung water
 - Hydrostatic edema
 - Permeability edema with diffuse alveolar damage (DAD): Acute respiratory distress syndrome (ARDS)
 - Permeability edema without DAD: Opiate overdose edema, transfusion-related lung injury (TRALI), highaltitude pulmonary edema (HAPE)
 - Mixed edema: Neurogenic pulmonary edema, reexpansion pulmonary edema

IMAGING

- Radiography
 - Hydrostatic edema
 - Perihilar haze, subpleural edema, peribronchial cuffing, septal thickening
 - Consolidation, batwing edema
 - Cardiomegaly, pleural effusion

- **ARDS**: Airspace disease, absence of cardiomegaly or septal lines
- HAPE: Asymmetric, perihilar, patchy, nodular airspace disease
- **Reexpansion edema**: Ipsilateral to prior effusion or pneumothorax
- Opiate overdose, TRALI, neurogenic edema: May mimic hydrostatic edema
- CT/HRCT
 - Not routinely used in evaluation of pulmonary edema
 - Hydrostatic edema
 - Smooth septal thickening, fissural thickening, bronchial wall thickening
 - Centrilobular, lobular, acinar, diffuse ground-glass opacities, consolidation
 - Cardiomegaly
 - Pleural effusion
 - Lymph node enlargement
 - o HAPE: Asymmetric, perihilar nodular airspace disease

(Left) Coned-down AP chest radiograph of a patient with hydrostatic cardiogenic edema shows short thin (Kerley B) lines \implies perpendicular to the lateral pleura and longer oblique (Kerley A) lines 🖂, typical radiographic manifestations. (Right) Coronal CECT of a patient with hydrostatic cardiogenic edema shows thick interlobular septa 🔁 and interlobar fissures 🔁 representing edema of the peripheral septal and subpleural interstitium, respectively, typical CT manifestations.





(Left) Axial CECT of a patient with interstitial edema shows smooth thickening of the interlobular septa 🔁 that form central polygonal arcades \implies that outline the margins of several secondary pulmonary lobules. (Right) Composite image with NECT of a normal right lower lobe (left) and CECT of interstitial edema (right) of the same patient shows bronchial wall thickening ⊇, mild septal thickening ⊇, and a small right pleural effusion 🔁. CT nicely demonstrates the early manifestations of interstitial edema.





Pulmonary Edema

TERMINOLOGY

Definitions

- Pulmonary edema: Abnormal accumulation of extravascular lung water
 - Hydrostatic edema
 - Common etiologies
 - Cardiogenic edema: Elevated pulmonary capillary pressure (left ventricular failure, mitral stenosis)
 - Fluid overload: IV fluid overadministration, renal failure
 - Permeability edema with diffuse alveolar damage (DAD)
 Acute respiratory distress syndrome (ARDS)
 - Permeability edema without DAD
 - Opiate overdose, IV cocaine, crack cocaine inhalation
 - Transfusion-related lung injury (TRALI): Dyspnea, hypoxemia, and bilateral pulmonary opacities within 6 hours after transfusion of blood products
 - High-altitude pulmonary edema (HAPE)
 - o Mixed edema: Both hydrostatic and permeability edema
 - Neurogenic pulmonary edema
 - Reexpansion pulmonary edema

IMAGING

Radiographic Findings

• Hydrostatic/cardiogenic edema

- Wide vascular pedicle: Marker of increased central venous pressure and increased circulating blood volume
 - Measures up to 58 mm in normal subjects
 - Variable width based on body habitus, mediastinal fat
- Pulmonary venous hypertension: Chronic elevation of left atrial pressure
 - Vascular redistribution/cephalization
- Interstitial edema
 - Perihilar haze or vascular indistinctness
 - Subpleural edema
 - Peribronchial thickening/cuffing
 - Interlobular septal thickening: Kerley B, A, and C lines
 - Increased lung density
- o Alveolar edema
 - Consolidation: Predilection for right lung
 - Batwing edema (< 10%): Rapid onset of heart failure
 - Asymmetry
 - Underlying lung disease, positional changes
 - □ Acute mitral regurgitation from papillary muscle
 - rupture: Preferential right upper lobe involvement
- Associated findings
 - Cardiomegaly, enlarged pulmonary vessels
 - Pleural effusion: Bilateral, right > left; intrafissural fluid
- ARDS
 - Evidence of mechanical ventilation
 - Exudative (acute) phase (1-7 days)
 - Bilateral symmetric heterogeneous opacities
 - Absence of temporal changes, cardiomegaly, or septal lines
 - Proliferative (organizing) phase (8-14 days)
 Coarse reticular opacities
 - Fibrotic (late) phase (> 15 days)
 - Slow resolution; reticular opacities

- Opiate overdose edema
 - o Consolidations: Bilateral, diffuse; may resolve rapidly
- TRALI • Bila
- Bilateral interstitial &/or alveolar pulmonary opacities
- HAPE
 - Central interstitial edema without septal lines
 - o Consolidations: Asymmetric, patchy, nodular
 - Spare lung apices and lung bases
 Rapid resolution with treatment
- Neurogenic edema
 - Acute onset following significant central nervous system insult
 - Bilateral, upper lobe-predominant airspace disease
 No cardiomegaly, rapid resolution
- Reexpansion edema
 - Follows rapid reexpansion of previously atelectatic lung (atelectasis duration > 3 days)
 - Post drainage of pleural effusion or pneumothorax
 - Progressive ipsilateral airspace disease; may progress to bilateral involvement

CT Findings

• Hydrostatic/cardiogenic edema

- o Interstitial edema
 - Interlobular septal thickening
 - □ Smooth; nodularity not typical but may occur
 - Outlines boundaries of secondary pulmonary lobule
 - □ Crazy-paving: Interstitial + alveolar edema
 - Subpleural edema: Thickened interlobar fissures
 - Peribronchovascular bronchial wall thickening
- o Alveolar edema
 - Ground-glass opacities, diffuse or patchy
 - Centrilobular ground-glass nodules
 - Lobular and acinar ground-glass opacities
 - Consolidation
 - □ Diffuse or patchy
 - Dependent (gravitational)
 - Central and perihilar in batwing edema
- Associated abnormalities
 - Cardiomegaly, pleural effusion, lymphadenopathy,
 - increased attenuation of mediastinal fat
- ARDS
 - Early phase
 - Anteroposterior gradient of lung involvement
 - Bilateral ground-glass opacities
 - Dense dependent consolidations
 - Bronchial dilatation
 - Pleural effusions
 - Late phase
 - Ground-glass opacities
 - Coarse reticular opacities and architectural distortion in nondependent lung
- HAPE
 - Asymmetric involvement
 - Perihilar ground-glass opacities and consolidations; nodular (acinar), nonuniform
- Reexpansion edema
 - o Ipsilateral ground-glass opacities
- TRALI, neurogenic edema: Rarely imaged with CT

Imaging Recommendations

- Best imaging tool
 - Chest radiography
 - CT/HRCT not indicated, but edema often identified when imaging performed for other reasons
 - HRCT may be useful for evaluation of fibrotic ARDS

DIFFERENTIAL DIAGNOSIS

Interstitial Edema

- Lymphangitic carcinomatosis
 - Nodular interlobular septal thickening
 - Patchy distribution

Alveolar Edema

- Pneumocystis jirovecii pneumonia
 - Severely immunocompromised state
- Ground-glass opacities, cysts
- Pneumonia
 - Signs and symptoms of infection
 - Focal or multifocal consolidation, cellular bronchiolitis
- Pulmonary hemorrhage
 - Ground-glass opacities, may exhibit crazy-paving pattern
 Centrilobular nodules

Interstitial and Alveolar Edema

- Pulmonary alveolar proteinosis
 - Crazy-paving pattern on CT
 - No cardiomegaly or pleural effusion

PATHOLOGY

General Features

- Etiology
 - Hydrostatic/cardiogenic edema
 - Increased capillary hydrostatic pressure
 - Left heart failure (may not be purely hydrostatic): Markedly ↑ capillary pressure may damage capillary endothelium leading to permeability edema
 Volume overload; overbydration
 - □ Volume overload; overhydration
 - Decreased intravascular oncotic pressure
 Hypoalbuminemia, hepatic/renal failure
 - ARDS
 - Respiratory symptoms within 1 week of clinical insult
 + bilateral pulmonary opacities on imaging + exclusion of heart failure or fluid overload as cause of symptoms
 - Opiate overdose
 - Unclear pathophysiology; postulated role of direct drug toxicity, hypoxia, and acidosis
 - TRALI
 - Susceptible recipients: Mechanical ventilation, positive fluid balance, smoking, chronic alcoholism, shock, liver/cardiac surgery
 - ↑ risk with transfusion of female plasma/whole blood
 - HAPE
 - Rapid ascent to altitudes > 3,000-4,000 meters
 - Excessive pulmonary artery pressures lead to nonuniform hypoxic vasoconstriction

- Resultant intraalveolar leakage of high molecular weight proteins, cells, and fluid

• Neurogenic edema

- Abrupt increase of intracranial pressure with activation of sympathetic system and resultant catecholamine release
- Effects on pulmonary capillary endothelium not understood
- Reexpansion edema
 - Postulated acute inflammatory response to reexpansion + alveolar capillary membrane damage

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Pulmonary edema: Respiratory distress, dyspnea, orthopnea, hypoxemia, cough (pink frothy sputum), crackles
 - **Hydrostatic/cardiogenic edema**: 3rd heart sound (S₃) (ventricular filling gallop)
 - ARDS: Symptoms within 6-72 hours from inciting event
 - Opiate overdose
 - High index of suspicion, appropriate history
 - Symptoms within hours of drug injection
 - Risk factors: Male sex, short duration of opiate use
 - **TRALI**: Symptoms within 6 hours of transfusion
 - HAPE
 - Risk factors: Individual susceptibility, male sex, cold temperature, preexisting pulmonary infection, vigorous exertion
 - Symptoms 2-4 days after arrival at high altitude
 - Neurogenic edema
 - Early stage: Symptoms within minutes to hours post neurologic injury
 - Late stage: Symptoms 12-24 hours post neurologic injury

Reexpansion edema

- Young patients with extreme sustained atelectasis
- ~ 64% with symptoms in 1st hour post pleural puncture

Natural History & Prognosis

- Hydrostatic/cardiogenic edema: Prognosis depends on severity and reversibility of underlying hemodynamic dysfunction
- ARDS: 26-58% mortality; increases with disease severity
- Opiate overdose edema: Rapid resolution with appropriate treatment
- **TRALI**: Majority of affected patients require ICU admission and ventilator support; 5-17% mortality
- HAPE: Favorable outcome with early recognition and prompt treatment
- Neurogenic edema: Prognosis based on severity of neurologic insult
- Reexpansion edema: 20% mortality reported

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Pulmonary Edema





(Left) Axial NECT of a patient with pulmonary edema shows centrilobular ground-glass $opacities \boxtimes and smooth$ interlobular septal thickening ➡, consistent with alveolar and interstitial edema. Note patchy distribution of airspace opacities and coexistence of normal and abnormal (thick) interlobular septa. (Right) Axial CECT shows interstitial and alveolar edema that manifest as asymmetric right upper lobe ground-glass opacities 🖾, interlobular septal thickening \square , and bronchial wall thickening \square .





(Left) Axial CECT of a patient with mitral valve disease and pulmonary edema shows diffuse bilateral ground-glass $opacities \supseteq$, small bilateral pleural effusions \supseteq , and minimal septal thickening \supseteq . (Right) Intermediate-power photomicrograph (H&E stain) of a specimen of predominant alveolar pulmonary edema shows edema fluid \supseteq and red blood cells ᠫ flooding the pulmonary airspaces. In this case, there is little interstitial edema as evidenced by normal thickness of the pulmonary interstitium 🔁.





(Left) Axial CECT shows alveolar edema manifesting as centrilobular and acinar ground-glass opacities 🔁. Note small right larger than left bilateral pleural effusions ➡. Alveolar edema has variable CT manifestations that range from ground-glass opacity to confluent consolidation. (Right) Axial CECT of the same patient shows pulmonary edema manifesting with patchy confluent 🔁 and lobular 🔁 ground-glass opacities. Note fissural pleural thickening 🔁 indicative of subpleural edema.

(Left) AP chest radiograph shows asymmetric alveolar edema that manifests as bilateral perihilar haze and consolidations, respectively. Note peribronchial cuffing 🔁, fissural pleural thickening 🖂 (subpleural edema), and bilateral pleural effusions. (Right) Axial NECT of a patient with batwing edema shows central perihilar consolidations *⊠* with intrinsic air bronchograms that spare the lung periphery. Batwing edema affects < 10% of patients with pulmonary edema and is associated with rapid onset of heart failure.





(Left) PA chest radiograph of a patient with acute mitral regurgitation shows preferential right upper lobe alveolar edema i Secondary to regurgitant flow of blood from an incompetent mitral valve, cardiomegaly, an enlarged left atrial appendage *⊡*, and bilateral pleural effusions. (Right) AP chest radiograph of a 58-year-old woman who developed acute respiratory distress within 6 hours of receiving a blood transfusion shows bilateral alveolar and interstitial edema, consistent with transfusion-related lung injury.





(Left) AP chest radiograph of a 55-year-old man who developed acute respiratory distress syndrome precipitated by sepsis shows asymmetric bilateral heterogeneous airspace disease. Note the absence of septal lines or pleural effusion. (Right) Coronal NECT of the same patient shows diffuse bilateral airspace disease with an anteroposterior gradient characterized by posterior consolidations 🖘 and anterior ground-glass opacities 🔁. The findings are characteristic of pulmonary edema secondary to diffuse alveolar damage.





Pulmonary Edema





(Left) PA chest radiograph of a 30-year-old man with acute pulmonary edema secondary to opiate overdose shows bilateral asymmetric heterogeneous alveolar opacities in the absence of septal lines or pleural effusion. (Right) Axial NECT of the same patient shows bilateral . asymmetric nodular $consolidations \implies that$ predominantly affect the right lung. These abnormalities typically resolve rapidly with appropriate treatment.





(Left) PA chest radiograph of a young man with high-altitude pulmonary edema shows asymmetric bilateral nodular opacities that predominantly affect the right lung. (Right) Axial NECT of the same patient shows asymmetric bilateral nodular consolidations that spare the lung periphery. The patchy distribution of the abnormalities reflects underlying nonuniform hypoxic vasoconstriction. Note the absence of pleural effusions or septal lines.





(Left) PA chest radiograph of a 26-year-old man with several days of chest pain shows a large left pneumothorax with associated complete atelectasis of the left lung \square and mass effect on the mediastinum. (Right) AP chest radiograph of the same patient after placement of a left thoracostomy tube 🖻 shows reexpansion of the left lung and development of ipsilateral airspace disease 🖂, consistent with reexpansion pulmonary edema. This entity typically affects young patients following relief of severe atelectasis.

KEY FACTS

TERMINOLOGY

- Pulmonary artery hypertension (PAH)
- Mean pulmonary artery pressure > 25 mm Hg at rest
 > 30 mm Hg during exercise
- Mean capillary wedge pressure and left ventricular enddiastolic pressure typically < 15 mm Hg

IMAGING

- **Radiography**: Enlarged pulmonary trunk and central pulmonary arteries
- CT/HRCT
 - Centrilobular nodules
 - Mosaic attenuation
 - o Interlobular septal thickening
 - Ground-glass opacities
- **CTA**
 - Enlarged pulmonary trunk > 30 mm
 - Peripheral pulmonary artery calcification
 - Eccentric filling defects

- Cardiac gated CTA
 - Decreased distensibility of pulmonary artery wall
- Angiography
 - Most reliable means of diagnosis
 - Direct measurement of right-sided pressures

TOP DIFFERENTIAL DIAGNOSES

- Congenital pulmonic valvular stenosis
- Idiopathic dilatation of pulmonary trunk
- Hilar lymphadenopathy

PATHOLOGY

• Nice Classification (2013): 5 groups

CLINICAL ISSUES

- Poor prognosis
- Treatment
 - o Medical therapy: Calcium channel blockers
 - o Idiopathic PAH: Prostaglandin I2 (epoprostenol)
 - Lung ± heart transplant

(Left) PA chest radiograph of a patient with pulmonary artery hypertension shows an enlarged pulmonary trunk \blacksquare , and enlarged left ight and right *▶* pulmonary arteries, and abrupt narrowing ("pruning") of peripheral pulmonary artery branches. (Right) Lateral chest radiograph of the same patient shows bilateral hilar masses 🔁 that represent enlarged pulmonary arteries. The patient has a patent ductus arteriosus (a left-toright shunt that represents a pre-capillary etiology, group 2 Nice classification of pulmonary hypertension).





(Left) Axial NECT of a patient with longstanding pulmonary artery hypertension shows marked enlargement of the right 🔁 and left 🄁 pulmonary arteries, intimal mural pulmonary artery calcification B, and an enlarged pulmonary trunk 🔁. (Right) Phase-contrast sagittal MR shows an enlarged pulmonary trunk 🔁 and enlarged proximal left and right pulmonary arteries ➡. Phase-contrast MR is useful for evaluating pulmonary artery morphology and determining the direction and velocity of blood flow.





TERMINOLOGY

Abbreviations

- Pulmonary artery hypertension (PAH)
- Pulmonary hypertension (PH)
- Pulmonary artery (PA)

Definitions

- Mean PA pressure > 25 mm Hg at rest
 > 30 mm Hg during exercise
- Mean capillary wedge pressure and left ventricular enddiastolic pressure typically < 15 mm Hg

IMAGING

General Features

Best diagnostic clue
 Enlarged pulmonary trunk ± enlarged left and right PAs

Radiographic Findings

- Radiography
 - **Enlarged pulmonary trunk**: Left superior mediastinal convexity on frontal radiography
 - Pruning of peripheral PA branches
 - Cardiac silhouette
 - Early: Normal
 - Late: Enlarged right atrium and ventricle
 - Chronic PAH: Intimal PA calcification

CT Findings

- HRCT
 - Centrilobular nodules
 - Severe PH; rarely untreated idiopathic PAH
 - Cholesterol granulomas, recurrent pulmonary hemorrhage, or plexogenic arterial lesions

• Mosaic attenuation

- Chronic thromboembolic pulmonary hypertension (CTEPH) is most common cause
- Regional differences in lung perfusion; alternating oligemia (low attenuation) and hyperemia (high attenuation)
- Vascular attenuation or obliteration in low attenuation lung; enlarged vessels in normal lung
- Interlobular septal thickening
 - Smooth (left heart disease), irregular (fibrosis; group 3), nodular (sarcoidosis or lymphangitic carcinomatosis; group 5)
- Ground-glass opacities
 - Pulmonary edema (group 2), interstitial lung diseases (group 3), connective tissue disorders (group 1), drug or toxic reactions (group 1)
- CTA
 - o General
 - Enlarged PAs: Pulmonary trunk > 30 mm
 - Right interlobar PA > 16 mm in men; > 14 mm in women
 - o Normal PAs
 - Pulmonary trunk: 28.6 mm; smaller than adjacent ascending aorta
 - Left PA: 28 mm; right PA: 24.3 mm
 - o Mural calcification
 - Long-standing PH; severe and late stages

- Longstanding cardiac shunts (typically ASDs) and Eisenmenger syndrome
- Eccentric filling defects
 - CTEPH: Mural thrombus or eccentric emboli; obtuse angles with PA wall, vessel stenosis ± irregular contour
 Poststenotic dilatation; rarely webs, beaded
 - vessels, obstructed thread-like arteries
- Intra-arterial soft tissue
 - Pulmonary intravascular tumor emboli
 - Tree-in-bud nodules: Distal or subsegmental involvement and dilated peripheral PAs
 - Malignancy: Breast, liver, kidney, lung, prostate, choriocarcinoma
- Cardiac gated CTA
 - Decreased distensibility of PA wall

MR Findings

- Less sensitive and specific than CT
- More difficult to perform in dyspneic patients
- Phase-contrast MR: PA morphology, blood flow direction and velocity, flow resistance, regurgitant fraction, PA strain

Angiographic Findings

- Most reliable means of diagnosis
- Direct measurement of right-sided pressures

Nuclear Medicine Findings

- Ventilation-perfusion scintigraphy
 - Usually low probability for PE
 - Chronic thromboemboli: High probability scans
 - Reduced quantity of particles necessary
 - Risk of acute right heart failure from capillary bed occlusion

Echocardiographic Findings

- Echocardiogram
 - Right ventricular pressure overload
 - Enlarged right atrium and ventricle
 - Right ventricular hypertrophy
 - Reduced global right ventricular function
 - Interventricular septum
 - □ Increased thickness; systolic flattening
 - □ IV septum: Posterior LV wall ratio > 1

Imaging Recommendations

- Best imaging tool
 - CECT: Quantification of PA enlargement; etiology (thromboembolism, lung abnormalities, cardiac morphology)
- Protocol advice
 - Multiplanar imaging for accurate measurements

DIFFERENTIAL DIAGNOSIS

Congenital Pulmonic Valvular Stenosis

- Enlarged pulmonary trunk and left PA
- ± thickening and calcification of pulmonic valve leaflets

Idiopathic Dilatation of Pulmonary Trunk

- Enlarged pulmonary trunk ± left and right PAs
- Diagnosis of exclusion
 - o Normal right-sided pressures

Hilar Lymphadenopathy

- Hilar enlargement
- Sarcoidosis, lymphoma, metastatic disease

PATHOLOGY

Staging, Grading, & Classification

- Nice Classification (2013)
 - Group 1: PAH
 - Idiopathic PAH
 - Heritable PAH: BMPR2; ALK1, ENG, SMAD9, CAV1, KCNK3; unknown
 - Drug and toxin induced
 - Associated with
 - Connective tissue disease
 - □ HIV infection
 - Portal hypertension
 - Congenital heart disease
 - □ Schistosomiasis
 - Pulmonary veno-occlusive disease (PVOD) &/or pulmonary capillary hemangiomatosis (PCH)
 Persistent PH of newborn (PPHN)
 - Group 2: PH due to left heart disease
 - 5 Group 2. PH due to tert field to disease
 - Left ventricular systolic dysfunctionLeft ventricular diastolic dysfunction
 - Valvular disease
 - Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
 - Group 3: PH due to lung diseases &/or hypoxia
 - Chronic obstructive pulmonary disease (COPD)
 - Interstitial lung disease
 - Other pulmonary diseases with mixed restrictive and obstructive pattern
 - Sleep-disordered breathing
 - Alveolar hypoventilation disorders
 - Chronic exposure to high altitude
 - Developmental lung disease
 - Group 4: CTEPH
 - Group 5: PH with unclear multifactorial mechanisms
 - Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
 - Systemic disorders: Sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
 - Metabolic disorders: Glycogen-storage disease, Gaucher disease, thyroid disorders
 - Others: Tumoral obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH

Microscopic Features

- Idiopathic PAH
 - Plexogenic pulmonary arteriopathy
 - Medial hypertrophy
 - Intimal proliferation
 - Necrotizing arteritis
- PVOD
 - o Microscopic findings of capillary hemangiomatosis
 - o Intimal fibrosis of pulmonary veins
 - Recanalized thrombi and webs
- Centrilobular cholesterol granulomas in 25% of cases

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea on exertion
- Other signs/symptoms
 - Fatigue, syncope, chest pain
 - PVOD may be preceded by flu-like illness

Demographics

- Age
 - o Idiopathic PAH: 3rd decade of life
- Sex
 - Idiopathic PAH: M:F = 1:3
 - Prevalence in men
 - 10% above age 35; 25% above age 65
- Epidemiology
 - o Schistosomiasis most common cause worldwide
 - PVOD: 1/3 children
 - 1% of acute thromboemboli become chronic thromboemboli

Natural History & Prognosis

- Diagnosis
 - Pulmonary artery catheterization
 - Normal resting mean PA pressure < 20 mm Hg
- Poor prognosis

Treatment

- Medical therapy
- o 30% response
- Calcium channel blockers
- Pulmonary thromboemboli
 - Anticoagulation
 - o Inferior vena cava filter
 - Selective thromboendarterectomy
- Idiopathic PAH
 - o Prostaglandin I2 (epoprostenol)
 - Vasodilator
 - Poor prognostic indicators on pre-treatment CT
 - Centrilobular ground-glass nodules
 - □ Interlobular septal thickening
 - Pleural and pericardial effusions
 - Lymphadenopathy
- Lung ± heart transplant

DIAGNOSTIC CHECKLIST

Consider

 PAH when imaging studies demonstrate pulmonary trunk size > 30 mm

Image Interpretation Pearls

• Evaluate mediastinum and lung parenchyma for possible etiologies

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- 2. Aluja Jaramillo F et al: Approach to pulmonary hypertension: from CT to clinical diagnosis. Radiographics. 38(2):357-73, 2018





(Left) PA chest radiograph of a patient with pulmonary hypertension shows a convex left mediastinal opacity 🔁 that represents an enlarged pulmonary trunk. (Right) Axial CECT of the same patient demonstrates enlargement of the pulmonary trunk \square and the left pulmonary artery 🔁 due to pulmonary hypertension. Pulmonary trunk enlargement is the most common imaging manifestation of pulmonary hypertension, with measurements > 30 mm typically used as a suggestive finding.





(Left) Axial CECT of a patient who presented with chest pain shows enlargement of the pulmonary trunk 🔿, peripheral thrombus 🖾 in the , left pulmonary artery, and a small left pleural effusion. (Right) Coronal CECT of the same patient shows extensive peripheral thrombus 🔁 in the left pulmonary artery and enlargement of a right pulmonary artery branch 🖂. These findings represent pulmonary hypertension due to chronic pulmonary thromboembolic disease (group 4, Nice classification).





(Left) PA chest radiograph of a patient with longstanding pulmonary hypertension demonstrates enlargement of the bilateral pulmonary arteries 🖂 (Right) Coronal CECT of the same patient demonstrates bilateral pulmonary mosaic attenuation. In pulmonary hypertension, mosaic attenuation is typically due to regional differences in lung perfusion, with regions of low attenuation (representing oligemia) 🔁 and high attenuation (representing hyperemia).

KEY FACTS

TERMINOLOGY

• Pulmonary hypertension with significant pulmonary venous &/or capillary wall proliferation (intimal hyperplasia)

IMAGING

- Radiography
 - Enlarged pulmonary arteries, cardiomegaly (right-heart), non-specific reticular opacities
- CT
 - Poorly-defined centrilobular ground-glass opacities
 - o Interlobular septal thickening
 - Findings of pulmonary hypertension (dilated pulmonary trunk ± enlarged right heart chambers)
 - o Normal size of central pulmonary veins and left atrium

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary arterial hypertension
- Chronic thromboembolic pulmonary hypertension

PATHOLOGY

- Key differences between PVOD/PCH and PAH
 - Location of vascular proliferation: Veins/venules in PCH, capillaries/precapillary arterioles in PAH
 - PAH arterial vasodilator treatment produces lifethreatening pulmonary edema in PVOD/PCH

CLINICAL ISSUES

- Rare, incidence of 0.2-0.5 cases/million persons/year
- EIF2AK4 mutation carriers have younger median age of diagnosis than non-mutation carriers
- Median survival: 2-3 years from diagnosis
- Treatment: Lung transplantation, avoidance of vasodilators

DIAGNOSTIC CHECKLIST

• Consider PVOD/PCH in patients with septal lines, groundglass opacities, and mediastinal/hilar lymphadenopathy in the setting of pulmonary hypertension with a normal-sized left atrium

(Left) Axial CECT of a 27-yearold woman with pulmonary venoocclusive disease/pulmonary capillary

hemangiomatosis shows smooth interlobular septal thickening 2 and enlarged right heart chambers 2, a classic combination of CT abnormalities in this disease. (Right) Coronal CECT of the same patient shows lower lobe predominant smooth interlobular septal thickening 2, upper lobe predominant ill-defined centrilobular ground-glass micronodules 2, and an enlarged left pulmonary artery 2.





(Left) Composite image with axial CECT of a 22-year-old patient with pulmonary venoocclusive disease/pulmonary capillary hemangiomatosis and pulmonary hypertension shows hilar lymphadenopathy □ a dilated pulmonary trunk ➡, and enlarged right-heart chambers 🔁. (Right) Axial NECT of the same patient shows ill-defined centrilobular ground-glass opacities, with a patchy distribution. A relatively small left atrium (not shown) is a non-specific but common finding described in affected patients.





Pulmonary Venoocclusive Disease/Pulmonary Capillary Hemangiomatosis

TERMINOLOGY

Abbreviations

- Pulmonary venoocclusive disease/pulmonary capillary hemangiomatosis (PVOD/PCH)
- Pulmonary arterial hypertension (PAH)

Definitions

• Pulmonary hypertension with significant pulmonary venous &/or capillary wall proliferation (intimal hyperplasia)

Classification

- Classified as group 1.6: PAH with overt features of venous/capillary (PVOD/PCH) involvement
 - Previously considered separate entities; currently thought to represent continuum

IMAGING

General Features

- Best diagnostic clue
 - Triad of septal lines, ground-glass opacities, and mediastinal/hilar lymphadenopathy in setting of pulmonary hypertension and normal-sized left atrium

Radiographic Findings

- Radiography
 - Enlarged pulmonary arteries, cardiomegaly (right-heart), non-specific reticular opacities

CT Findings

- HRCT/CT
 - Centrilobular ground-glass opacities: Diffuse, perihilar, patchy
 - Thick interlobular septa
 - o Mediastinal &/or hilar lymphadenopathy
 - Pulmonary hypertension (dilated pulmonary trunk and central pulmonary arteries ± enlarged right heart chambers)
 - o Normal size of central pulmonary veins and left atrium

Imaging Recommendations

- Best imaging tool
 - HRCT/CT to differentiate PVOD/PCH from other causes of PAH

DIFFERENTIAL DIAGNOSIS

Pulmonary Arterial Hypertension

- Centrilobular ground-glass opacities in 1/3
- Septal thickening extremely uncommon

Chronic Thromboembolic Pulmonary Hypertension

- Peripheral filling defects on pulmonary CTA
- Mosaic attenuation (from differential perfusion)

PATHOLOGY

General Features

- Etiology
 - Bi-allelic *EIF2AK4* gene mutations described for hereditary PVOD/PCH
 - Non-genetic causes of PVOD/PCH
 - Exposure to organic solvents such as trichloroethylene

- Chemotherapy using alkylating drugs (cyclophosphamide, mitomycin C, cisplatin)
- Other: Scleroderma, sarcoidosis, human immunodeficiency virus, fenfluramine

• Key differences between PVOD/PCH and PAH

- Location of vascular proliferation: Veins/venules in PCH, capillaries/precapillary arterioles in PAH
- PAH arterial vasodilator treatment produces lifethreatening pulmonary edema in PVOD/PCH
- Pathophysiology: Capillary and venule wall vascular proliferation produces increase in capillary hydrostatic pressure leading to pulmonary hypertension

Microscopic Features

- Capillary and venule mural vascular proliferation produces thrombosis &/or obstruction leading to increased pressures
- Absence of plexiform arteriopathy (characteristic of PAH)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Similar to PAH (dyspnea on exertion, syncope, heart palpitations)
 - Vasodilators may exacerbate pulmonary edema and result in death

Demographics

- Sex
- M=F
- Rare; incidence of 0.2-0.5 cases/million persons/year
- *EIF2AK4* mutation carriers have younger median age at diagnosis (26 years, range: 0-50.3) compared to non-mutation carriers (60 years, range: 6.7-81.4)

Natural History & Prognosis

• Median survival: 2-3 years from diagnosis

Treatment

- Lung transplantation (survival rate post-transplant of 75% at 3 years)
 - Arterial vasodilators (standard treatment for other causes of PAH) may induce fatal pulmonary edema

Diagnosis

- Based on CT findings, and low DLCO/VA (< 55%)
- Biopsy is diagnostic gold standard but contraindicated in setting of PAH (high complication rate)

DIAGNOSTIC CHECKLIST

Consider

 PVOD/PCH in patients with triad of septal lines, groundglass opacities, and mediastinal/hilar lymphadenopathy in the setting of pulmonary hypertension with a normal-sized left atrium

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KEY FACTS

TERMINOLOGY

- Pulmonary embolism (PE)
- Embolized thrombus to pulmonary arteries, from lower extremity or abdominopelvic veins

IMAGING

- Radiography
 - o Nonspecific radiographic findings; 10% normal
 - Oligemia (Westermark sign); vascular obstruction
 - Subsegmental atelectasis (Fleischner lines)
 - Pleural effusion
 - Pulmonary infarction: Hampton hump; lower lobe
- CTA
 - Standard of care for suspected PE
 - Direct visualization of intraluminal clot
 - Pulmonary hypertension, right ventricular strain
 - Subsegmental atelectasis
 - Pulmonary infarct
 - Detection of disease other than PE in 70%

- Ventilation perfusion (V/Q) scintigraphy
 High sensitivity, low specificity
- Dual-energy CT pulmonary angiography
 o Increasing utility with advances in scanner technology

TOP DIFFERENTIAL DIAGNOSES

- Hilar or peribronchial lymph nodes
- Pneumonia &/or atelectasis
- Flow-related or motion artifacts
- In situ pulmonary artery thrombus

PATHOLOGY

- Risk factors: Immobilization, malignancy, hypercoagulable/excess estrogen state, prior PE/deep venous thrombosis
- Epidemiology: 3rd most common cause of death

CLINICAL ISSUES

- Good outcome with appropriate therapy
- Mortality in untreated disease, up to 30%

(Left) Axial CTA of a patient with chest pain and dyspnea shows significant thromboembolism burden. A saddle embolus \supseteq in the pulmonary trunk bifurcation extends into the bilateral pulmonary arteries 🛃. (Right) Axial CTA of a patient with large burden pulmonary embolism shows bibasilar subsegmental pulmonary artery emboli (not shown) and characteristic findings of right heart strain including rightsided chamber enlargement and flattening of the interventricular septum 🔁 (RV:LV ratio > 1).





(Left) Coronal CTA shows a right basilar pulmonary infarct that manifests as a peripheral consolidation with central lucency \supseteq and surrounding ground-glass attenuation 🔁. The offending embolus 🔁 propagates into a lateral basilar subsegmental artery E. (Right) Composite image with axial CECT obtained 9 days (left) and 2 months (right) after acute thromboembolic disease shows the melting sign. The well-defined subpleural right lower lobe pulmonary infarct ➡ decreases in size ➡ as it "melts" away.





TERMINOLOGY

- Abbreviations
- Pulmonary embolism (PE)

Definitions

• Embolized thrombus to pulmonary arteries, often originating in lower extremity or abdominopelvic veins

IMAGING

General Features

- Best diagnostic clue
- Arterial intraluminal filling defect(s) on CTALocation
 - o Central, lobar, segmental, subsegmental arteries
- Size
- o May occlude large central or small peripheral arteries
- Morphology
 - Usually tubular; casts of systemic veins
 - Well-defined discrete margins; typically convex in relation to vessel lumen

Radiographic Findings

- Nonspecific radiographic findings; 10% normal
- Subsegmental atelectasis (Fleischner lines); airspace opacities, elevated hemidiaphragm(s), volume loss
- Pleural effusion
- Pulmonary artery abnormalities
 - Regional oligemia (**Westermark sign**); vascular obstruction
 - Enlarged central pulmonary artery (**knuckle sign**); endoluminal clot
- Pulmonary infarct (uncommon); < 10% of emboli
 - Hampton hump: Subpleural peripheral wedge-shaped opacity, rounded apex pointing to hilum
 - o Usually basilar
 - Typically: 0-72 hours after acute PE
 - **Melting sign**: Initial ill-defined opacity involutes over time → decreases in size, becomes well-defined
 - **50% clear completely** within 3 weeks; may leave linear scars (**Fleischner lines**)

CT Findings

- NECT
 - Intraluminal hyperattenuating (30-60HU) thrombus
 - Low sensitivity, high specificity (> 90%); detection may require narrow window widths
 - Subsegmental atelectasis
 - Pulmonary infarct
 - Peripheral subpleural wedge-shaped consolidation
 - No contrast enhancement
 - Consolidation with central lucency; high likelihood ratio for infarction
 - Vessel sign; pulmonary artery leading to consolidation
- CTA
 - Standard of care for suspected PE; rapid, noninvasive, readily available
 - $\circ~$ Direct visualization of intraluminal thrombus
 - Filling defect; frequently central in vessel lumen

- Partial filling defect, sharp interface, surrounded by contrast
- Cutoff of vascular enhancement, arterial occlusion, may enlarge vessel caliber

• Right ventricular strain/failure

- Right ventricular dilatation (RV:LV ratio > 1)
- Leftward bowing/flattening interventricular septum
 Reflux of contrast into dilated inferior vena cava (IVC)
- and hepatic veins • **Pulmonary hypertension**; enlarged pulmonary trunk (≥ 2.9-3.1 cm)
- Dual-energy CT pulmonary angiography
 - Increased utility with advances in scanner technology; radiation dose-neutral protocols
 - Pulmonary blood volume (iodine map) images:
 Assessment of iodine distribution → objective analysis of enhancement
 - May ↑ sensitivity for PE detection; differentiation of lung abnormalities (infarct, consolidation, atelectasis)
- Indeterminate or false-negative CTA
 - Poor bolus, large body habitus, image noise
 - Failure to recognize subsegmental emboli
 - Potential pitfalls/artifacts
 - Artifacts: Beam hardening, volume averaging, motion
 Thin-section and multiplanar reformations helpful
 - Transient contrast interruption: Admixing of unopacified IVC blood during deep inspiration
 End evolution breath held instructions image
 - □ End-expiratory breath-hold instructions/image acquisition ↓ incidence
 - Flow-related ("smoke") artifacts: Nonuniform opacification, amorphous, ill-defined filling defects
 - Technical and physiologic factors: Admixture of unopacified blood
 - Poor cardiac output, increased vascular resistance (pulmonary hypertension, parenchymal atelectasis/consolidation)

MR Findings

- MR Angiography: Limited role; increasing utility with advances in scanner technology, availability
- Visualization of central, lobar, and segmental emboli
- Sensitivity approximately 90%; specificity 80-95%

Angiographic Findings

- Never gained widespread acceptance, not universally available
- Vascular filling defect, abrupt occlusion or pulmonary artery pruning, oligemia
- Potential to miss central and subsegmental emboli

Nuclear Medicine Findings

- Ventilation perfusion (V/Q): Modified PIOPED II criteria for PE
 - o Criteria used to assign one of three interpretations
 - PE present, nondiagnostic, or negative for PE
 PE present: Two or more large mismatched segmental perfusion defects
 - More likely to provide diagnosis when lungs free of parenchymal abnormality
 - High sensitivity; poor specificity
 - Normal perfusion scan excludes PE

Ultrasonographic Findings

- Lower extremity ultrasound: Low sensitivity, high specificity
- When positive, optional pulmonary artery CTA
- 50% of patients with PE: No deep venous thrombosis (DVT)

Imaging Recommendations

- Best imaging tool
 - o CT angiography; lower extremity ultrasound
 - Pregnant patient with normal chest radiograph; consider perfusion scan only for dose reduction
- Protocol advice
 - Guidelines for regnant patients with suspected PE
 - Chest radiography: 1st radiation-associated imaging study
 - Nuclear scintigraphy if normal chest radiograph
 - CTA if abnormal chest radiograph
 - Pregnant patient: Maternal and fetal radiation reduction
 - Reduction in tube current and voltage
 - External shielding: Bismuth breast shield + lead apron
 - Internal fetal shielding with oral barium preparation
- Advantages of CTA
 - Detection of disease other than PE in 70%
 - Pneumonia, lung cancer, metastases, pneumothorax
 Pericarditis, acute myocardial infarction, aortic dissection

DIFFERENTIAL DIAGNOSIS

Hilar and Peribronchial Lymph Nodes

• Reformatted images to show extraluminal location

Flow-Related ("Smoke") or Motion Artifacts

• Nonuniform vascular opacification mimics filling defect

Pneumonia &/or Atelectasis

- CTA: Vessel enhancement within consolidated lung
- Pneumonia and edema "fade"; infarcts "melt"

Intravascular Tumor Emboli

- Direct invasion or vascular dissemination of malignancy
- Dilated beaded peripheral pulmonary arteries; tree in bud

In Situ Pulmonary Artery Thrombus

- Associated with radiation therapy: underrecognized complication of central chest radiation
- Pneumonectomy: Pulmonary artery stump

Pulmonary Artery Sarcoma

• Enhancing endoluminal mass, often eccentric, irregular margins

Embolized Foreign Bodies

Smaller and thinner than thrombi; metallic density
 Fractured IVC filter tines, vertebroplasty cement

PATHOLOGY

General Features

- Etiology
 - Risk factors: Hypercoagulability
 - Acquired: Malignancy, immobilization, trauma, postoperative, burns, infection (COVID-19), excess estrogen (pregnancy, oral contraceptives)

- Inherited: Factor V Leiden, Proteins C/S, antithrombin deficiency
- History of prior PE or DVT
- Epidemiology
 - 3rd most common cause of cardiovascular death
 - PE in 1.5% of CECT performed for other reasons
 - 2-20% of pregnant patients with suspected PE proven to have PE

Gross Pathologic & Surgical Features

- Thrombus fragments in right heart; average of 8 pulmonary vessels embolized
- Hemodynamic consequences: > 50% reduction of capillary bed, pulmonary hypertension, right heart strain

Microscopic Features

• Intraluminal thrombus, branching lines of fibrin-platelet aggregates, surrounded by red and white blood cells

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Dyspnea, tachypnea, pleuritic chest pain, syncope, or
- o Dysphea, tachyphea, pleuritic chest pain, syncope, or asymptomatic
- No signs, symptoms, or laboratory studies strongly correlate with PE
 - D-Dimer assay: Highly sensitive (normal value essentially excludes large PE)

Demographics

- Age: Disproportionately affects older adults (> 70 years at 3x higher risk than 45-60 years)
- Sex: M = F

Natural History & Prognosis

- Most pulmonary emboli resolve without sequelae
- Outcome: Good with appropriate therapy
- Good after negative CTA (< 1% embolic rate)
 Mortality in untreated disease up to 30%
- Mortality in untreated disease, up to 30%
- Chronic thromboembolic pulmonary hypertension (~ 5% of patients after acute PE)

Treatment

- Anticoagulation and fibrinolysis; hemorrhage complications in 2-15%
- Catheter directed thrombolysis in selected patients: Hemodynamic compromise, contraindications for systemic fibrinolytics
- IVC filter: Contraindication to anticoagulation, recurrent emboli

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Incidental PE found in 4% of patients with malignancy on restaging CECT

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- 2. Martinez Licha CR et al: Current management of acute pulmonary embolism. Ann Thorac Cardiovasc Surg. 26(2):65-71, 2020





(Left) Axial CTA shows a large, nearly occlusive pulmonary embolus in the right interlobar pulmonary artery that extends into basilar segmental branches. (Right) Axial dualenergy CTA pulmonary blood volume image of the same patient shows asymmetrically reduced parenchymal perfusion throughout the basilar right lower lobe 🛃 with decreased enhancement of attenuated, subsegmental arteries 🔁. A subsegmental embolus in the lateral basilar left lower lobe \bowtie resulted in a similar reduction in perfusion.





(Left) AP chest radiograph of a 63-year-old man with intermittent chest pain and progressive dyspnea shows regional lucency in the right upper lung (Westermark sign) \square , exaggerated in this patient with concurrent cardiogenic pulmonary edema. (Right) Perfusion lung scintigraphy of the same patient shows the large segmental perfusion defect of the entire right upper lobe apical segment 🔁 and additional large segmental perfusion defects in the basilar right lower lobe 🔁 and the apicoposterior and lingular left upper lobe 🔁





(Left) Axial NECT of a 78-yearold woman with metastatic breast cancer and chronic kidney disease undergoing surveillance imaging shows a hyperattenuating saddle thromboembolus 🔁. Narrow window width helps increase conspicuity. (Right) Coronal oblique CTA shows large thromboembolic burden involving both the left and right pulmonary arteries 🔁 and propagation into lobar and segmental pulmonary arteries 🔁 Reconstructed oblique images are often helpful for identification of pulmonary emboli.

KEY FACTS

TERMINOLOGY

- Chronic thromboembolic pulmonary hypertension (CTEPH)
- Pulmonary embolism
- Organization of thromboemboli after acute pulmonary embolism; resultant pulmonary vascular obstruction/obliteration

IMAGING

- **Radiography**: Normal vs. findings of pulmonary arterial hypertension (PAH)
- **CTA**: Luminal thrombi, peripheral thrombi, pulmonary artery occlusion, webs
 - Enlarged pulmonary arteries related to PAH
 - Mosaic perfusion of lung parenchyma
 - Cardiac chamber enlargement from PAH
 - Hypertrophied bronchial arteries
- V/Q scan: Multiple mismatched defects
 Perfusion defect on dual-energy CT (DECT)

TOP DIFFERENTIAL DIAGNOSES

- Acute pulmonary embolism
- Pulmonary artery sarcoma
- Takayasu arteritis
- Congenital interruption of pulmonary artery

PATHOLOGY

• Factor VIII, high frequency of antiphospholipid antibodies, lupus anticoagulant; may be risk factors

CLINICAL ISSUES

- 5% incidence in patients with acute PE
- Symptoms: Progressive exertional dyspnea
- Treatment: Inferior vena cava filter, lifetime anticoagulation, surgical thromboendarterectomy in selected patients

DIAGNOSTIC CHECKLIST

• Consider chronic PE in patients with chronic dyspnea, PAH, and eccentric or web-like thrombi or mosaic lung perfusion

(Left) Composite image with axial CECT (left) and axial CTA obtained 3 weeks later (right) shows a right lower lobe pulmonary embolus 🔁, which manifests as a thin linear endoluminal web 🛃 on follow-up imaging. (Right) Axial CTA of a patient with severe pulmonary hypertension and chronic pulmonary emboli shows superimposed acute emboli in left lower lobe segmental pulmonary arteries 🔁, dilatation of the right cardiac chambers, and flattening of the interventricular septum \∃≥\.





(Left) Axial CECT of a young woman on long-term oral contraception who presented with dyspnea shows an acute right upper lobe pulmonary embolus 🔁. (Right) Axial CECT of the same patient shows a chronic left upper lobe pulmonary embolus manifesting as a long peripheral wall-adherent filling defect 🔁 in the pulmonary artery lumen. Patients with chronic pulmonary thromboembolic disease may develop acute pulmonary emboli (acute on chronic pulmonary emboli).





TERMINOLOGY

Abbreviations

- Chronic thromboembolic pulmonary hypertension (CTEPH)
- Pulmonary embolism (PE)

Synonyms

• Chronic pulmonary arterial thromboembolic disease

Definitions

• Thromboemboli organization after acute PE with resultant pulmonary vascular obstruction/obliteration

IMAGING

General Features

- Best diagnostic clue
 - Eccentric, wall-adherent, low-density filling defect; dilated pulmonary artery(ies)

Radiographic Findings

- Radiography
 - o Normal chest radiograph
 - Findings of pulmonary arterial hypertension (PAH)
 Pulmonary artery/right heart enlargement
 - Subpleural opacities from prior pulmonary infarcts
 - Hypo- and hyperperfused lung regions
 - Rarely peripheral cavitary lesions; infarcts

CT Findings

• HRCT

- Mosaic perfusion of pulmonary parenchyma
 - Heterogeneous lung attenuation from differential perfusion
 - Decreased attenuation from decreased perfusion; small intrinsic pulmonary arteries
- Subpleural opacities from prior pulmonary infarcts

• CTA

- CTA allows direct visualization of luminal thrombi, organized mural thrombi, arterial occlusion, webs
 - Eccentric thrombi
 - Smooth or nodular vessel wall thickening
 - Rarely eccentric wall-adherent pulmonary artery calcifications
 - Webs
 - Eccentric linear filling defects with partial intraluminal extension
 - □ Webs represent remote episodes of PE
 - Commonly CTEPH exhibit webs but webs do not necessarily imply CTPEH; ancillary findings that support CTEPH include pulmonary hypertension and dilatation of right heart chambers

- Abrupt vessel narrowing or occlusion

- "Pruning" of peripheral arteries
- Peripheral neovascularity in longstanding PAH
- Enlarged pulmonary arteries related to PAH
 - Pulmonary artery (PA):aorta ratio > 1
 - Pulmonary trunk diameter > 29 mm
- Cardiac chamber enlargement from PAH
- Enlarged RV: RV/LV diameter > 1 at midventricular level

- Straight or left-bowing interventricular septum
- D-shaped LV cavity on short axis view

Large hypertrophied bronchial arteries

- Increased bronchopulmonary collaterals distinguish CTEPH from 1° PAH
- Exclude alternative causes of PAH
 - Congenital cardiovascular disease: Atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage
 - Parenchymal disease: Emphysema, interstitial fibrosis
 - Other pulmonary vascular diseases: Veno-occlusive disease, capillary hemangiomatosis, vascular occlusions from mediastinal fibrosis, pulmonary artery sarcoma
- Perfusion defects on dual-energy CT (DECT)
 96%-100% sensitivity and 76%-92% specificity

MR Findings

MRA

- Correlates well with CTA to segmental level; cannot reliably detect smaller thrombi
- Eccentric, low signal defects along arterial wall on SSFP, MRA, and C+ GRE sequences
- o Vessel occlusions, intraluminal webs and bands
- Time-resolved MRA (TR-MRA) for assessment of lung perfusion pattern
- MR cine
 - Allows qualitative and quantitative assessment of ventricular function
 - Phase-contrast imaging measures flow in systemic and pulmonary vessels; assessment of treatment outcomes
 Pre- and post-pulmonary thromboendarterectomy

Echocardiographic Findings

- Evidence of PAH
- Right atrial and ventricular enlargement/dysfunction
- Tricuspid regurgitation
- Exclusion of cardiac causes of PAH (e.g., patent foramen ovale, septal defect)

Angiographic Findings

- Vascular occlusions, webs, stenoses, mural thrombi
- 2 orthogonal views essential for surgical planning
- Right ventricular and pulmonary artery hemodynamics

Nuclear Medicine Findings

- V/Q scan
 - Normal V/Q scan excludes chronic PE
 - o Multiple mismatched segmental or larger defects
 - Magnitude of perfusion defects often underestimates degree of obstruction
 - o 97% sensitivity with 90%-95% specificity

Imaging Recommendations

- Protocol advice
 - Contrast bolus timing for opacification of pulmonary circulation
 - Pulmonary trunk as ROI for bolus tracking; 80-100 mL of contrast at 3 cc/sec; 1.5-mm collimation
 - ECG may be synchronized with CT scan to assess RV function; more radiation to patient
MR/MRA sequences: Axial SSFP, cine SSFP of heart, coronal time-resolved MRA (for perfusion), coronal C+ MRA, axial and coronal post-contrast T1 GRE

DIFFERENTIAL DIAGNOSIS

Acute Pulmonary Embolism

- Vascular filling defects more likely central than peripheral; no webs
- Right ventricle may be enlarged but not hypertrophic
- No mosaic lung attenuation

Pulmonary Artery Sarcoma

- Usually irregular, lobulated, wall-adherent
- Contrast enhancement (best on MR) seen in sarcoma (vascular); not in thrombus (usually avascular)
- May involve pulmonary valve and extend retrograde into RV infundibulum; does not occur in chronic PE

Takayasu Arteritis

- Mural thickening in pulmonary vasculitis may resemble eccentric thrombus
- Other vessels involved (e.g., aorta)
- CT and MR may identify circumferential inflammatory mural thickening
 - MR better than CT for assessment of mural enhancement; differentiates active vs. chronic vasculitis
- FDG PET shows intense uptake in active disease

Proximal Interruption of Pulmonary Artery

• Affected lung is hypoplastic

PATHOLOGY

General Features

- Etiology
 - Unresolved pulmonary emboli that organize, become adherent, and incorporate into arterial wall
 - 75% of all patients with CTEPH have prior history of acute PE
 - 25% of all patients with CTEPH without history of PE
 - Severe remodeling and microvasculopathy of distal pulmonary arteries
 - Chronic infection and inflammation
 - Presence of *Staphylococcus aureus* within thrombi
 - Higher levels of C-reactive protein, interleukin-6, and interferon gamma-induced protein 10
 - Proximal PA occlusion and arteriopathy contribute to elevated pulmonary vascular resistance
- Associated abnormalities
 - Patients may have altered coagulation
 - Factor VIII, high frequency of antiphospholipid antibodies, lupus anticoagulant; may be risk factors
 - Cancer and ventriculoarterial shunts
 - Splenectomy may increase risk of CTEPH

Gross Pathologic & Surgical Features

- Emboli transform into fibrous tissue; incorporation into pulmonary artery intima and media
- Small vessel vasculopathy in remaining open vessels, subjected to high flow

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Progressive exertional dyspnea
- Exercise intolerance
- Other signs/symptoms
 - Exertional chest painPresyncope, syncope
 - Fatigue, palpitation. hemoptysis

Demographics

- Epidemiology
 - 5% incidence in patients with acute PE
 - Older adult patients; M = F

Natural History & Prognosis

- 2/3 of affected patients may have no history of acute PE
- Often misdiagnosed as asthma, heart failure, chronic obstructive pulmonary disease, physical deconditioning, or psychogenic dyspnea
- Extent of vascular obstruction: Major determinant of development of PAH
- Low survival rate without intervention for PAH
 - 5-year survival rate of 30% with mean pulmonary artery pressure \geq 40 mm Hg
 - 5-year survival rate of 10% with mean pulmonary artery pressure ≥ 50 mm Hg

Treatment

- Potentially correctable cause of PAH
- IVC filter placement
 - Lifetime anticoagulation
- Medical therapy or balloon angioplasty for non-surgical candidates
 - o Riociguat, Macitentan, Selexipag
- Surgical thromboendarterectomy in selected patients
 - Location/extent of proximal thromboembolic obstructions; critical determinants of operability
 - Occluding thrombi must involve main, lobar, or proximal segmental arteries

DIAGNOSTIC CHECKLIST

Consider

• Chronic PE in patient with chronic dyspnea, PAH, and eccentric or web-like thrombi or mosaic lung perfusion

Image Interpretation Pearls

- Eccentric web-like thrombi, differential lung perfusion, vessel calcifications, and right heart strain favor chronic PE
- Intimal hyperplasia in congenital heart disease with central shunting may mimic chronic PE
 - Intravascular ultrasound helps to differentiate

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(Left) Axial CTA of a patient with chest pain and dyspnea shows bilateral large lower lobe pulmonary emboli ₽. The right lower lobe pulmonary embolus nearly occludes the vessel lumen, while the left lower lobe embolus expands the vessel. (Right) Axial CTA of the same patient obtained 6 months later shows complete recanalization of the left lower lobe pulmonary artery without residual embolus and a right lower lobe pulmonary artery web \blacksquare , consistent with chronic thromboembolic disease.





(Left) Axial CTA of a patient with pulmonary hypertension secondary to chronic pulmonary thromboembolic disease shows a large peripheral filling defect 🔁 extending from the pulmonary trunk into the enlarged left pulmonary artery. Note marked hypertrophy of bronchial arteries 🔁 (Right) Axial CTA of the same patient shows a peripheral right lower lobe chronic pulmonary embolus 🛃 and a linear left lower lobe web 🛃 associated with marked bronchial artery hypertrophy 🔁.





(Left) Coronal CTA MIP reformatted image of a patient with pulmonary hypertension shows chronic pulmonary emboli manifesting as bilateral eccentric endoluminal soft tissue 🔁 that partially encases vessel lumina. (Right) Axial CECT of a patient with pulmonary artery hypertension from chronic pulmonary thromboembolic disease shows mosaic attenuation with differential caliber of pulmonary arteries, larger caliber 🛃 arteries in the hyperperfused lung than in those 🛃 in the hypoperfused lung.

Sickle Cell Disease

KEY FACTS

TERMINOLOGY

- Sickle cell disease (HbSS): Inherited hemoglobinopathy; abnormal hemoglobin molecule deforms when deoxygenated
- Acute chest syndrome: Respiratory symptoms ± fever in HbSS patients and new chest radiographic abnormalities
- Sickle cell chronic lung disease: Sequelae of recurrent acute chest syndrome

IMAGING

- Radiography
 - o Airspace disease: Lobar, segmental, subsegmental
 - Preferential lower lobe involvement
 - Cardiomegaly ± enlarged central pulmonary arteries
 - Rib expansion, H-shaped vertebrae, absent or small calcified spleen
- **CT**: Mosaic perfusion ± infarcts/consolidations
- **CECT**: High osmolarity contrast contraindicated; may induce sickling

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary edema
- Infectious pneumonia
- Pulmonary infarction ± thromboembolism

PATHOLOGY

- Autosplenectomy: Risk of pneumonia by encapsulated bacteria (*Staphylococcus*, *Haemophilus*)
- Progressive multi-organ damage

CLINICAL ISSUES

- Acute chest syndrome
 - Children: Cough, wheezing, fever (often pneumonia)Adults: Chest pain, dyspnea, limb pain (often fat emboli)
- Pulmonary hypertension (up to 40%)

DIAGNOSTIC CHECKLIST

• Consider acute chest syndrome HbSS patient with new respiratory complaints/pain and new pulmonary opacities

(Left) Frontal chest radiograph of a 50-year-old woman with sickle cell disease and acute chest syndrome shows cardiomegaly and hazy lung opacities, greater in the right upper lobe 🛃. (Right) Coronal NECT of the same patient shows a hyperdense liver 🕰, an absent spleen \implies , and a dilated pulmonary trunk 🔁 from pulmonary hypertension. The low-attenuation left ventricular blood pool 🔁 reflects clinical anemia. Chronic hemolysis and repeated transfusions may lead to hepatic iron overload, cirrhosis, and hepatitis.

(Left) Composite image with axial NECT of the same patient shows mosaic perfusion and multilobar peripheral wedge-shaped ground-glass opacities that suggest pulmonary infarcts. Subpleural bands 🛃 reflect chronic lung scarring related to prior episodes of acute chest syndrome. (Right) Composite image with axial NECT of the same patient obtained one year later shows mosaic attenuation related to microvascular occlusion and peripheral reticulation and small subpleural densities \square , likely healed lung infarcts.









Abbreviations

- Sickle cell disease (HbSS)
- Acute chest syndrome (ACS)

Definitions

- **HbSS**: Inherited hemoglobinopathy; abnormal hemoglobin molecule deforms when deoxygenated
- Spectrum of inherited blood disorders
- Acute chest syndrome: Respiratory symptoms ± fever in HbSS patients and new chest radiographic abnormalities
 Often preceded by vaso-occlusive crisis with bone pain
 - Orten preceded by vaso-occlusive crisis with bone pa – ~ 80% adults with ACS
 - May be precipitated by lung infection ± infarction
 - Adult patients face greater severity and risk of death
- Sickle cell chronic lung disease: Result of recurrent ACS
- Sickle cell trait: Strictly not HbSS; benign clinical course

IMAGING

General Features

- Best diagnostic clue
- Expanded ribs, H-shaped vertebrae, absent/small spleenLocation
 - o Lower lobe predominant opacities

Radiographic Findings

- Radiography
 - Lung parenchyma
 - Initial chest radiograph may be normal (50%)
 - Lobar, segmental, subsegmental opacities
 - Pneumonia, atelectasis, infarct
 Preferential lower lobe involvement
 - Interstitial thickening from prior episodes of ACS
 - Pleura
 - Pleural effusion: Pneumonia, infarct, left heart failure
 - Heart
 - Cardiomegaly: Chronic anemia and high output heart failure, ventricular dilatation and compensatory hypertrophy, cor pulmonale from pulmonary hypertension (PH)

• Mediastinum

- Paravertebral mass; extramedullary hematopoiesis
 Unilateral or bilateral, sharply marginated
- Enlarged pulmonary trunk from PH
- Skeletal
 - Avascular necrosis (AVN) of humeral heads
 - H-shaped vertebrae (10%)
 - Step-off deformity of superior and inferior endplates (Reynold sign)
 - Enlarged ribs due to marrow expansion
 - Osseous sclerosis due to bone infarcts
- o Upper abdomen
 - Small or absent spleen, may be calcified (autosplenectomy)

CT Findings

- Consolidation
 - o Involves at least one complete lung segment
 - Pneumonia, pulmonary infarction, fat embolism

- Mosaic perfusion from regional microvascular occlusion
 - Geographic areas of hypoperfusion: Areas of decreased attenuation contain small vessels
 - Geographic areas of hyperperfusion: Areas of groundglass opacity contain normal or enlarged vessels
 - Flow redistribution to lung with less microvascular occlusion
 - Ventilation-perfusion mismatch increases red cell sickling
 Ground-glass opacity: Fluid overload or reperfusion injury
- Pulmonary thromboembolism (PE)
 - ~ 10% positivity when imaged emergently with CECT
 In situ thrombosis vs. venous thromboembolism
- CECT: High osmolarity contrast contraindicated; may induce sickling
- Sequelae of recurrent ACS
 - Fibrosis with reticulation, traction bronchiectasis
 - Parenchymal bands, septal thickening, peripheral wedgeshaped opacities

Nuclear Medicine Findings

- Bone scan
 - Foci of decreased or increased radiotracer uptake in ribs; bone infarcts
 - Increased spleen uptake; calcification from autosplenectomy
 - Delayed renal uptake
- Tc-99m sulfur colloid
 - Uptake in extramedullary hematopoiesis
- V/Q scan
 - Limited clinical use in ACS: May mimic pulmonary embolism
 - Etiology: Sickling erythrocytes, pneumonia, fat emboli
 - Findings resolve quickly with supportive therapy

Imaging Recommendations

- Best imaging tool
 - Chest radiographs often provide sufficient information for evaluation and treatment
- Protocol advice
 - CT more sensitive for parenchymal abnormalities but usually not necessary; excess radiation dose in young patients

DIFFERENTIAL DIAGNOSIS

Chest Pain

- Pulmonary edema
- Lung opacities more diffuse and bilateral
- Infectious pneumonia
 - May be lobar or multifocal
- Pulmonary infarction ± pulmonary embolism
 Clearing opacities may show distinct margins
- Acute coronary syndrome ± myocardial infarction

PATHOLOGY

General Features

- Etiology
 - Complex interaction of sickled erythrocytes, circulating co-factors, host immunity, endothelial activation
 - Cascade of microvascular vaso-occlusion, intravascular hemolysis, and multi-organ tissue damage

- ACS: Acute lung injury, cause rarely determined
 - Pneumonia (often community-acquired) ± infarctions (from thrombosis or fat emboli)
 - Rib infarction \rightarrow pain \rightarrow splinting \rightarrow linear atelectasis
 - Central vessel thrombosis (acute or chronic) unusual

• Pneumonia

- Documented in 30% of ACS cases
- More common cause of ACS in children.
- Most common pathogens: Chlamydia pneumoniae, Mycoplasma pneumoniae, respiratory syncytial virus
- Upper lobe consolidation more likely pneumonia; oxygen tension highest in upper lung zones due to high V:Q ratio

Pulmonary fat embolism

- Emboli contain fat and necrotic marrow in 10-16%
- Found in 40-77% of adults with ACS
- Diagnosis supported by lipid-laden macrophages in bronchoalveolar lavage fluid

Pulmonary hypertension

- Develops in up to 40% of patients; Group 5 PH
- Multifactorial: Vaso-occlusion, hemolysis, left heart failure, hepatic cirrhosis

• Rib infarction

- High correlation between rib infarction and pulmonary opacity
- Rib pain may result in splinting and atelectasis
- Incentive spirometry may decrease atelectasis

Left ventricular dysfunction

- High output failure due to anemia, especially when hemoglobin ≤ 7 gm/dL
- Fluid imbalance from renal regurgitation (from microinfarction of renal papillae)
- Microvascular myocardial ischemia
- Autosplenectomy: Impaired immunity due to functional asplenia
 - Risk of pneumonia from encapsulated organisms:
- Streptococcus pneumoniae, Haemophilus influenzae Genetics
- Valine substitution for glutamine in hemoglobin beta subunit (HbS): autosomal recessive mutation
- o Sickle cell anemia
 - When exposed to low oxygen tension, HbS forms large polymers
 - Erythrocytes distort, less pliable (sickle cells) \rightarrow widespread vaso-occlusion and hemolysis

Microscopic Features

- Arteries, capillaries, venules clogged with sickled erythrocytes ± in situ thrombi
- Occasional fat and necrotic bone marrow emboli
- Alveolar septal edema, hemorrhage, necrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - ACS: New pulmonary opacity on radiography + fever, cough, tachypnea, wheezing, chest pain
 - Infectious vs. noninfectious etiology
 - Wheezing, cough, and fever typical in patients < 10 years

- Adults: Chest, arm, and leg pain; often afebrile
- ACS often preceded by vaso-occlusive crisis (adults)
 - Fat embolism suggested when pulmonary and radiographic findings preceded by severe bone pain
- Other signs/symptoms
 - Hyperreactive airway disease, ~ 40% of affected children
 - o Cerebrovascular events: Stroke, cerebral hemorrhage

Demographics

- Epidemiology
 - o Global annual incidence: 300,000-400,000 neonates
 - HbSS most prevalent inherited disorder among African Americans
 - HbSS occurs in 0.15% of African American population
 - HbSA occurs in 8% of African American population
 - Average life expectancy: 42 years (men), 48 years (women)
 - ACS occurs in up to 50% of patients with HbSS
 - Recurrent episodes in 80%
 - Children 100x more susceptible to pneumonia; recurrence rate 30%

Natural History & Prognosis

- ACS: Leading cause of death in HbSS
 - Up to 25% of deaths; ↑ mortality due to PH
 - > 20% have fatal pulmonary complications, thromboembolism in 15-48% at autopsy
 - 2nd most common cause of hospitalization in patients with HbSS
- Higher risk of bacterial pneumonia and sepsis from encapsulated organisms; related to functional asplenia
- Chronic sequelae of recurrent ACS
 - Sickle cell chronic lung disease (5%)
 - High output cardiac failure
 - Pulmonary artery hypertension (up to 40%); cor pulmonale
- Progressive end-organ damage

Treatment

- Supportive
 - o Oxygen, hydration, pain control
 - Incentive spirometry, bronchodilators
 - Empiric antibiotics
 - Blood transfusion
- Prevention
 - Penicillin prophylaxis
 - Pneumococcal and Haemophilus influenzae vaccination
- Hematopoietic stem cell transplantation (HSCT)

DIAGNOSTIC CHECKLIST

Consider

 ACS in patient with HbSS with new-onset respiratory complaints/pain and new pulmonary opacities

SELECTED REFERENCES

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- Carstens GR et al: Clinical relevance of pulmonary vasculature involvement in 2. sickle cell disease. Br J Haematol. 185(2):317-26, 2019
- Ware RE et al: Sickle cell disease. Lancet. 390(10091):311-23, 2017 3.

Sickle Cell Disease





(Left) PA chest radiograph of a 57-year-old man with sickle cell anemia shows cardiomegaly, pulmonary venous hypertension \blacksquare , and interstitial and alveolar edema. (Right) Axial CECT of the same patient shows alveolar edema, an enlarged pulmonary trunk \square from pulmonary hypertension, and a small right pleural effusion ➡. Left ventricular failure likely results from high-output failure due to anemia, , overhydration, or renal regurgitation. Pulmonary hypertension is a late complication.





(Left) Axial CECT of the same patient shows a right paravertebral soft tissue mass Secondary to extramedullary hematopoiesis, which occurs in response to chronic, severe anemia. Right heart enlargement 🔁 is secondary to pulmonary hypertension. (Right) Axial NECT of a patient with sickle cell anemia with restrictive lung disease shows diffuse scattered reticular opacities and honeycombing \supseteq . Fibrosis is a rare complication that can occur following recurrent episodes of acute chest syndrome.





(Left) PA chest radiograph of a 17-year-old woman with sickle cell anemia shows a right upper lobe consolidation $\overline{\Longrightarrow}$, cardiomegaly, H-shaped vertebral bodies \boxtimes , and absence of the splenic shadow ∠, all stigmata of sickle cell disease. (Right) Lateral chest radiograph of the same patient shows the right upper lobe consolidation \blacksquare and Hshaped vertebrae 🛃 due to microinfarctions at vertebral endplates. Round pneumonias due to Streptococcus pneumoniae may affect , patients with autosplenectomy.

Fat Embolism

KEY FACTS

TERMINOLOGY

- Fat embolism (FE): Release of fat globules into venous system
- Fat embolism syndrome (FES): Pulmonary, cerebral, and cutaneous manifestations

IMAGING

- Best diagnostic clue: Diffuse bilateral airspace disease in trauma setting
- Radiography
 - Chest radiograph may be normal
 - Patchy or diffuse bilateral opacities
- CT
 - Focal or diffuse consolidation ± ground-glass opacity
 Nodules < 10 mm; centrilobular and subpleural
- CTA
- Fat density endoluminal filling defect (rare finding)
- V/Q scan
 - Peripheral V/Q mismatches

TOP DIFFERENTIAL DIAGNOSES

- Acute respiratory distress syndrome
- Cardiogenic and noncardiogenic pulmonary edema
- Infection
- Pulmonary embolism

CLINICAL ISSUES

- FE
 - o > 90% of patients with traumatic bone injury
 - Asymptomatic in most cases
- FES
 - Develops within 1-3 days of injury
 - Clinical triad of hypoxemia, neurologic abnormalities, and petechial rash
 - o Mortality: 5-15%; worse in older adults, severe injuries

DIAGNOSTIC CHECKLIST

• Consider FES in patient who develops chest radiographic abnormalities 1-3 days after bone trauma

(Left) PA chest radiograph of a 68-year-old woman with acute respiratory distress three days after sustaining a femoral fracture shows diffuse bilateral heterogeneous pulmonary opacities diagnosed as fat embolism syndrome based on clinical criteria. (Right) AP radiograph of the right femur of the same patient shows a comminuted displaced fracture 🔁 through the mid femoral shaft. Patchy or diffuse pulmonary opacities on chest radiography in the setting of bone trauma should suggest pulmonary fat embolism.





(Left) Axial CECT of a patient with a recent long bone fracture demonstrates an endoluminal filling defect 🖂 in a left upper lobe pulmonary artery compatible with fat embolism. The Hounsfield unit value was less than -40. The identification of fat in such emboli is a rare observation. (Right) Axial CECT of a patient who presented with shortness of breath due to fat embolism syndrome shows bilateral ground-glass opacities with interlobular septal thickening and a crazy-paving pattern 🔁





Abbreviations

- Fat embolism (FE)
- Fat embolism syndrome (FES)

Definitions

- FE
 - $\circ~$ Release of fat globules into venous system
- Typically benign course
- FES
 - o Pulmonary, cerebral, cutaneous manifestations

IMAGING

General Features

Best diagnostic clue
 Bilateral airspace disease in trauma setting

Radiographic Findings

- Radiography
 - Early: Chest radiograph may be normal
 - Late: Patchy or diffuse bilateral opacities
 - Airspace, interstitial, ± nodular

CT Findings

- NECT
 - Focal or diffuse consolidation ± ground-glass opacity
 Nodules < 10 mm
 - Centrilobular and subpleural
 - Upper lung zones
- CECT
 - Rarely endoluminal filling defect exhibiting fat attenuation

Nuclear Medicine Findings

- V/Q scan
 - Peripheral V/Q mismatches

Imaging Recommendations

Best imaging tool
 Chest radiography for identification and monitoring

DIFFERENTIAL DIAGNOSIS

Acute Respiratory Distress Syndrome

- Imaging and time course overlap
- Distinguish with Gurd and Wilson criteria

Cardiogenic Pulmonary Edema

• Cardiomegaly, Kerley lines, pleural effusions

Noncardiogenic Pulmonary Edema

• Normal heart size and appropriate clinical setting

Infection

• Signs and symptoms of infection

Pulmonary Hemorrhage

• Consolidation and septal thickening

Pulmonary Embolism

• Pulmonary artery filling defects on CTA

PATHOLOGY

General Features

- Etiology
 - Intramedullary veins damaged by bone trauma: Intravasation of marrow fat; obstruction of pulmonary microvasculature
 - Hydrolysis of fat emboli: Liberation of free fatty acids, ↑ capillary bed permeability, delayed pulmonary failure
 - Platelet aggregation: Stimulated by fat globules, local serotonin and histamine release; resultant edema, hemorrhage and vascular disruption

Microscopic Features

• Widespread microvascular occlusion by fat emboli

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - FE: Asymptomatic in most cases
 - FES: Clinical triad of hypoxemia, neurologic abnormalities, and petechial rash
- Clinical profile
 - Clinical diagnosis: Gurd and Wilson criteria
 - At least 1 major and 4 minor criteria
 - Major criteria
 - Hypoxemia
 - Pulmonary edema
 - Central nervous system depression
 - Petechial rash in vest distribution
 - Minor criteria
 - Tachycardia
 - Pyrexia
 - Retinal emboli
 - Jaundice
 - □ Sudden drop in hematocrit or platelets
 - □ Increased erythrocyte sedimentation rate
 - □ Fat globules in sputum and urine

Demographics

- Epidemiology
 - FE: > 90% of patients with traumatic bone injury
 - FES: 3-4% of patients with FE

Natural History & Prognosis

- FES: Develops within 1-3 days of injury
- Mortality: 5-15%; worse in older adults and in severe injuries

Treatment

- Adequate oxygenation and hemodynamic stability
- Reduced risk: Early immobilization and stabilization

DIAGNOSTIC CHECKLIST

Consider

 FES in patient who develops chest radiographic abnormalities 1-3 days after bone trauma

SELECTED REFERENCES

1. Rothberg DL et al: Fat embolism and fat embolism syndrome. J Am Acad Orthop Surg. 27(8):e346-55, 2019

TERMINOLOGY

- Hepatopulmonary syndrome (HPS)
 - Intrapulmonary vascular dilatation
 - ↑ alveolar-arterial oxygen gradient on room air
 - o Liver disease

IMAGING

- Best diagnostic clue: Dilated intrapulmonary vessels, peripheral telangiectasias, and arteriovenous communications
- Radiography: Normal or basilar reticulonodular opacities
- **CT**: Dilated basilar lung vessels, peripheral telangiectasias, arteriovenous communications
- Nuclear medicine: Tc-99m macroaggregated albumin for shunt quantification
- Pulmonary angiography
 - Documentation of arteriovenous malformations
 - o May show spider-like peripheral vasculature

TOP DIFFERENTIAL DIAGNOSES

- Portopulmonary hypertension
- Hepatic hydrothorax
- Interstitial lung disease

PATHOLOGY

• Postulated excess circulating pulmonary vasodilators (e.g., nitric oxide)

CLINICAL ISSUES

- Symptoms/signs
 - o Dyspnea, cyanosis, clubbing, hypoxemia
 - HPS in 15-20% of patients with cirrhosis; increased risk of death and decreased functional status
 - Orthotopic liver transplant, most effective treatment

DIAGNOSTIC CHECKLIST

• Consider HPS in patients with cirrhosis, hypoxemia, and dilated basilar peripheral pulmonary vessels on CT

(Left) PA chest radiograph of a patient with hepatic cirrhosis shows bilateral basilar reticulonodular opacities 🔁. The dilated intrapulmonary vasculature and the arteriovenous communications seen in hepatopulmonary syndrome occur predominantly in the lower lobes. (Right) Composite image with CECT of the same patient shows dilated peripheral lower lobe pulmonary vessels 🔁 that are approximately twice the size of the adjacent bronchi and enlarged subpleural vessels \nearrow .





(Left) Axial CECT MIP reformatted image of a patient with hepatopulmonary syndrome shows dilated lower lobe vessels \square and relative sparing of upper lobe vessels. Vessel dilatation is thought to be due to increased circulating vasodilators. (Right) Axial CECT of a patient with cirrhosis shows abnormal communications 🔁 between peripheral pulmonary arteries and veins. Such communications are not always visible on CT, but arteriovenous shunting may be demonstrated and quantified on nuclear scintigraphy.





Abbreviations

• Hepatopulmonary syndrome (HPS)

Definitions

- Syndrome composed of triad
 - Intrapulmonary vascular dilatation
 - 1 alveolar-arterial oxygen gradient on room air
 - Liver disease

IMAGING

General Features

- Best diagnostic clue
 - Dilated intrapulmonary vessels, peripheral telangiectasias, and arteriovenous communications in patients with liver cirrhosis
- Location
 - More common in **lower lobes**

Radiographic Findings

- Chest radiography may be normal
- Basilar nodular or reticulonodular opacities

CT Findings

- **Dilated subpleural vessels**; arteriovenous communications may not be visible
- Nodular dilatation of peripheral pulmonary vessels, representing arteriovenous communications
 May see dilated feeding artery and draining vein
- Dilatation of pulmonary artery in relation to accompanying bronchus

Nuclear Medicine Findings

- V/Q scan
 - Ventilation perfusion mismatch and shunt
- Tc-99m-labeled macroaggregated albumin
 - Activity in brain, kidney, liver, spleen from intrapulmonary arteriovenous shunting
 - Allows shunt quantification
 - Does not differentiate intracardiac from intrapulmonary shunts

Echocardiographic Findings

- Contrast echocardiography with microbubbles at 4th-6th cardiac cycle
 - Bubbles before 3rd cardiac cycle more common in intracardiac shunts

DIFFERENTIAL DIAGNOSIS

Portopulmonary Hypertension

- Pulmonary arterial hypertension accompanying portal hypertension
- May be secondary to vasoactive substances, venous thromboembolism, or increased cardiac output
- 2-5% of patients with liver cirrhosis

Hepatic Hydrothorax

- Pleural effusion, usually right-sided
- Postulated leakage of ascitic fluid into pleural space via diaphragmatic defects

Arteriovenous Malformation

• May be sporadic or familial

Interstitial Lung Disease (ILD)

- Sarcoidosis associated with interferon therapy
- Methotrexate for treatment of primary biliary cirrhosis
 Centrilobular nodules, patchy ground-glass opacities
 Fibrosis has been reported

Metastatic Disease

• Tumor emboli from hepatocellular carcinoma may cause dilated pulmonary vasculature

Portosystemic Collateral Vessels

• Esophageal, paraesophageal, cardiophrenic varices

PATHOLOGY

General Features

- Etiology
 - Postulated excess circulating **pulmonary vasodilators** (e.g., nitric oxide)

Staging, Grading, & Classification

- Type 1 (most common): Subpleural telangiectasia and peripheral vessel dilatation
- Type 2: Arteriovenous communications

Microscopic Features

- Dilated precapillary arterioles and pleural vessels
- Arteriovenous communications

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Shortness of breath, cyanosis, clubbing
 - Cutaneous spider nevi
- Other signs/symptoms
 - o Hypoxemia
 - o Increased alveolar-arterial oxygen gradient
 - DLCO shows decreased diffusion capacity

Demographics

Epidemiology
 0 15-20% of patients with cirrhosis

Natural History & Prognosis

• HPS confers ↑ risk of death and poor functional status

Treatment

Orthotopic liver transplant, most effective treatment

DIAGNOSTIC CHECKLIST

Consider

• HPS in patient with cirrhosis, hypoxemia, and dilated basilar peripheral pulmonary vessels on CT

SELECTED REFERENCES

- 1. Bansal K et al: Hepatopulmonary Syndrome 2021
- Folador L et al: Hepatopulmonary syndrome has low prevalence of pulmonary vascular abnormalities on chest computed tomography. PLoS One. 14(10):e0223805, 2019

TERMINOLOGY

• Spectrum of pulmonary complications related to use of inhaled or intravenous illicit drugs

IMAGING

- Excipient lung disease
 - Early: Diffuse centrilobular micronodules
 - Late: Signs of pulmonary hypertension and cor pulmonale
 - Talc deposition may coalesce into larger hyperattenuating opacities
- Septic embolism
 - Multiple peripheral cavitary lung nodulesReversed halo sign is common feature
- Infection
 - Consolidation, ground-glass opacities, nodules
- Pulmonary edema related to cocaine, methamphetamines, heroin
- Emphysema

TOP DIFFERENTIAL DIAGNOSES

- Small nodules (< 1 cm)
 - Excipient lung disease
 - Infectious bronchiolitis or respiratory bronchiolitis
 - o Hypersensitivity pneumonitis
- Large nodules (1-3 cm)
 - o Septic embolism
 - Fungal or mycobacterial infection
- Consolidation or ground-glass opacity
 - o Infection
 - o Pulmonary edema
 - Pulmonary hemorrhage
- Decreased lung attenuation
 - Air-trapping
 - o Emphysema

DIAGNOSTIC CHECKLIST

• Consider illicit drug use in young adult with unexplained lung disease

(Left) AP chest radiograph of a crack cocaine user who presented to the emergency department with chest pain and dyspnea shows bilateral ill-defined pulmonary opacities. (Right) Axial CECT of the same patient shows bilateral perihilar ground-glass opacities and consolidations that suggest alveolar pulmonary edema. Consider illicit drug use when pulmonary edema is seen in a young patient without a history of cardiac disease.





(Left) PA chest radiograph of a patient who presented with syncope after intravenous injection of oxycodone intended for oral use shows *diffuse bilateral pulmonary* micronodules and enlarged central pulmonary arteries 🚬 (Right) Axial CTA of the same patient shows diffuse bilateral centrilobular micronodules that represent impaction of excipient in the pulmonary arterioles. Note also right atrial and right ventricular enlargement, consistent with cor pulmonale from pulmonary hypertension.





Definitions

- Spectrum of pulmonary complications related to use of inhaled or intravenous (IV) illicit drugs
 - Typical drugs: Heroin, cocaine ("crack"), methamphetamine ("speed"), codeine, methadone, methylphenidate (Ritalin)
- Excipient: Insoluble filler materials that bind active drug, and contribute to shape and lubrication for improved oral ingestion
 - Talc, cellulose, crospovidone, starch

IMAGING

Imaging Features

- Excipient lung disease (ELD): IV injection of crushed oral medications; a.k.a. "foreign body granulomatosis"
 - Early: Diffuse centrilobular micronodules
 - Late: Enlarged central pulmonary arteries (pulmonary hypertension), dilated right heart (cor pulmonale)
 - Talc deposition may coalesce into larger hyperattenuating opacities with perihilar confluence, similar to progressive massive fibrosis
- Septic embolism
 - Multiple angiocentric nodules with peripheral distribution, frequently cavitate over time
 - o Reversed halo sign
- Infection: Increased risk due to malnutrition, immunosuppression, or coexisting HIV infection
 - Consolidation, ground-glass opacities
 - Centrilobular pulmonary nodules
- Aspiration: Due to altered consciousness • Dependent consolidation, ground-glass opacity
- Dependent tree-in-bud opacities
- Pulmonary edema: Cocaine, methamphetamines, heroin
 - Bilateral perihilar consolidation or ground-glass opacities, septal thickening
 - ± pleural effusion
- Pulmonary hemorrhage: Multifocal, bilateral airspace disease
- Emphysema
 - IV injection of methylphenidate: Panacinar emphysema with lower lobe predominance
 - Mimics a-1 antitrypsin deficiency
 - o Cocaine smokers: Emphysema with upper lobe predominance
- Small airways disease: Cocaine, other inhaled substances • Asthma and constrictive bronchiolitis
 - Geographic areas of increased lucency

Imaging Recommendations

- Best imaging tool
 - Chest radiographs for initial evaluation and follow-up
 - CT more sensitive for detection and further characterization if chest radiograph does not explain persistent clinical symptoms

DIFFERENTIAL DIAGNOSIS

Small Nodules (< 1 cm)

- Infectious bronchiolitis or respiratory bronchiolitis
- Hypersensitivity pneumonitis

Large Nodules (1-3 cm)

- Septic embolism
- Fungal or mycobacterial infection
- Organizing pneumonia

Consolidation or Ground-Glass Opacity

- Infection: Bacterial, viral, pneumocystis
- Pulmonary edema
- Aspiration
- Pulmonary hemorrhage •
- Organizing or eosinophilic pneumonia •

Decreased Lung Attenuation

- Air-trapping
 - o Asthma/constrictive bronchiolitis
 - Foreign body aspiration
- Emphysema
 - Upper lung zone: Cigarette smoking
 - ο Basilar: IV Ritalin; α-1 antitrypsin

PATHOLOGY

General Features

- Etiology
 - ELD
 - Embolization of talc or other fillers (cellulose, crospovidone, starch) to pulmonary arterioles and capillaries
 - Foreign body granulomatous reaction and fibrosis

• Septic emboli

- Source: Subacute bacterial endocarditis and tricuspid vegetations, septic thrombophlebitis, direct injection of infected fluid
- Staphylococcus most common organism
- Pulmonary edema
 - May be cardiogenic &/or related to pulmonary capillary damage with increased permeability
- Emphysema
 - Damage and obliteration of capillary bed; direct drug toxicity or intermediate immune response

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea, cough, wheezing, chest pain o Hemoptysis

Demographics

- Aae
 - Any; primarily 18-25 years
- Sex
 - Males > females
- Epidemioloav • Over 1.5 million IV drug users in North America

SELECTED REFERENCES

Blinick R et al: Cracking the opium den: cardiothoracic manifestations of 1. drug abuse. J Thorac Imaging. 36(2):W16-31, 2020

TERMINOLOGY

• Calcification of valve leaflet or annulus

IMAGING

• Radiography

- Aortic stenosis: Bicuspid or degenerative; left ventricular configuration, aortic dilatation
- Mitral stenosis: Left atrial/appendage enlargement, pulmonary venous hypertension
- Mitral annulus calcification: Reverse C-shaped calcification
- Pulmonic stenosis: Enlarged pulmonary trunk and left pulmonary artery
- NECT: Characterization of calcification
 - Caseous calcification of mitral annulus (CCMA): Centrally hypodense, peripheral calcification
- Echocardiography: Procedure of choice to assess valve morphology and function

TOP DIFFERENTIAL DIAGNOSES

- Pericardial calcification
- Ventricular calcification
- Coronary artery calcification
- Great vessel calcification

PATHOLOGY

- Aortic valve leaflets: Degenerative, congenital bicuspid aortic valve
 - o Bicuspid aortic valve: 90% calcified at surgery
- Aortic annulus: Atherosclerosis
- Mitral valve leaflets: Rheumatic heart disease
- Mitral annulus: Degenerative, end-stage renal disease
- CCMA: Degenerative

CLINICAL ISSUES

- Surgical replacement of abnormal valves
- Aortic and mitral valves most commonly replaced

(Left) PA chest radiograph of a patient with multiple valve replacements shows a tricuspid annuloplasty ring 🔁 and artificial mitral 🔁 and pulmonic 🔁 valves. (Right) Lateral chest radiograph of the same patient shows a tricuspid annuloplasty ring 🔁 and artificial mitral 🛃 and pulmonic 🔁 valves. Knowledge of the anatomic location of the cardiac valves allows radiographic identification of calcified valve leaflets and annuli.





(Left) Axial NECT of an asymptomatic patient who underwent lung cancer screening shows dense aortic valve calcification 🖂. Three patterns of aortic valve calcification are described: Commissure (or linear), complete or partial ring, and plaque-like calcification. (Right) Axial CECT of a patient with treated lung cancer shows thick, curvilinear calcification \supseteq of the mitral annulus. Mitral annular calcification is associated with a higher incidence of new coronary events and systemic atherosclerosis.





Abbreviations

- Caseous calcification of mitral annulus (CCMA)
- Mitral annular calcification (MAC)

Definitions

• Calcification of valve leaflet or annulus

IMAGING

General Features

- Best diagnostic clue
 - Calcification in expected position of cardiac valve

Radiographic Findings

• Aortic valve

- Frontal radiograph: Projects over spine
- Lateral radiograph: Between anterior and posterior cardiac borders, above line from carina to sternodiaphragmatic junction
- 3 patterns of calcification
 - Commissure calcification: Linear
 - Complete or partial ring calcification
 - Plaque-like calcification
- Bicuspid aortic valve calcification
 - Circular calcification with internal linear focus (fused raphe)
- Strong marker for aortic stenosis
 - Secondary findings
 - □ Left ventricular configuration,
 - Poststenotic dilatation of ascending aorta
- Aortic annulus calcification
 - Usually seen in conjunction with leaflet calcification
 - May extend into ascending aorta or interventricular
- septum
- Mitral valve
 - Frontal radiograph: Left of spine, below aortic valve
 - Lateral radiograph: Below line from carina to sternodiaphragmatic junction
 - Mitral stenosis
 - Left atrial enlargement

• Double density sign

- o Enlarged left atrial appendage
- o Pulmonary venous hypertension and edema
- Longstanding: Hemosiderosis associated interstitial lung disease

MAC and CCMA

- Uniform, reverse C-shaped calcification
 - Junction between ventricular myocardium and posterior mitral leaflet
- O-shaped with involvement of anterior mitral leaflet

• Pulmonic valve

- Frontal radiograph: Below and medial to pulmonary trunk border, between spine and left atrial appendage
- Lateral radiograph: Upper anterior heart, behind sternum
- Most cephalad of cardiac valves
- Congenital pulmonic valvular stenosis
 - Enlarged pulmonary trunk and left pulmonary artery
 - Decreased pulmonary vascularity when severe

• Tricuspid valve

- Below pulmonic valve
- Separated from pulmonic valve by infundibulum of pulmonary outflow track
- Tricuspid stenosis
 - Right heart enlargement and clockwise rotation of cardiac apex
 - Medial displacement and dilatation of superior vena cava (SVC)
 - Leftward bowing of interventricular septum

• Tricuspid annulus calcification

- Mirror image of mitral annulus
- Uniform, C-shaped calcification

CT Findings

- CECT
 - Leaflet (central); annulus (peripheral)
 - Quantification of aortic valve calcification with CECT not reliable
 - Contrast material may simulate calcification
 - NECT with ECG gating preferred
 - o CCMA
 - Centrally hypodense mass with peripheral calcification
 - No enhancement
 - Usually involves posterior annulus; may involve entire annulus when large
- Cardiac gated CTA
 - Assessment of motion abnormalities

Echocardiographic Findings

- Calcification appears as increased echogenicity
- CCMA: Round mass with increased peripheral echogenicity, decreased central echogenicity
- Severity of stenosis determined by orifice size
- Calculation of valve jet velocities
 - Higher aortic valve calcium scores on CT correlate with higher jet velocities

Imaging Recommendations

- Best imaging tool
 - **Echocardiography**: Procedure of choice to assess valve morphology and function

DIFFERENTIAL DIAGNOSIS

Pericardial Calcification

- Focal or curvilinear calcification; follows cardiac contour; most commonly atrioventricular (AV) grooves
- No predilection for cardiac apex (unlike myocardial calcification)
- Infection, trauma, iatrogenic

Ventricular Calcification

- Thin or thick curvilinear calcification following ventricular contour
- Myocardial infarction, metastatic calcification, thrombus, tumor, aneurysm, pseudoaneurysm

Coronary Artery Calcification

- Curvilinear or tram-track calcification
- Involvement of 1 wall may mimic calcified infarct

Great Vessel Calcification

- Rim-like aortic wall calcification: Atherosclerosis
- Pulmonary artery wall calcification: Chronic pulmonary hypertension

PATHOLOGY

General Features

- Etiology
 - Aortic valve leaflets: Degenerative, congenital bicuspid aortic valve
 - Rheumatic heart disease (RHD), syphilis, ankylosing spondylitis
 - Aortic annulus: Atherosclerosis
 - o Mitral valve leaflets: RHD
 - o Mitral annulus: Degenerative, end-stage renal disease
 - CCMA: Degenerative
 - Pulmonic valve leaflets: Congenital pulmonic valvular stenosis, chronic pulmonary arterial hypertension
 - o Tricuspid valve leaflets: RHD, septal defects, endocarditis
 - Tricuspid annulus: RHD, congenital pulmonic valvular stenosis
- Dystrophic calcification is usually degenerative
- Calcification begins at points of maximal cusp flexion (margins of attachment)
- Calcific masses may eventually prevent cusp opening

Gross Pathologic & Surgical Features

- Bicuspid aortic valve: 90% calcified at surgery
- MAC: 6% at autopsy
- CCMA: 2.7% at autopsy

Microscopic Features

• CCMA: Calcium, fatty acids, cholesterol

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Aortic stenosis
 - Classic triad
 - Angina pectoris
 - □ Syncope
 - □ Heart failure
 - Exertional dyspnea
 - "Pulsus parvus et tardus" on physical exam
 - Crescendo-decrescendo systolic ejection murmur with paradoxical S2 split
 - Mitral stenosis
 - Exertional dyspnea, cough, wheezing
 - Abrupt onset atrial fibrillation
 - Stress-induced pulmonary edema
 - Loud S1 followed by S2 and "opening snap"; lowpitched, rumbling diastolic murmur
 - CCMA
 - Usually asymptomatic
 - Mitral stenosis if mass becomes obstructive
 - Pulmonic stenosis
 - Exertional dyspnea and fatigue
 - Systolic ejection click louder on expiration; ejection murmur at left upper sternal border

• Tricuspid stenosis

- Fatigue
- Edema secondary to systemic venous congestion
- Widely split S1 with single S2; diastolic murmur along left sternal border

Demographics

- Age
 - Aortic valve leaflets
 - < 70 years of age: Bicuspid aortic valve
 - □ > 90% have calcification by 40 years of age
 - > 70 years of age: Degenerative disease
 - o Mitral valve leaflets: 20-30 years old
 - Mitral annulus: > 60 years old
- Sex
 - Mitral valve leaflets: M > F
 - o Mitral annulus: F > M
- Epidemiology
 - Aortic valve leaflets
 - Degenerative calcification: 2-7% prevalence in patients > 70 years
 - Bicuspid aortic valve: 2% of population
 - MAC: 6% of population
 - o CCMA: 0.06-0.07% overall; 0.6% on echocardiography

Natural History & Prognosis

- Aortic annulus
 - Extension into conducting system may lead to heart block
 - High association with systemic atherosclerosis
- MAC
 - Higher incidence of new coronary events
 - Right bundle branch block
 - High association with systemic atherosclerosis
 - Associated with aortic stenosis
- CCMA
 - o Usually benign
 - Rare valvular dysfunction

Treatment

- Surgical replacement of abnormal valves
- Aortic and mitral valves most common
- o Valvuloplasty
- Widening of stenotic valve using balloon catheter
- o Valvulotomy or commissurotomy
 - Incision of commissures
- o Valve replacement
 - Percutaneous or traditional open-heart techniques

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Valve and annular calcification often detected on radiography
- NECT with ECG gating optimal for quantifying calcification
- Echocardiography optimal for assessment of valve morphology and function

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1. Fletcher AJ et al: Imaging aortic valve calcification: significance, approach and implications. Clin Radiol. 76(1):15-26, 2021





(Left) Lateral chest radiograph of a patient who presented with chest pain shows subtle calcification \supseteq in the expected anatomic location of the aortic valve. (Right) Sagittal CECT of the same patient demonstrates dense calcifications \supseteq involving the aortic valve. Degenerative disease and bicuspid aortic valve morphology are the most common etiologies of aortic valve calcification. Aortic valve calcification on imaging is a strong marker for aortic valve stenosis.





(Left) Coronal CECT of the same patient shows dense $calcification \supseteq affecting the$ aortic valve. Note dilatation of the ascending thoracic aorta 🔁. Aortic stenosis should be suspected when findings such a left ventricular configuration &/or poststenotic dilation of the ascending aorta are present. (Right) Lateral chest radiograph obtained several months later shows interval surgical aortic valve replacement *⊡* and associated sequela of median sternotomy.





(Left) Lateral chest radiograph of an asymptomatic patient demonstrates calcification 🔁 in the region of the mitral annulus. Mitral annular calcification is associated with right bundle branch block and aortic stenosis. (Right) Sagittal CECT of the same patient shows extensive dense calcification \supseteq of the mitral annulus. Although mitral annular calcification may be seen in isolation, the presence of left atrial enlargement should raise suspicion for mitral stenosis.

Aortic Valve Disease

KEY FACTS

TERMINOLOGY

- Aortic regurgitation (AR)
- Aortic stenosis (AS)
- Aortic valve disease: AR and AS

IMAGING

- Best diagnostic clue
 - AR: Retrograde flow of blood into left ventricle on echocardiography and MR
 - AS: Systolic jet into proximal aorta on MR
- AS: Aortic valve calcification
 Quantification of calcification on NECT
- **ECG-gated CTA**: Thickening and calcification of aortic valve leaflets
 - AR: Incomplete coaptation of aortic valve leaflets
 - AS: Measurement of aortic valve orifice
- MR: Volumes, velocities, and gradients quantification

TOP DIFFERENTIAL DIAGNOSES

- Subvalvular aortic stenosis
- Supravalvular aortic stenosis

PATHOLOGY

- Acute AR: Endocarditis, dissection, trauma
- Chronic AR: Valve disease, aortic root dilation
- AS: Degenerative, bicuspid valve, rheumatic heart disease

CLINICAL ISSUES

- AR: Chest pain, dyspnea
 - Variable progression to left ventricular failure
 - Surgery for acute AR with hypotension and pulmonary edema
- AS: Angina, syncope, dyspnea
 - Degenerative > 70 years; bicuspid valve < 70 years
 - Surgery for severe, symptomatic AS; left ventricular dysfunction; critical stenosis

(Left) Graphic illustrates normal and abnormal appearances of the aortic valve. Aortic valve disease secondary to degeneration and congenital bicuspid aortic valve are characterized by thickening and calcification of the valve leaflets, resulting in incomplete valve opening or closure and aortic valve dysfunction. (Right) Coneddown lateral chest radiograph of a patient with aortic stenosis shows calcification ightarrowin the anatomic location of the aortic valve.





(Left) Cine MR through the aortic valve of a patient with aortic stenosis demonstrates marked narrowing of the aortic valve orifice \supseteq and thickening of the aortic valve leaflets. (Right) Coronal MR cine demonstrates hypointense retrograde flow of blood 🔁 into the left ventricle, consistent with aortic regurgitation. MR cine and echocardiography allow calculation of the regurgitant fraction and help determine the severity of aortic regurgitation.





Definitions

• Aortic valve disease: Aortic regurgitation (AR), aortic stenosis (AS)

IMAGING

General Features

- Best diagnostic clue
 - **AR**
 - Retrograde flow of blood into left ventricle on echocardiography and MR
 - o AS
 - Systolic jet into proximal aorta on MR

Radiographic Findings

- Radiography
 - AR
 - Acute: Normal heart size, pulmonary edema
 - Chronic
 - □ Left ventricular enlargement
 - □ Dilatation of aortic root ± ascending aorta
 - Pulmonary venous hypertension

o AS

- **Calcification** in expected position of aortic valve
 - Frontal radiograph: Projects over spine
 - Lateral radiograph: Between anterior and posterior cardiac borders, above line from carina to sternodiaphragmatic junction
- 3 patterns of calcification
 - Commissure calcification: Linear
 - Complete or partial ring calcification
 - Plaque-like calcification
- Left ventricular configuration
- Heart size increases with increased AS severity
- Poststenotic dilation of ascending aorta

CT Findings

- NECT
 - Quantification of aortic valve calcification
- CECT
 - **AR** – Left ventricular enlargement
 - Dilatation of aortic root ± ascending aorta
 - Effacement of sinotubular junction
 - Annuloaortic ectasia
 - AS
 - Aortic valve calcification
 - Central location allows distinction from peripheral aortic annulus calcification
 - Bicuspid valve: Early thickening and calcification of valve leaflets
 - Degenerative valve: Greater calcification than bicuspid valve
 - Left ventricular hypertrophy
 - Poststenotic dilatation of ascending aorta
- Cardiac gated CTA
 - o AR
 - Incomplete coaptation of aortic valve leaflets
 Accurate for moderate to severe AR

- Mild AR frequently overlooked
- Thickening and calcification of valve leafletsLeft ventricular enlargement
- AS
 - Measurement of aortic valve orifice
 - Thickening and calcification of valve leaflets

MR Findings

- MR cine
- ∘ AR
 - Retrograde blood flow into left ventricle in diastole on cine GRE
 - Left ventricular enlargement in chronic AR
 - Holodiastolic flow reversal highly sensitive and specific for severe AR
 - Volumes and ejection fraction quantification
 - Regurgitant fraction calculation
 - AS
 - Systolic jet into proximal aorta on bright blood sequences
 - Morphology: Bicuspid aortic valve
 - Volumes and ejection fraction quantification
 - Calculation of peak systolic velocities and gradients

Echocardiographic Findings

- Echocardiogram
 - AR
 - Incomplete coaptation of aortic valve leaflets
 - Left ventricular enlargement in chronic AR
 - Calculation of regurgitant fraction
 - o AS
 - Identification of stenotic valve and determination of etiology
 - Quantification of diastolic ± systolic dysfunction
 - Quantification of left ventricular hypertrophy
 - Assessment of coexisting disorders

Angiographic Findings

- Conventional
 - o **AR**
 - Regurgitant jet in left ventricle
 - o AS
 - Aortic valve calcification
 - Systolic jet into aorta
 - Measurement of aortic valve orifice size
 - Quantification of gradient across stenotic valve

Imaging Recommendations

- Best imaging tool
- Echocardiography
- Protocol advice
 - ECG-gated CTA for evaluation of leaflets, orifice, and function

DIFFERENTIAL DIAGNOSIS

Subvalvular Aortic Stenosis

- Idiopathic hypertrophic subaortic stenosis (IHSS)
- Fixed, hemodynamically significant obstruction of left ventricular outflow tract (LVOT)
- Left ventricular hypertrophy and cardiac dysfunction

Supravalvular Aortic Stenosis

- Hourglass narrowing of proximal ascending aorta above aortic valve
- Associated with Marfan and Williams syndromes

PATHOLOGY

General Features

- Etiology
- o AR
 - Acute: Endocarditis, dissection, trauma
 - Chronic
 - Valve disease: Degenerative, bicuspid valve, rheumatic heart disease
 - D Aortic root dilatation: Marfan, syphilis
- o AS
 - Degenerative, bicuspid valve, rheumatic heart disease
- Associated abnormalities
 - o AS
 - Bicuspid aortic valve, aortic coarctation

Staging, Grading, & Classification

- Classification by echocardiography
- AR
 - Mild: Central jet width < 25% of LVOT; vena contracta < 0.3 cm; regurgitant volume < 30 mL/beat; regurgitant fraction < 30%; effective regurgitant orifice area < 0.10 cm²
 - o Moderate: Measurements between mild and severe AR
 - Severe: Central jet width ≥ 65% of LVOT; vena contracta
 > 0.6 cm; regurgitant volume ≥ 60 mL/beat; regurgitant fraction ≥ 50%; effective regurgitant orifice area ≥ 0.30 cm²
- AS
 - o Aortic sclerosis: Aortic jet velocity ≤ 2.5 m/s
 - Mild: Aortic jet velocity 2.6-2.9 m/s; mean gradient < 20 mm Hg; AVA > 1.5 cm²; AVA/BSA > 0.85 cm²/m²
 - Moderate: Aortic jet velocity 3.0-4.0 m/s; mean gradient 20-40 mm Hg; AVA 1.0-1.5 cm²; AVA/BSA 0.60-0.85 cm²/m²
 - **Severe**: Aortic jet velocity > 4 m/s; mean gradient > 40 mm Hg; AVA < 1 cm²; AVA/BSA < 0.60 cm²/m²

Gross Pathologic & Surgical Features

- AR
- Valve fibrosis and thickening in rheumatic heart disease
- AS
 - Thickening and calcification of leaflets
 - Occurs earlier in bicuspid valves
 - Calcification begins at base of cusps
 - o Valve fibrosis and thickening in rheumatic heart disease

Microscopic Features

- AS
 - Accumulation of lipid and inflammatory cells

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o AR
 - Chest pain, dyspnea

- Usually asymptomatic until valve area is reduced to 1 cm²
- o AS
 - Angina, syncope, dyspnea

Demographics

- Age
- o AR
 - Variable depending on etiology
- o AS
 - < 70 years of age: Bicuspid valve</p>
- >70 years of age: Degenerative disease
- Sex
- o AS
 - M:F = 3:1
- o AS
 - Bicuspid valve: M:F = 4:1
- Epidemiology
 - AR: Prevalence of 4.9%
 - AS: Prevalence of 2-5% > 65 years of age

Natural History & Prognosis

- AR
 - Variable progression to left ventricular failure
 - Poor prognosis if valve not replaced prior to development of failure
- AS
 - Degenerative: Long asymptomatic period prior to development of symptoms
- Treatment
- AR
 - o Surgery
 - Acute AR with hypotension and pulmonary edema
 - Medical management
 - Mild to moderate AR
 - Poor surgical candidates
 - Vasodilators ± inotropic agents
- AS
 - Surgical valve replacement
 - Severe, symptomatic AS
 - Left ventricular dysfunction
 - Critical stenosis by echocardiography
 - Coronary bypass or other valve surgery
 - o Medical management
 - Endocarditis prophylaxis ± inotropic agents

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Echocardiography: Diagnosis and severity classification
- ECG-gated CTA: Evaluation of leaflets and orifice size
- Cine MR: Quantification of volumes, gradients, and function

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Aortic Valve Disease





(Left) Cardiac CT of a patient with aortic stenosis shows extensive calcification 🔁 involving the aortic valve leaflets. Left ventricular hypertrophy and poststenotic dilation of ascending aorta may also be present on imaging. (Right) Coronal MR cine shows thickening of the aortic valve leaflets 🛃 and a hyperintense systolic jet 🄁 into the ascending aorta, consistent with aortic stenosis. MR cine can quantify the gradient across the stenotic aortic valve and help determine the severity of disease.





(Left) Cardiac CTA of a patient with aortic stenosis demonstrates thickening and calcification of the aortic valve leaflets with resultant gross narrowing of the aortic valve orifice. (Right) Cardiac CTA of the same patient shows measurement of the aortic valve orifice. The severity of aortic stenosis is determined by several parameters, one of which is the aortic valve orifice area.





(Left) Coronal MR cine demonstrates hypointense retrograde flow of blood ≥ into the left ventricle, consistent with aortic regurgitation. MR cine and echocardiography allow calculation of the regurgitant fraction and help determine the severity of aortic regurgitation. (Right) DSA shows retrograde flow of contrast ≥ into the left ventricle in this patient with aortic regurgitation.

Mitral Valve Disease

KEY FACTS

TERMINOLOGY

- Mitral regurgitation (MR): Retrograde blood flow across mitral valve (MV) from left ventricle to left atrium
 Most common valve dysfunction in USA
 - o Mitral regurgitation synonymous with MR
- MV prolapse: Protrusion of MV leaflet(s) > 2 mm into left atrium
- Flail leaflet: Rupture of papillary muscle or chordae tendineae with systolic eversion of leaflet tip into atrium
- Mitral stenosis (MS): Restricted left ventricular inflow across MV
- Mitral annular calcification (MAC): Excessive calcification of mitral annulus

IMAGING

- Echocardiography: Primary diagnostic tool
- MR: Left atrial enlargement
- Chronic MR: Left ventricle enlargement

- Acute MR: Localized right upper lobe asymmetric pulmonary edema
- Cardiac MR: MR quantification (imaging method of choice)

TOP DIFFERENTIAL DIAGNOSES

- Mitral valve masses
- Dilated cardiomyopathy
- Ventricular septal defect
- Left atrial myxoma

CLINICAL ISSUES

• Surgical complications include paravalvular abscess, paravalvular leak, dehiscence, valve malfunction

DIAGNOSTIC CHECKLIST

- Chronic MR causes left atrial and ventricular enlargement
- MS less common than regurgitation and almost always secondary to rheumatic heart disease

(Left) Composite image with PA (left) and lateral (right) chest radiographs of a patient with mitral stenosis secondary to rheumatic heart disease shows left atrial enlargement manifesting with the double density sign 🖂 and mitral valve calcifications 🔁. Rheumatic heart disease is the most common cause of mitral stenosis in adults. (Right) Graphic shows the morphologic features of mitral stenosis. Thickening of the mitral valve results in abnormal valve leaflet motion and poor valve function.





(Left) Four-chamber MR cine of a 67-year-old patient with thickened mitral valve leaflets shows mitral regurgitation (seen as dark dephasing jet 🔁 due to incomplete valve closure) and severe left atrial dilatation 🖂 (Right) Coronal oblique CECT of a 78-year-old patient obtained through the mitral valve plane shows extensive mitral annulus calcification. This is characterized by calcification of the mitral annulus &/or leaflets, and affects more frequently the lateral and posterior portions of the mitral annulus.





Abbreviations

- Mitral valve (MV)
- Mitral regurgitation (MR)
- Mitral stenosis (MS)

Synonyms

• Mitral regurgitation = MR

Definitions

- **MR**: Systolic blood backflow from left ventricle to left atrium across MV
 - Acute versus chronic
 - Most common valve dysfunction in USA
- **MV prolapse**: Protrusion of MV leaflet(s) > 2 mm into left atrium
 - Important cause of MR
- Flail leaflet: Rupture of papillary muscle or chordae tendineae with systolic eversion of leaflet tip into atrium
 Strongly associated with acute and severe MR
- **MS**: Restricted opening of MV leaflets causing impaired left ventricular inflow across MV
- Mitral annular calcification (MAC): Excessive calcification of mitral annulus
 - Central degeneration may lead to liquefaction, termed caseous MAC

IMAGING

General Features

- Best diagnostic clue
 - Left atrial enlargement
 - MV calcification
- Normal MV morphology
 - o Bicuspid valve: Anterior and posterior leaflets
 - Leaflets attached to D-shaped annulus; annulus in fibrous continuity with aortic valve
 - Papillary muscles and chordae tendineae have no septal attachment

Radiographic Findings

- Radiography
 - Findings of left atrial enlargement
 - Frontal chest radiograph
 - Double density over right heart: Enlarged left atrium superimposed on right heart
 - Elevation of left main stem bronchus
 - Splaying of carina
 - Convexity or straightening of left atrial appendage along left heart border
 - Lateral chest radiograph
 - Posterior convexity of left atrial borderPosterior displacement of left mainstem bronchus
 - Localized right upper lobe asymmetric pulmonary edema in acute MR
 - Left ventricle enlargement in chronic MR
 - Cephalization of flow due to pulmonary venous hypertension
 - MS: Enlarged central pulmonary arteries from pulmonary hypertension

CT Findings

- CECT
 - Left atrial enlargement
 - Chronic atrial fibrillation may cause intraatrial thrombus, particularly in left atrial appendage
 - Thrombus may calcify
 - Pulmonary edema: Interlobular septal thickening, ground-glass opacities
 - o Chronic MR: Left ventricular enlargement
- Cardiac gated CTA
 - o Valve leaflet thickening and calcification
 - Fish-mouth deformity from commissural fusion and leaflet thickening
 - Identification of MAC or caseous degenerative mitral annulus
 - MV prolapse or flail leaflet in systole
 - MV orifice area measured during early diastole
 - Normal: 4-6 cm²
 - Mild MS: 1.6-3.9 cm²
 - Moderate MS: 1.0-1.5 cm²
 - Severe MS < 1.0 cm²
 - Regurgitant or stenotic contrast jet
 - Best tool to evaluate postsurgical complications

MR Findings

- T1WI
 - o Left atrial enlargement
 - Chronic MR: Left ventricular enlargement
 - MS: Left atrial enlargement, pulmonary artery enlargement, right ventricular enlargement
- T2* GRE
 - MR: Regurgitant dephasing jet projects from MV into left atrium during systole
 - MS: Stenotic dephasing jet projects from mitral valve into left ventricle during diastole
- SSFP white blood cine
 - Multiplanar imaging shows abnormal valve motion (MV prolapse, flail leaflet)
 - Bowing of thick anterior leaflet with hockey stick appearance in rheumatic MS
 - o Assessment of MS valve opening area
- Velocity-encoded phase contrast imaging used to quantify regurgitant fraction
 - o Mild < 30%; moderate 30-50%; severe >50%

Echocardiographic Findings

- Echocardiogram
 - o Assessment of left atrial and ventricular size
 - MR: Color Doppler shows jet extending from MV into left atrium during systole
 - MS: Color Doppler shows jet extending from MV into left ventricle during diastole
 - Mean valve orifice area; gradient and estimated pulmonary pressures can be calculated
 - MV prolapse well demonstrated

Angiographic Findings

- Conventional
 - o MR can be quantified on 0 (none) to 4 (severe) scale
 - Calculation of regurgitant volume

Imaging Recommendations

- Best imaging tool
 - Echocardiography is primary diagnostic tool for screening, diagnosis, and surveillance
 - o Cardiac MR
 - MR quantification (imaging method of choice)
 - Valvular motion analysis
 - Blood flow velocity assessment
 - CT: Visualization of mitral annular &/or leaflet calcifications
- Protocol advice
 - 2-chamber long-axis plane perpendicular to MV; best imaging plane

DIFFERENTIAL DIAGNOSIS

Mitral Valve Masses

- Vegetations and thrombus may mimic valve thickening
- Neoplasms rare: Metastatic disease, papillary fibroelastoma, myxoma, lymphoma, sarcoma

Dilated Cardiomyopathy

- Generalized cardiac enlargement
- Signs of heart failure due to left ventricular dysfunction

Ventricular Septal Defect

- Left atrial enlargement; may mimic MR
- Right ventricular enlargement; enlarged pulmonary trunk due to shunt vascularity

Left Atrial Myxoma

- MV obstruction may mimic MS
- May calcify

PATHOLOGY

General Features

- Etiology
 - o MR
 - Usually caused by myxomatous degeneration
 - Infective endocarditis, collagen vascular disease, ischemic cardiomyopathy
 - **MS**
 - Up to 95% due to rheumatic heart disease in adults (most prevalent cause in low- and middle-income countries)
 - Collagen vascular disease, endocarditis
 - Substantial MAC
 - MV prolapse
 - Due to elongation/rupture of chordae tendineae
 - Connective tissue disorders, Marfan syndrome
- Associated abnormalities
 - Rheumatic fever: Aortic and tricuspid valve involvement may also occur

Gross Pathologic & Surgical Features

• MS: Thickened leaflets with commissural fusion

Microscopic Features

 MR: Myxomatous degeneration may be evident in MV prolapse

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute MR: Sudden onset of pulmonary edema
 - Chronic MR: Shortness of breath, orthopnea, paroxysmal nocturnal dyspnea
 - MR: Holosystolic murmur
 - MS: Diastolic murmur, accentuated 1st heart sound, opening snap
- Other signs/symptoms
 - Palpitations due to atrial fibrillation
 - Atypical chest pain due to MV prolapse

Demographics

- Age
 - Patients with MR from rheumatic fever; younger
 - MS: Age of symptom onset is 20-50 years
- Sex
 - o MR and MS more common in women
 - $\circ~$ MV prolapse affects ~ 6% of women
- Epidemiology
 - MR: Rheumatic fever most common in developing world; MV prolapse accounts for majority of cases in developed countries
 - MS occurs early in developing world among patients with rheumatic fever

Natural History & Prognosis

- Acute MR: Poorly tolerated
- Chronic MR: Volume overload may be asymptomatic for years
- 5-year survival of patients with chronic MR: 80%
- Atrial fibrillation and heart failure may occur

Treatment

- Options, risks, complications
 - Acute MR: Treatment of pulmonary edema
 - Chronic MR: Medical treatment with diuretics and afterload-reducing agents
 - MV surgical repair or replacement indicated in severe MR with symptoms, decreased ejection fraction, or heart failure
 - Percutaneous balloon valvuloplasty in MS with heart failure or pulmonary hypertension
 - Severe calcification, fibrosis, or valve thickening are contraindications
 - Otherwise, surgical MV replacement
 - Antibiotic prophylaxis in MV prolapse
 - Surgical complications include paravalvular abscess, paravalvular leak, dehiscence, valve malfunction

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Chronic MR causes left atrial and ventricular enlargement
- MS less common than regurgitation and almost always secondary to rheumatic heart disease

SELECTED REFERENCES

1. Garg P et al: Assessment of mitral valve regurgitation by cardiovascular magnetic resonance imaging. Nat Rev Cardiol. 17(5):298-312, 2020

Mitral Valve Disease





(Left) PA chest radiograph of a patient with papillary muscle rupture and acute mitral regurgitation shows cardiomegaly and right upper lobe airspace disease that represents localized pulmonary edema. Right upper lobe edema results from the preferential direction of the regurgitant blood flow. (Right) Axial CECT of a patient with atrial fibrillation and dyspnea shows thickened mitral valve leaflets *Æ*, severe left atrial dilatation, and a large left a trial throm bus thatextended from the left atrial appendage.





(Left) Four-chamber SSFP MR of a 75-year-old patient with mitral regurgitation shows severe left atrial dilatation ≥. (Right) Three-chamber SSFP MR of the same patient shows a systolic regurgitation jet \square into the left atrium secondary to poor closure of the mitral valve leaflets during systole. Color Doppler echocardiography and cine MR are both sensitive for detecting systolic or diastolic jets, which indicate valvulopathy (i.e., regurgitation or stenosis).





(Left) Composite image with diastolic (top) and systolic (bottom) cardiac gated CTA of a patient with mild mitral regurgitation shows mild anterior mitral valve leaflet thickening \supseteq and systolic valve leaflet prolapse \blacksquare into the left atrium. (Right) Axial CECT of the same patient shows peripheral calcification with central low attenuation, characteristic of caseous mitral annulus calcification, which most commonly affects the posterior annulus and is reported to cause mitral stenosis when large.

TERMINOLOGY

• Left atrial wall calcification

IMAGING

- Radiography
 - Linear/curvilinear calcification along left atrial contour; may encase left atrium
- CT
 - Identification/characterization of left atrial calcification
 - Thin, punctate or linear calcifications involving endocardium and myocardium
 - MacCallum patch: calcifications of posterosuperior left atrial wall due to mitral regurgitant flow
- **Cardiac-gated CECT**: Chamber assessment, exclusion of thrombus
- Cardiac MR
 - Cine SSFP: Depiction of mitral valve leaflet mobility
 - Phase-contrast velocity-encoded sequences: Quantification of mitral valve regurgitation

TOP DIFFERENTIAL DIAGNOSES

- Mitral annular calcification
- Left atrial thrombus calcification
- Myxoma
- Pericardial calcifications

CLINICAL ISSUES

- Extent of calcifications considered marker of untreated disease
- If extensive, may involve conduction system and produce cardiac arrhythmias or A-V block
- Treatment: Total endoatrioectomy with mitral valve replacement

DIAGNOSTIC CHECKLIST

• Presence of left atrial calcifications is highly suspicious for rheumatic heart disease, specially if associated with mitral annular calcifications and mitral stenosis

(Left) Coned-down lateral chest radiograph of a patient with rheumatic heart disease and longstanding mitral stenosis shows dense crescentic left atrial calcifications 🛃. (Right) Axial NECT of a 68-year-old woman with rheumatic heart disease and mitral stenosis shows fine linear left atrial wall calcifications
estimates and calcifiedmitral valve leaflets 🛃. When extensive, atrial calcifications may involve the conduction system and produce cardiac arrhythmias or A-V block.





(Left) Coronal NECT of a patient with rheumatic heart disease shows left atrial enlargement and characteristic curvilinear calcifications → along the posterosuperior left atrial wall that represent the so-called MacCallum patch, which results from mitral regurgitant flow. (Right) Coronal oblique graphic shows the morphologic features of left atrial calcification → affecting the left atrial wall.





- Abbreviations
- Rheumatic heart disease (RHD)

Synonyms

- Porcelain atrium
- Coconut atrium

Definitions

• Calcification of left atrial walls

IMAGING

General Features

- Best diagnostic clue
- Linear/curvilinear calcification along left atrial contour
 Location
 - Left atrium wall and appendage
- o Mitral valve
- Morphology
 - o Variable, usually curvilinear
 - o Follows left atrium contour

Radiographic Findings

- Linear/curvilinear calcifications along left atrium; may encase left atrial chamber
- MacCallum patch: Posterior mural left atrial calcifications due to mitral regurgitant flow
- Calcified left atrial thrombus: Thick, laminar, may involve left atrial appendage

CT Findings

- NECT
 - Thin, punctate, or linear calcifications involving endocardium and myocardium
 - o Usually located on posterosuperior left atrial wall
 - o Greater extent of calcification compared to radiography
- Cardiac gated CTA
 - Allows assessment of cardiac chambers and exclusion of thrombus

MR Findings

- SSFP cine
 - Depiction of mitral valvular leaflet mobility
- Phase-contrast velocity-encoded sequences
 Allow quantification of mitral valvular regurgitation

Imaging Recommendations

- Best imaging tool
 NECT for optimal characterization of left atrial calcification (location and extent)
- Protocol advice
 ECG-gating for motion correction

DIFFERENTIAL DIAGNOSIS

Mitral Calcification

- Mitral annular calcifications: May be bulky, association with mitral stenosis; often seen in end-stage renal disease
- Leaflet calcifications: May be punctate; association with RHD in adults

Left Atrial Thrombus Calcification

• Thick, laminar; usually in left atrial appendage

Myxoma

- May exhibit intrinsic scattered calcifications
- Usually abuts fossa ovalis, may be attached to mitral valve

Pericardial Calcification

• Located on pericardial surface, usually along AV grooves

PATHOLOGY

General Features

- Etiology
 - RHD
 - Mitral stenosisEnd-stage renal failure
 - Usually associated with metastatic calcifications and mitral annular calcification

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dyspnea
 - Atrial fibrillation
 - o Mitral stenosis

Demographics

- Age
- 6th decade
- Sex
 - o 2/3 cases in women

Natural History & Prognosis

- Extent of calcification considered marker of untreated disease
- Up to 50% of patients present with atrial fibrillation
- When extensive, may involve conduction system and produce cardiac arrhythmia or A-V block
- Severe left atrial calcification has hazard ratio of 4.4 (95% CI: 1.7-11.6) for major adverse cardiac events (MACE); adjusted for age, sex, renal failure, atrial fibrillation

Treatment

• Total endoatrioectomy with mitral valve replacement

DIAGNOSTIC CHECKLIST

Consider

• Left atrial calcifications are highly suspicious for RHD, especially if associated with mitral annular calcification and mitral stenosis

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TERMINOLOGY

- Dystrophic calcification
- Metastatic calcification

IMAGING

- Best diagnostic clue: Calcification along ventricular contour
 Left > right ventricle
 - Aneurysm > pseudoaneurysm
- Morphology
 - Dystrophic: Curvilinear, thin or thick
 - Metastatic: Diffuse, globular, amorphous
- Radiography: Linear or curvilinear cardiac calcification
- **CT**: Localization and characterization of calcification
 - Mural curvilinear left ventricular calcification
 - Myocardial infarction: Hypoenhancing myocardium, nonenhancing mural thrombus
 - Aneurysm: Wide neck; apical or anterolateral wall
 - Pseudoaneurysm: Narrow neck; posterior, lateral, or diaphragmatic wall

TOP DIFFERENTIAL DIAGNOSES

- Pericardial calcification
- Valve and annular calcification
- Coronary artery calcification
- Great vessel calcification

PATHOLOGY

- Myocardial calcification: Myocardial infarction, end-stage renal disease
- Cardiac chamber calcification: Tumor, thrombus
- Aneurysm and pseudoaneurysm

CLINICAL ISSUES

- Myocardial infarction most common > 45 years
- Coronary artery disease: 40-70 years
 M > F; > 70 years, M = F
- Calcified infarct: Increased risk of sudden death
- Aneurysm resection: Heart failure, arrhythmia
- Pseudoaneurysm resection: Risk of rupture

(Left) Axial CECT of a patient with a history of myocardial infarction shows dystrophic subendocardial calcification \square along the ventricular apex and associated low-density thrombus 🔁. (Right) Axial CECT of a patient with prior myocardial infarction demonstrates calcification earrowalong the left ventricular apex and the distal interventricular septum. Ventricular calcifications typically develop 6 years after myocardial infarction and impart an increased risk of sudden death.





(Left) Axial CECT of a patient with end-stage renal disease shows amorphous metastatic calcification \supseteq of the left ventricular myocardium. (Right) Coronal NECT of a patient hospitalized for management of severe sepsis demonstrates extensive calcification \supseteq in the left ventricular myocardium. The calcification seen in this case is dystrophic calcification and represents the sequela of local tissue damage &/or cellular necrosis.





Synonyms

- Dystrophic calcification
- Metastatic calcification

Definitions

- Dystrophic calcification
 - Sequela of local tissue damage &/or cellular necrosis leading to calcification
 - o Normal serum calcium and phosphorus levels
 - Most prevalent myocardial calcification: Previous myocardial infarction (MI) leading to myocyte necrosis

Metastatic calcification

- Sequela of systemic process (e.g., abnormalities of calcium homeostasis)
- o Elevated calcium or parathyroid hormone levels
- May occur in normal tissue

IMAGING

General Features

- Best diagnostic clue
 - Calcification following ventricular contour
- Location
 - Left > right ventricle
 - Associated with previous MI: Interventricular septum and apex
 - Aneurysm > pseudoaneurysm
- Morphology
 - Dystrophic: Curvilinear, thin or thick
 - o Metastatic: Diffuse, globular, amorphous

Radiographic Findings

- Linear or curvilinear calcification
- Frontal radiography: Left of midline
- Lateral radiography: Follows left ventricular contour

CT Findings

- NECT
 - Mural curvilinear calcification in left ventricular myocardium
- CECT
 - Mural curvilinear left ventricular calcification
 - MI: Hypoenhancing myocardium, nonenhancing endoluminal mural thrombus
 - Aneurysm: Wide neck
 - Apical or anterolateral wall
 - Pseudoaneurysm: Narrow neck
 - Posterior, lateral, or diaphragmatic wall

Imaging Recommendations

- Best imaging tool
 - o CT for localization and characterization of calcification

DIFFERENTIAL DIAGNOSIS

Pericardial Calcification

- Linear or curvilinear calcification along pericardium
 Typically on right and along atrioventricular groove, spares apex (unlike myocardial ca++)
- Causes: Infection, trauma, iatrogenic

Valve and Annular Calcification

- Aortic valve calcification
 - Usually associated with valvular sclerosis or hemodynamically significant stenosis
- Mitral valve calcification
 - Leaflet: May be thin, delicate
 - Characteristic of rheumatic mitral stenosis
 - Annular: Dense, ring-like clumps, on posterior atrioventricular ring
 - F > M; common in end-stage renal disease (ESRD)
 - Normal valve function
 - □ If dysfunctional, regurgitation > > stenosis

Coronary Artery Calcification

• Curvilinear or tram-track calcification

Great Vessel Calcification

- Rim-like aortic wall calcification in atherosclerosis
- Pulmonary artery calcification in chronic pulmonary hypertension

Tumor Calcification

• Left atrial myxoma calcifies in 10% of cases

PATHOLOGY

General Features

- Etiology
 - Myocardial calcification
 - Calcification in 8% of cases 6 years after MI; M > F
 - Sepsis
 - Metastatic calcification in ESRD
 - Calcification within cardiac chambers
 - Thrombus calcification: 20-60% of patients post MI
 - Tumor calcification
 - More common in left atrium
 - Myxoma most common primary cardiac tumor
 - Aneurysm and pseudoaneurysm: Most common post MI

CLINICAL ISSUES

Demographics

- Age
 - MI most common after 45 years
- Sex
 - o Sequela of MI due to coronary artery disease (CAD)
 - 40-70 years, M > F
 > 70 years, M = F

- Natural History & PrognosisCalcified infarction: Increased risk of sudden death
- Associated with ventricular tachycardia
- Associated with ventricular tachycardia
 Pseudoaneurysm: Increased risk of rupture

Treatment

- Medical ± surgical therapy for CAD
- Aneurysm resection: Heart failure, arrhythmia
- Pseudoaneurysm resection

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TERMINOLOGY

- Coronary artery calcification (CAC)
- Coronary artery disease (CAD)

IMAGING

- Cardiac-gated MDCT
 - Most sensitive detection method
 - High temporal and spatial resolution
 - Recommended: > 64-channel multidetector CT

• CAC quantification

• Agatston, volume, and mass routinely included

• Screening low-dose CT

• Visual identification and qualitative assessment correlates with Agatston score

• Impact of CAC measurements

- CAC correlates with extent of CAD
- CAC < 0: Powerful negative risk factor
- CAC: Strongly and independently associated with incident CVD events

TOP DIFFERENTIAL DIAGNOSES

- Coronary artery stent
- Mitral annular calcification
- Pericardial calcification
- Aortic root calcification

CLINICAL ISSUES

- CAC provides improved clinical risk prediction in asymptomatic individuals
- Adults at intermediate risk: CAC measurement allows risk reclassification
- CAC correlates with extent of CAD
- CAC < 0 is powerful negative risk factor
- High CAC scores associated with major adverse cardiac events and higher likelihood of stress-induced ischemia

DIAGNOSTIC CHECKLIST

• Cardiac-gated unenhanced MDCT improves clinical risk prediction in intermediate-risk asymptomatic individuals

(Left) Graphic demonstrates the characteristic locations and morphologic features of coronary artery calcification in the left main and proximal left anterior descending coronary arteries. (Right) Axial CECT shows moderate coronary artery calcification in the distal left main ➡, left anterior descending 🛃, and ramus intermedius 乏 coronary arteries. Coronary artery calcification is more common in the left coronary arteries than in the right and is most pronounced in the proximal aspects of the vessels.





(Left) Axial cardiac gated NECT shows mild coronary artery calcification \supseteq along the proximal left anterior descending coronary artery. CT is more sensitive than radiography for detection of coronary artery calcification. (Right) Axial CTA shows heavy coronary artery calcification in the distal left main 🔁, left anterior descending *Æ*, ramus intermedius \mathbf{E} , and left circumflex \blacksquare coronary arteries. Although coronary artery CTA underestimates calcium scores, it is useful for evaluating stenosis and occlusion.





Abbreviations

- Coronary artery calcification (CAC)
- Coronary artery disease (CAD)
- Coronary Artery Disease reporting and Data System (CAD-RADS)

Definitions

• Calcium deposits in coronary arteries

IMAGING

General Features

- Best diagnostic clue
 Linear CAC
- Location
 - Coronary arteries and branches
 - Left > right
 - Proximal > distal
- Morphology
- o Spotty, parallel, tubular

Radiographic Findings

• Only evident in severe cases

CT Findings

- CAC Morphology
 - o Spotty calcifications associated with unstable plaque
 - Extensive calcification associated with stable plaque
- Cardiac-gated MDCT
 - Most sensitive detection method
 - o Recommended: > 64-channel multidetector CT (MDCT)
 - High temporal and spatial resolution

• Electron Beam CT (EBCT)

• Original publications and technique described on EBCT

CAC quantification

- Agatston score: Most widely used and studied
 - Measures calcified lesions
 - □ Gated imaging; 3-mm thick slices
 - □ Lesions with area > 3 contiguous pixels > 130 HU
 - For each lesion cofactor derived from its peak attenuation
 - □ Agatston score: Plaque area x cofactor
 - Agatston score/calcium score category/cardiovascular risk
 - □ 0: Absent/very low
 - □ 1-10: Minimal/low
 - □ 11-100: Mild/moderate
 - □ 101-400: Moderate/moderately high
 - $\Box \geq 400$: Extensive/high
- o Volume
 - Identifies all voxels > 130 HU, multiplies serial number of calcium areas by total calcium areas
 - Underestimates high CAC

o Mass

- Not based on HU threshold, uses fitting equations to calculate mineral mass
- Requires calibration with phantom

Cardiac gated CTA

• Identification and assessment of stenosis

- o Allows assessment of non-calcified plaques
- o Vulnerable (high-risk) plaque findings
 - Combination of two or more high-risk features necessary to designate plaque as high-risk for CAD-RADS (modifier "V")
 - Positive remodeling
 - □ Ratio of outer vessel diameter at plaque divided by average outer diameter of proximal and distal vessel > 1.1 {Av/[(Ap + Ad)/2] > 1.1}
 - Low attenuation plaque
 - Noncalcified plaque with internal attenuation < 30 HU
 - Napkin-ring sign
 - Central low attenuation plaque with peripheral rim of higher CT attenuation
 - Spotty calcium
 - □ Small calcified plaque within plaque (density ≥ 130 HU separately visualized from lumen, diameter < 3 mm in any direction)
- Dual-source imaging: Higher temporal resolution
- Underestimates calcium scores (when dedicated noncontrast CAC estimation is omitted)

• Screening low-dose CT (LDCT)

- Patients that qualify for LDCT for lung cancer screening share major risk factors for CAD
- Visual identification and qualitative assessment has been correlated with AU

Qualitative CAC assessment

- Described for use on nongated low-dose chest CT
- Simple visual assessment of entire coronary circulation for CAC
- Categories
 - □ None
 - 🗆 Mild
 - □ Moderate
 - Heavy
- Can separate patients into risk categories: Based on coronary heart disease death or all-cause mortality with good interreader agreement
- CAC identification should be included on reports, especially in cases with moderate/heavy CAC

• CAC progression

- Percentage of change: [(CAC follow-up CAC baseline) / CAC baseline] x 100
- Significant progression (Berry method)
 - For CAC baseline > 0 and ≤ 100: (CAC follow-up CAC baseline) > 10 unit increase/year
 - For CAC baseline > 100: [(CAC follow-up CAC baseline) / CAC baseline] > 10% increase/year

Imaging Recommendations

- Best imaging tool
 - Cardiac-gated non-enhanced MDCT for CAC quantification
 - o Cardiac-gated CTA for stenosis evaluation

DIFFERENTIAL DIAGNOSIS

Coronary Artery Stent

• Similar appearance to CAC on NECT

Mitral Annular Calcification

- May be misinterpreted as CAC
- May be bulky; may be associated with mitral stenosis

Pericardial Calcification

• Located on pericardial surface, usually over AV grooves

Aortic Root Calcification

• May be misinterpreted as ostial calcifications

PATHOLOGY

General Features

- Etiology
 - Risk factors
 - Diabetes
 - Hypercholesterolemia
 - Smoking
 - Obesity
 - Hypertension
 - Family history
 - Premature CAC development
 - Familial hypercholesterolemia
 - Mediastinal radiotherapy

Gross Pathologic & Surgical Features

- Deposition of lipids, platelets, fibrin, cellular debris, and calcium
- Gross findings: Fatty streaks, atheromatous plaque

Microscopic Features

- Calcification occurs on intima (compared to peripheral arteries where medial calcification is predominant)
- Mediastinal radiation therapy may produce coronary sclerosing intimal fibrosis, which calcifies

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - May be asymptomatic
 - Angina most common symptom
- Other signs/symptoms
 - Shortness of breath
 - Dyspnea on exertion
 - o Arhythmia

Demographics

- Age
 - o M > 45 years, F > 55 years
- Ethnicity
 - MESA study showed CAC differences (adjusted to all relevant variables): Whites > Asians > Hispanics > African Americans
- Sex
 - o Disease delayed in women by 10-15 years compared to men
 - CAC greater in men compared to women up to 6th decade; similar by 7th decade
- Epidemiology
 - Atherosclerotic heart disease is **leading cause of death** in developed world

Natural History & Prognosis

- CAC correlates with extent of CAD
- Impact of CAC measurements
 - Improved clinical risk prediction in asymptomatic individuals
 - Especially in intermediate Framingham Risk Scores ranging from 5% to 20%
 - CAC < 0 is powerful negative risk factor
 - Minimal CAC (1-10): Hazard ratio (HR) of 1.99 for allcause mortality
 - High CAC scores associated with major adverse cardiac events (MACE) similar to populations on secondary prevention and higher likelihood of stress-induced ischemia
 - CAC is strongly and independently associated with incident cardiovascular disease (CVD) events independent of age, sex, and baseline risk factor burden
 - In adults at intermediate risk, CAC measurement allows risk reclassification
 - CAC ≥ 100 or CAC ≥ 75th percentile have MACE rates, which make initiation of statin therapy reasonable
 - CAC scores of 0 have 10-year event rates in very low ranges, and statin therapy may be of limited value
- CAC higher in diabetic patients
 - Correlates with total plaque burden
 - Independent risk factor for adverse outcomes
 - May not represent accurately severity of local stenosis

Treatment

- Lifestyle modifications
- Medical therapy
 - CAC may progress after statin treatment
 - Associated with high-intensity statin therapy (HIST)
 - Mechanism: Increased calcification of necrotic core leads to plaque stabilization and reduced risk of coronary events
- Procedural therapy
 - Percutaneous intervention
 - Coronary artery bypass graft (CABG)

DIAGNOSTIC CHECKLIST

Consider

 Cardiac-gated unenhanced MDCT improves clinical risk prediction in intermediate-risk asymptomatic individuals

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Coronary Artery Calcification





(Left) Composite image with axial cardiac gated NECT for calcium score quantification shows hyperattenuating foci of in the left anterior descending coronary artery \blacksquare , consistent with mild coronary artery calcification. A label 🛃 is placed on the calcification using software designed for calcium score calculation. (Right) Calcium score quantification of the same patient (in chart format) lists the total number of calcified lesions ₽, the volume \blacksquare , the equivalent mass of calcification \boxtimes , and the calcium score \triangleright .





(Left) Curved multiplanar reformatted coronary CTA shows calcification in the left anterior descending coronary artery ➡. Coronary CTA may be performed with prospective or retrospective ECG gating. Dual-source imaging provides higher temporal resolution than conventional CT. (Right) Curved multiplanar reformatted coronary CTA shows calcification within the *left circumflex coronary artery* ■. Reformatted images provide better coronary artery visualization and more precise vessel stenosis characterization.





(Left) Axial cardiac gated NECT obtained for calcium score calculation shows calcification in the right coronary artery 🛃. Cardiac gated NECT is more sensitive than radiography for detection of calcification. Higher calcium scores are associated with a higher risk of complications, such as myocardial infarction, stroke, and cardiovascular death. (Right) Curved multiplanar reformatted coronary CTA of the same patient shows calcification in the proximal \square , mid \square , and distal 🔁 right coronary artery segments.

TERMINOLOGY

- Inflammatory response to cardiac injury (surgery, myocardial infarction) with pericardial &/or pleural effusion
- Etiologies: Cardiac surgery, pericardiotomy, myocardial infarction, pacemaker or defibrillator lead implantation

IMAGING

• Radiography

- Abnormal (> 90%): Enlarged cardiac silhouette (globular shape), pleural effusion
- CT
 - Mild to moderate pericardial &/or pleural effusion
 - Careful inspection of pacemakers lead tips (especially atrial ones)
- MR
 - Pericardial effusion
 - Accurate pericardial thickness measurement
 - Simple effusion: Low signal on T1WI, high signal on T2WI and STIR

- Echocardiography: Main imaging tool for diagnosis and follow-up
- **Cardiac MR**: Can be performed in poor acoustic window conditions

PATHOLOGY

• Pericarditis leading to pericardial effusion, mediated by autoimmune hypersensitivity reaction

CLINICAL ISSUES

- Pleuritic chest pain (80%), low-grade fever (50-60%), dyspnea (50-60%) 1-3 weeks after cardiac injury
- Elevated inflammatory markers (C-reactive protein)

DIAGNOSTIC CHECKLIST

 Consider post cardiac injury syndrome in any patient who develops pericardial or pleural effusion after cardiac procedure

(Left) Axial CECT of a patient who developed chest pain, fever, and cardiomegaly on radiography (not shown) 3 weeks after cardiac surgery shows pericardial fluid 🄁 expanding pericardial recesses and sinuses and findings of prior median sternotomy 🔁. Patients with post cardiac injury syndrome often have abnormal chest radiographs. (Right) Coronal CECT of a patient with chest pain after active fixation lead pacemaker placement shows right ventricular perforation by a lead 🔁 (see inset) and mild pericardial effusion 🔁.





(Left) Axial CECT of 60-yearold man with post cardiac injury syndrome who presented with chest pain, fever, and dyspnea ten days after aortic valve replacement shows a moderate pericardial effusion 🔼, and sternotomy wires 🔁 in place, with absence of sternal healing given the brief post-operative period. (Right) Coronal CECT MIP reformatted image of the same patient shows the prosthetic aortic valve \supseteq and a moderate pericardial effusion ₽.





Abbreviations

• Post cardiac injury syndrome (PCIS)

Synonyms

- Post pericardiotomy syndrome (PPCS)
- Postmyocardial infarction syndrome (Dressler syndrome)

Definitions

- Inflammatory response to cardiac injury (surgery, myocardial infarction) that leads to pericardial &/or pleural effusion
- Etiologies: Cardiac surgery (PPCS), pericardiotomy (PPCS), myocardial infarction (Dressler), pacemaker or cardiac defibrillator lead implantation

IMAGING

General Features

- Best diagnostic clue
 - Pericardial effusion (&/or small pleural effusion) 1-3 weeks after cardiac injury
- Normal pericardium
 - Normal pericardial fluid: 15-30 mL; usually located in pericardial recesses and sinuses
 - Normal pericardial thickness on CT or MR: < 2 mm (optimally identified on T1WI black-blood SE sequences)
- Pericardial effusion
 - Pericardial thickness > 5 mm anterior to right ventricular free wall: Moderate pericardial effusion (100-500 mL)

Radiographic Findings

• Abnormal chest radiograph (> 90%)

- Enlarged cardiac silhouette (globular shape)
- Oreo cookie sign: Water density material between anterior mediastinal and subepicardial fat on lateral radiography
- Pleural effusion: Usually left-sided, mild-moderate size
- Right atrial lead lateral or anterior orientation associated with PCIS

CT Findings

- Mild to moderate pericardial &/or pleural effusion
- Careful inspection of pacemakers lead tips (especially atrial leads); windowing and post-processing to minimize underlying streak artifact
- Pericardial tamponade
 - Pericardial effusion, atrial dilatation
 - Dilated superior vena cava, inferior vena cava, hepatic veins
 - Elongated ventricles
 - Abdominal ascites

MR Findings

- Black blood SE
 - Allows accurate measurement of pericardial thickness
 - Simple effusion: Low signal on T1WI, high signal on T2WI and STIR
 - Hemorrhagic effusion: Increased signal on T1WI

Echocardiographic Findings

- Pericardial effusion
 - May relate to pacer wire perforation (confirmation with ECG gated CT)

Imaging Recommendations

- Best imaging tool
 - Echocardiography is main imaging tool for diagnosis and follow-up

DIFFERENTIAL DIAGNOSIS

Pericardial effusion

- Etiologies: Drugs, viral infection, hydrostatic edema, metastases, collagen-vascular disease, idiopathic
- Indistinguishable from PCIS on imaging; appropriate history may suggest diagnosis
- Inflammatory process commonly associated with pericardial thickening

PATHOLOGY

General Features

- Etiology
 - Pericarditis leading to pericardial effusion, mediated by autoimmune hypersensitivity reaction
- Laboratory findings
 - Elevated C-reactive protein
 - AHA (anti-heart antibodies) levels parallel severity of autoimmune reaction

CLINICAL ISSUES

Presentation

 Most common signs/symptoms
 Pleuritic chest pain (80%), low-grade fever (50-60%), dyspnea (50-60%); 1-3 weeks after cardiac injury

Demographics

- Sex
- o F:M of 2:1

Natural History & Prognosis

- PCIS occurs 2-3 weeks after cardiac surgery or pericardiotomy in 10-40% of patients
- 0.5-5% of permanent pacemaker implantations; stronger association with active fixation leads (suspected microperforation)

Treatment

• Empirical anti-inflammatory therapy and adjunctive colchicine

DIAGNOSTIC CHECKLIST

Consider

 PCIS in any patient who develops pericardial or pleural effusion (especially left pleural effusion) after cardiac procedure

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TERMINOLOGY

• Fluid in pericardial space

IMAGING

- Radiography
 - Frontal: Water bottle sign; globular enlargement of cardiopericardial silhouette
 - Lateral: Fat pad sign; pericardial fluid outlined by surrounding fat
- CT
 - Low-attenuation fluid: Uncomplicated effusion
 - High-attenuation fluid: Hemorrhage, purulent fluid, malignancy
 - o Associated pericardial thickening and calcification
 - Cardiac chambers: Constriction and tamponade
- MR: Assessment of complicated effusion
 93% accuracy for constrictive pericarditis
- Echocardiography: Imaging modality of choice

TOP DIFFERENTIAL DIAGNOSES

- Pericardial cyst
- Pericardial malignancy
- Dilated cardiomyopathy

CLINICAL ISSUES

- Signs/symptoms
 - May be asymptomatic
 - Chest pain, friction rub
 - Cardiac tamponade: Rate of fluid accumulation more significant than volume or composition
- Treatment
 - Small effusions may not require treatment
 - o Increased hemodialysis in chronic renal failure
 - Anti-inflammatory agents for acute idiopathic/viral pericarditis
 - Percutaneous or surgical drainage
 - Emergent management of tamponade

(Left) Graphic shows features of pericardial effusion. Pericardial fluid is located in the potential space between the serous parietal 🔁 and visceral pericardium or epicardium 🛃. (Right) PA chest radiograph shows a large pericardial effusion manifesting with the water bottle sign, characterized by globular enlargement of the cardiopericardial silhouette and a normal vascular pedicle. Pericardial fluid may slowly accumulate and attain a large volume without producing cardiac tamponade.





(Left) Lateral chest radiograph of the same patient shows the fat pad sign. A water density stripe *→* represents pericardial fluid visible between the retrosternal mediastinal fat \square and the subepicardial fat 🛃. (Right) Graphic depicts the anatomic basis for the fat pad sign. Fluid in the pericardial space \implies will appear as a water density stripe outlined by the fat density retrosternal mediastinal fat \triangleright and the subepicardial fat 🛃 located beneath the serous visceral pericardium or epicardium.





Definitions

- Fluid in pericardial space
- **Cardiopericardial silhouette**: Combined pericardial and cardiac silhouette on radiography

IMAGING

General Features

- Best diagnostic clue
 - Radiography: Fat pad (Oreo cookie) sign on lateral radiograph
 - CT/MR: Fluid in pericardial space
- Location
 - CT and MR
 - Small effusion: Posterior; along left ventricle and left atrium
 - Large to moderate effusion: Anterior; along right ventricle
 - Very large effusion: Circumferential
- Anatomic considerations
 - Pericardium surrounds heart and portions of pulmonary trunk, vena cava, and ascending aorta
 - **Fibrous pericardium**: Contiguous with ascending aorta and pulmonary trunk adventitia
 - Serous pericardium: Within fibrous pericardium
 - Serous visceral pericardium (epicardium): Lines heart
 - Serous parietal pericardium: Lines fibrous pericardium
 - 2 apposed pericardial layers with intervening
 - (potential) pericardial space
 - May contain 15-50 mL of fluid normally
- Normal pericardium
 - Radiography: Not visible
 - CT: Thin soft tissue linear structure; 0.7-2 mm thick
 - o MR: Thin low-signal linear structure on T1 and T2WI
 - o CT and MR
 - Pericardium between retrosternal mediastinal and subepicardial fat
 - No distinction between serous and fibrous pericardial layers
 - Frequent visualization of physiologic fluid and fluidfilled pericardial sinuses and recesses

Radiographic Findings

- Frontal chest radiography
 - May be normal with small pericardial effusion
 - Moderate-large (> 250 mL) pericardial effusion
 - Water bottle sign
 - Globular symmetric enlargement of cardiopericardial silhouette
 - Normal vascular pedicle
 - Documentation of slow or rapid cardiopericardial silhouette enlargement on serial radiography
- Lateral chest radiography
 - > 2-mm fluid density stripe between retrosternal and subepicardial fat
 - Fat pad sign: Oreo cookie, sandwich, or bun sign
- > 200 mL of fluid: Enlarged cardiopericardial silhouette

CT Findings NECT

- Direct assessment of pericardial abnormalities
- Low-attenuation pericardial fluid
- Heart failure, renal failure, malignancy
- High-attenuation pericardial fluid
 - Hemorrhage, pus, malignancy
 - Hemopericardium: High attenuation initially; attenuation decreases over time
- High sensitivity for pericardial thickening and calcification
- CECT
 - o Assessment for thickening, nodules, masses
 - Pericardial thickening, enhancement of serous pericardium: Inflammation
 - Associated mediastinal fat stranding
 - Assessment of cardiac chambers
 - Signs of constriction: Tubular ventricles, flattened/sigmoid interventricular septum
 - Signs of cardiac tamponade
 - Flattened anterior heart surface, right cardiac chambers
 - Flattened or bowed interventricular septum
 - Enlarged vena cava; periportal edema; reflux of contrast into inferior vena cava, azygos, hepatic/renal veins
 - Compression of coronary sinus

MR Findings

- General
 - Uncomplicated effusion
 - T1WI: Low signal; T2WI: High signal
 - Complicated effusion: Septations, debris
 - Hemorrhagic effusion
 - T1WI: High signal; T2WI: Low signal
 - Hemopericardium
 - □ Acute phase: Homogeneous high signal
 - □ **Subacute phase** (1-4 weeks): Heterogeneous signal, foci of high signal on T1 and T2WI
 - Chronic phase: Low signal intensity foci (calcification, fibrosis), dark peripheral rim
 No contrast enhancement
 - Assessment of pericardium and cardiac chambers to exclude constriction
 - MR: 93% accuracy for differentiation between constrictive pericarditis (pericardial thickening of > 4 mm) and restrictive cardiomyopathy

Ultrasonographic Findings

• High sensitivity for pericardial fluid

- Anechoic space between pericardial layers
- Decreased pericardial motion
- Assessment of constrictive pericarditis
- Assessment of suspected tamponade
 - Mass effect
 - Diastolic compression/collapse of right heart chambers; abnormal cardiac filling
 - Compression of pulmonary trunk and thoracic inferior vena cava
 - Abnormal motion
 - Cardiac swing within pericardium
- Doppler flow velocity paradoxus: Respiratory variation in Doppler velocities
- Paradoxical motion of interventricular septum
- Lack of inspiratory collapse of dilated inferior vena cava

Imaging Recommendations

- Best imaging tool
 - Echocardiography: Modality of choice for pericardial imaging
 - CT/MR: Visualization of entire pericardium; evaluation of complications of pericardial effusion (hemorrhage, loculation)
 - Contrast-enhanced cardiac MR: Evaluation of constrictive pericarditis

DIFFERENTIAL DIAGNOSIS

Pericardial Cyst

- Focal water attenuation round or ovoid lesion abutting pericardium
- Rare; prevalence of 1 in 100,000; 7% of mediastinal masses
- May mimic loculated pericardial effusion

Pericardial Malignancy

- 10-12% of patients with malignancy at autopsy
- Lung cancer in 1/3 of cases
- Pericardial nodular thickening, effusion, enhancement, mass

Dilated Cardiomyopathy

- Marked cardiomegaly
- May mimic pericardial effusion

PATHOLOGY

General Features

- Etiology
 - General: Obstruction of lymphatic or venous drainage
 - Most common causes: Myocardial infarction, left ventricular failure
 - **Uremic effusion**: 50% of patients with chronic renal failure
 - Infection
 - Acute pericarditis: 90% idiopathic or viral
 - Tuberculosis
 - Most common cause of constrictive pericarditis in developing world
 - Tamponade, frequent complication
 - Blunt/penetrating trauma
 - Thermal injury
 - Endocarditis, sepsis
 - Cardiac surgery: Typical spontaneous resolution
 - Up to 6% may become clinically significant; cardiac tamponade
 - Autoimmune disease
 - Rheumatoid arthritis: Effusion in 2-10%
 - Systemic lupus erythematosus: Symptomatic effusion in up to 50%
 - Systemic sclerosis: Small effusion in up to 70%
 - Neoplasia
 - Hypoalbuminemia, myxedema

- Drug reaction, radiation, trauma
- Effusive constrictive pericarditis
 - Constrictive physiology ± associated pericardial effusion or tamponade
 - Persistent elevated right chamber pressures after pericardial fluid drainage

Pathophysiology

- Pericardial effusion: Rate of fluid accumulation
 - Gradual increase in pericardial fluid: May accommodate > 1 L without tamponade
 - Rapid increase in pericardial fluid: Cardiac tamponade; impaired cardiac filling
- Cardiac tamponade
 - ↓ intracardiac volume, ↑ diastolic filling pressures
 - ↑ intrapericardial pressure with cardiac compression
 - Rate of fluid accumulation more significant than fluid volume or composition

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - May be asymptomatic
 - Chest pain: Worse with inspiration and supine position
 - Pericardial friction rub in acute pericarditis
- Other signs/symptoms
 - Pericardial tamponade
 - Anxiety, dyspnea, chest pain, jugular vein distention
 - Tachycardia, hypotension
 - Paradoxical pulse: > 10-mm Hg drop in systolic arterial pressure during inspiration
 - **Beck triad**: Muffled heart sounds, hypotension, jugular vein distention

Treatment

- Small pericardial effusions may not require treatment
- Increased hemodialysis; renal failure-related effusion
- Increasing effusion or effusion > 250 mL
 - Pericardiocentesis (image guided)
 - 93% success rate
 - o Surgical drainage
 - Preferred for hemopericardium, purulent effusion
 - Pericardial window, subxiphoid pericardiotomy
 - Pericardiectomy
 - Balloon pericardiotomy in recurrent tamponade
 Emergent management of tamponade
- Anti-inflammatory agents for acute idiopathic/viral pericarditis

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Recognition of normal fluid-filled pericardial recesses, which may mimic lymph nodes and congenital cysts

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Pericardial Effusion





(Left) Axial NECT shows a large pericardial effusion manifesting as water attenuation fluid in the pericardial space. The intrapericardial portions of the ascending aorta 🛃 and pulmonary trunk 🛃 are also surrounded by pericardial fluid. (Right) Axial NECT of the same patient shows water attenuation pericardial fluid completely surrounding the heart. The serous parietal 🛃 and visceral \blacksquare pericardial layers are not visible, but their anatomic location is inferred by the pericardial fluid boundaries.





(Left) Coronal cine MR of a patient with a pericardial effusion shows homogeneous high signal intensity fluid surrounding the heart and proximal great vessels. Portions of the pulmonary $trunk \supseteq and ascending a orta$ *≥* are intrapericardial and are therefore surrounded by fluid in cases of moderate to large pericardial effusion. (Right) Graphic shows the anatomy of the pericardium, which envelops the heart, the distal superior vena cava, the proximal ascending aorta, and the pulmonary trunk, forming pericardial recesses.





(Left) Composite image of a patient with acute pericarditis with short-axis SSFP (left) and contrast-enhanced (right) images shows a small circumferential pericardial $effusion \supseteq$ and pericardial thickening and enhancement (Right) Composite image of a patient with constrictive pericarditis with short-axis SSFP (left) and contrastenhanced (right) images shows a thick enhancing pericardium ➡ and no pericardial fluid. Interventricular septal dependence and absence of pericardial motion indicate constrictive physiology.

(Left) SSFP cine MR short-axis image of a patient with a large pericardial effusion shows high signal pericardial fluid completely surrounding the heart. The combined parietal serous and fibrous pericardial layers manifest as a thin low-signal linear structure regional surrounding thefluid. (Right) SSFP cine MR 4chamber view of the same patient shows high-signal pericardial fluid surrounding the heart and a visible serous visceral pericardium \supseteq (a.k.a. epicardium).





(Left) Axial CECT of a patient with a loculated pericardial effusion shows a right inferior pericardial collection of water attenuation and a small component of pericardial fluid posterior to the left ventricle. (Right) Axial CECT of a patient with pericarditis shows enhancement of the serous pericardium. The serous parietal pericardium 🔁 lines the fibrous pericardium. The serous visceral 🛃 pericardium lines the heart and subepicardial fat and is also known as the epicardium.





(Left) Axial CECT of a patient with tuberculous pericarditis shows a large pericardial effusion, enhancement of the serous parietal pericardium \square , infiltration of the adjacent mediastinal fat, right paraesophageal $lymphadenopathy \square$, and bilateral pleural effusions. (Right) Coronal CECT of a patient with infectious pericarditis secondary to penetrating trauma shows low-attenuation fluid and gas \blacksquare within the pericardial space and enhancement of the serous parietal pericardium \rightarrow





Pericardial Effusion





(Left) Axial NECT of a patient with malignant pericardial effusion shows highattenuation pericardial fluid and bilateral pleural effusions. Malignant pericardial effusion, purulent pericardial fluid, and hemopericardium may manifest with highattenuation fluid. (Right) Axial CECT of a patient who presented with metastatic disease shows enhancing pericardial nodules 🛃 in the superior aortic pericardial recess and mediastinal $lymphadenopathy \square$, consistent with metastases.





(Left) Axial CECT of a patient with a Stanford type A aortic dissection shows highattenuation pericardial fluid *▶* secondary to hemopericardium. (Right) Axial CECT of a patient with pericardial tamponade after traumatic dialysis catheter placement shows highattenuation pericardial fluid due to extravasated contrast from superior vena cava laceration and mass effect on the right ventricle. The intrapericardial location of the superior vena cava injury resulted in hemopericardium and cardiac tamponade.





(Left) Axial CECT of a patient with lung cancer, malignant pericardial effusion, and cardiac tamponade shows a large pericardial effusion and bilateral small pleural effusions with features of loculation. Note mass effect on the right cardiac chambers \blacksquare (particularly the right atrium) by the pericardial fluid. (Right) Axial CECT of the same patient shows pericardial fluid-producing mass effect on the right atrium and right ventricle and flattening of the interventricular septum, CT signs of cardiac tamponade.

Constrictive Pericarditis

KEY FACTS

TERMINOLOGY

• Pericardial stiffening/adhesions + clinical hemodynamic changes and right heart failure

IMAGING

- Clinical evidence of physiologic constriction
- Radiography: Pericardial calcification
- CT
 - Pericardial thickening/calcification highly suggestive of constrictive pericarditis
 - o Tubular ventricles, dilated atria
 - Waist-like narrowing of atrioventricular groove
- MR
 - Septal bounce: Paradoxical diastolic motion of interventricular septum
 - Pericardial enhancement with acute inflammation
 - More sensitive for distinction of constrictive pericarditis from restrictive cardiomyopathy

TOP DIFFERENTIAL DIAGNOSES

- Restrictive cardiomyopathy
- Pericarditis without constriction

PATHOLOGY

- Infectious: Viral, bacterial, mycobacterial
- Postsurgical or radiation injury
- Inflammatory: Systemic lupus erythematosus, rheumatoid arthritis

CLINICAL ISSUES

- Symptoms of right heart failure
- Surgical pericardiectomy when chronic

DIAGNOSTIC CHECKLIST

- Pericardial thickening and calcification can confirm constrictive pericarditis when clinically suspected
- Absence of pericardial thickening &/or calcification does not exclude constrictive physiology

(Left) Lateral chest radiograph of a patient with constrictive pericarditis shows curvilinear calcification 🔁 surrounding the heart. Lateral radiography is more sensitive than frontal radiography for visualization of pericardial calcification. (Right) Axial NECT (bone window) of a patient with constrictive pericarditis shows thick, irregular pericardial calcifications 🛃 in the atrioventricular grooves with resultant ventricular waistlike narrowing and tubular configuration. Pericardial calcification is suggestive but not diagnostic of constriction.





(Left) Short-axis T1WI MR shows diffuse circumferential pericardial thickening \square , identified as a low signal intensity band between the high signal intensity mediastinal and subepicardial fat. Note associated straightening of the interventricular septum 🖂 (Right) Four-chamber T1WI C+ MR of a patient with pericardial constriction shows delayed enhancement \blacksquare of the pericardium along the left ventricle and right atrium, indicating fibrosis or inflammation. Biatrial enlargement is also present.





Definitions

• Pericardial stiffening/adhesions + clinical hemodynamic changes and right heart failure

IMAGING

General Features

- Best diagnostic clue
 - Normal pericardial thickness: < 3 mm
 - **Pericardial thickening/calcification** highly suggestive of constrictive pericarditis
- Morphology
 - Atrial enlargement, tubular ventricles
 - Prominent leftward convexity or sigmoid shape of interventricular septum

Radiographic Findings

- Radiography
 - Linear or nodular pericardial calcification, best seen on lateral radiography
 - Usually diffuse, right-sided, along atrioventricular groove or diaphragmatic surface
 - o Pleural effusion

CT Findings

- Pericardial calcification highly suggestive of constriction
- **Tubular ventricular configuration**, straightened or sinusoidal interventricular septum
- Waist-like narrowing of atrioventricular groove
- Dilated atria and vena cava
- Pleural effusions, ascites, hepatic venous congestion

MR Findings

- T1WI
 - Low signal intensity band between high signal intensity mediastinal and subepicardial fat
- T1WIC+
 - Pericardial enhancement denotes acute inflammatory process
- SSFP white blood cine
 - Septal bounce: Paradoxical diastolic motion of interventricular septum
- MR more sensitive in distinguishing between pericardial effusion, constrictive pericarditis, and restrictive cardiomyopathy
- Myocardial tagging
 - Perturbation of magnetization marks stripes across myocardium and pericardium
 - Pericardial adhesions prevent normal step-off or break of stripes during cardiac cycle

Echocardiographic Findings

- Echocardiography is primary diagnostic tool
- Transesophageal more sensitive than transthoracic
- Can differentiate pericardial thickening from effusion
- Respirophasic changes in diastolic filling

Imaging Recommendations

- Best imaging tool
 - Imaging of patients with **clinical evidence of physiologic constriction**

- Echocardiography is primary tool to investigate pericardial effusion and cardiac hemodynamics
- CT and MR useful for assessment of entire pericardium
- CT and MR useful to distinguish myocardial from pericardial disease

DIFFERENTIAL DIAGNOSIS

Restrictive Cardiomyopathy

- Similar physiologic changes by echocardiography and cardiac catheterization
- Look for myocardial thickening or enhancement

Pericarditis Without Constriction

- Distinction based on physiologic changes
- Constriction may be transient after acute pericarditis

Myocardial Calcification

• Thin, linear calcification of left ventricular wall

Pericardial Neoplasm

- Enhancing pericardium suggests metastatic disease, especially in association with known malignancy
- Primary pericardial neoplasms are rare

PATHOLOGY

General Features

- Etiology
 - Infectious: Viral (Coxsackie B, influenza), bacterial, mycobacterial
 - Postsurgical, radiation injury
 - Inflammatory: Systemic lupus erythematosus (SLE), rheumatoid arthritis
 - o Metabolic: Uremia

CLINICAL ISSUES Presentation

- resentation
- Most common signs/symptoms
 - Symptoms of right heart failure
 - Dyspnea, orthopnea
 - Hepatomegaly, ascites
 - **Kussmaul sign**: Increased jugular venous pressure during inspiration

Treatment

- Medical management when subacute
- Surgical pericardiectomy when chronic
- May recur

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Pericardial thickening and calcification can confirm constrictive pericarditis when clinically suspected
- Absence of pericardial thickening &/or calcification does not exclude constrictive physiology

- 1. Goldstein JA et al: Hemodynamics of constrictive pericarditis and restrictive cardiomyopathy. Catheter Cardiovasc Interv. 95(6):1240-8, 2020
- Alajaji W et al: Noninvasive multimodality imaging for the diagnosis of constrictive pericarditis. Circ Cardiovasc Imaging. 11(11):e007878, 2018

KEY FACTS

TERMINOLOGY

- Metastases to heart and pericardium
 - Lymphatic spread
 - Direct extension
 - Hematogenous spread
 - Transvenous spread

IMAGING

- **Radiography**: Findings related to pericardial effusion • Associated signs of malignancy: Mediastinal lymphadenopathy, pleural effusions
- **CT**: Pericardial effusion
 - ± thickening/enhancement, nodules/masses• Associated signs of malignancy
- **MR**: T1WI: Usually low signal intensity; melanoma/hemorrhagic metastases may be T1 hyperintense
 - o T2WI: High signal relative to myocardium
 - o Most metastases enhance

TOP DIFFERENTIAL DIAGNOSES

- Primary cardiac neoplasms
- Treatment effects
- Myopericarditis

PATHOLOGY

 Immunohistochemical markers may be needed to distinguish metastatic disease from primary cardiac sarcoma

CLINICAL ISSUES

- Very poor prognosis
- 1/3 of affected patients die within 1 month of detection

DIAGNOSTIC CHECKLIST

- Malignant pericardial effusion is often 1st sign of cardiac or pericardial metastatic disease
- Assessment for signs of cardiac tamponade and coronary artery involvement

(Left) AP chest radiograph of a 35-year-old woman with metastatic melanoma shows an abnormal contour \supseteq of the left heart border and a moderate left pleural effusion. In a patient with a history of malignancy, short-interval morphologic changes of the cardiac silhouette and unilateral pleural effusion should be considered suspicious for metastatic disease. (Right) Axial fused FDG PET/CT of the same patient shows FDG-avid cardiac 🔁 and left subscapularis muscle 🔁 metastases.





(Left) Cine 4-chamber MR of a patient with metastatic melanoma shows an *intermediate signal intensity* mass \supseteq centered in the right ventricular myocardium with associated pericardial effusion. Among primary malignancies, melanoma has the highest frequency of cardiac metastases. (Right) Axial CECT of a patient with mediastinal sarcoma shows a large mediastinal mass 🔁 that invades the pericardium and the subepicardial fat and abuts and partially encases the right ventricular outflow tract 🔁.





Definitions

- Metastases to heart and pericardium
 - Lymphatic spread: Most common route; lung and breast cancer
 - Hematogenous spread: Typically melanoma; other sites usually involved
 - **Direct extension**: Lung cancer and other thoracic malignancies; rarely mesothelioma
 - Transvenous spread
 - Inferior vena cava from renal cell carcinoma, hepatocellular carcinoma, adrenal and uterine malignancies
 - Pulmonary vein from lung cancer
- Pericardial involvement in ~ 5-10% of late-stage cancer
- Malignant pericardial effusion in ~ 40% of patients with metastases to heart and pericardium

IMAGING

General Features

- Best diagnostic clue
 - Multiple cardiac and pericardial masses
 - o Associated malignant pericardial effusion
 - Other extracardiac thoracic metastases
- Location
 - Pericardium may extend variable distance above aorta and pulmonary trunk
 - Malignant pericardial effusion; diffuse or loculated
 - Transvenous spread to atria
 - Hematogenous spread: Multiple randomly distributed myocardial/pericardial nodules and masses
- Morphology
 - Pericardial nodularity and thickening
 - Pericardial fluid may exhibit heterogeneous attenuation; may be loculated in irregular collections

Radiographic Findings

- Radiography
 - Initial abnormality detected may be lung or mediastinal mass
 - Typical findings of pericardial effusion
 - May simulate cardiomegaly (fluid > 250 mL)
 - "Water bottle" heart if large
 - Oreo cookie sign on lateral radiography
 - Separation of mediastinal and subepicardial fat by water density
 - May produce unusual cardiac contour
 - Associated signs of malignancy
 - Mediastinal lymphadenopathy in 80%
 - Pleural effusions in 50%
 - Osseous metastases

CT Findings

- NECT
 - Pericardial effusion
 - Calcifications rare except in certain tumors
 - Osteosarcoma
 - Angiosarcoma
 - Tumors with psammomatous calcification

- Associated signs of malignancy
 - Lung metastases
 - Lymphadenopathy
 - Pleural effusion
 - Osseous metastases
- CECT
 - Pericardial effusion
 - ± thickening/enhancement
 - ± pericardial nodules/masses
 - o May better demonstrate solid and cystic components
 - o May demonstrate associated myocardial involvement
 - Visualization of central masses extending to heart via pulmonary veins
 - o Associated lymphadenopathy

MR Findings

- T1WI
 - Metastases are usually of low signal intensity
 - Melanoma and hemorrhagic metastases may show high signal intensity
- T2WI
 - o High signal intensity relative to myocardium
- T1WIC+
 - Most metastases enhance
 - Differentiation from thrombus (chronic thrombus may enhance peripherally)
- Better assessment of extent of disease than with CT
 - Superior contrast resolution allows better detection of myocardial metastases and pericardial disease
- Cardiac functional impairment can be detected and quantitated

Echocardiographic Findings

- Procedure of choice for initial evaluation of suspected pericardial effusion
 - Moderate effusion: Echo-free space 10-20 mm
 Severe effusion: Echo-free space > 20 mm
- Evaluation of right and left ventricular function
- Identification of signs of tamponade: Right ventricular or atrial diastolic collapse

Imaging Recommendations

- Best imaging tool
 - Echocardiography for initial evaluation
 - Limited evaluation of right ventricle
 - May not show entire pericardium
 - Poor demonstration of associated findings, lymphadenopathy
 - o Cardiac-gated MR for comprehensive evaluation

DIFFERENTIAL DIAGNOSIS

Primary Cardiac Neoplasms

- Very rare
- May mimic metastases with multifocal myocardial involvement or pericardial invasion
- Aggressive neoplasms
 - Sarcomas: Angiosarcoma, leiomyosarcoma, rhabdomyosarcoma
 - Primary cardiac lymphoma
- Differentiation between primary cardiac sarcoma (e.g., osteosarcoma) and metastases may be difficult

Treatment Effects

- Drug- or radiation-induced myopericarditis and pericardial thickening
 - o Radiation dose usually exceeds 3,000 cGy
 - o Common drugs: Doxorubicin and cyclophosphamide
- Nephrotic syndrome with pericardial effusion

Myopericarditis

- Infectious, inflammatory, or drug induced
- Enhancing, nodular pericardium, and epicardial enhancement on MR may mimic metastases

Pericardial Cyst

- Congenital, typically unilocular
- Homogeneous water attenuation, imperceptible wall
- Well marginated; no soft tissue components

Loculated Pleural Effusion

- Fluid attenuation on CT
- Usually separate from pericardium

PATHOLOGY

General Features

- Etiology
 - Most common neoplasms metastatic to heart and pericardium: Lung, breast, melanoma, lymphoma
 - Metastases to heart in ~ 1% of autopsies; ~ 10% when malignant neoplasm known
- Malignant pericardial effusions overwhelmingly secondary to metastases
 - Primary cardiac neoplasms are very rare

Gross Pathologic & Surgical Features

• > 90% of epithelial origin (e.g., lung, breast)

Microscopic Features

- Immune markers may discriminate among cell types
- Psammoma bodies (lung cancer, ovarian cancer)
- Immunohistochemical markers may be needed to distinguish metastatic from primary cardiac sarcoma

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Asymptomatic (50%)
 - Typically related to impaired cardiac function (30%) from pericardial effusion and tamponade
 - Hypotension and tachycardia
 - Dyspnea out of proportion to radiographic abnormality
 - Chest pain, cough, peripheral edema
 - Arrhythmia common
- Other signs/symptoms
 - Signs of **cardiac tamponade**
 - **Kussmaul sign**: Increased distention of jugular veins with inspiration
 - Friedreich sign: Rapid diastolic descent of venous pulse
 - Pulsus paradoxus: Decrease of > 10 mm Hg in diastolic pressure on inspiration

Demographics

- Age
 - Age determined by incidence of primary malignancy
- Sex
 - Equal sex distribution
- Epidemiology
 - Melanoma has highest rate of cardiac metastases (46-71%), followed by leukemia
 - o 1/3 of pericardial metastases from lung cancer
 - 1/3 of patients with lung cancer have pericardial metastases at autopsy
 - 1 in 4 patients with malignant pericardial effusion has breast cancer
 - 1 in 4 patients with breast cancer has malignant pericardial effusion at autopsy
 - 15% of pericardial metastases from hematologic malignancy
 - Other common primary malignancies
 - Esophageal cancer; can lead to esophageal-pericardial fistula
 - Papillary thyroid carcinoma, thymoma
 - Rare primary malignancies
 - Mesothelioma, endometrial cancer, osteosarcoma

Natural History & Prognosis

- Very poor prognosis
- Over 80% die within 5 years of detection
 - ~ 1/3 die within 1 month of detection, usually from cardiac tamponade
 - Other causes of death: Heart failure, coronary artery invasion, arrhythmia
- Cardiac tamponade from pericardial fluid accumulation
 - Decreased cardiac output, progressive decrease in cardiac diastolic filling
 - Rapid fluid accumulation poorly tolerated
 - Recurrent pericardial effusion in 50%

Treatment

- Surgical resection for palliation
- Treatment of cardiac tamponade from malignant pericardial effusion
 - Pericardiocentesis or pericardial window: Primary treatment choice with catheter drainage
 - Pericardial sclerosis or pericardiectomy
 - Radiation therapy

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Malignant pericardial effusion is often 1st sign of cardiac or pericardial metastatic disease
- Assessment for signs of cardiac tamponade and coronary artery involvement

- 1. Bussani R et al: Cardiac tumors: diagnosis, prognosis, and treatment. Curr Cardiol Rep. 22(12):169, 2020
- Maleszewski JJ et al: Neoplasia and the heart: pathological review of effects with clinical and radiological correlation. J Am Coll Cardiol. 72(2):202-27, 2018





(Left) Short-axis SSFP MR of a patient with left upper lobe adenocarcinoma shows a large left upper lobe mass ➡ that invades the fibrous and serous parietal pericardium and a small pericardial effusion 🔁. (Right) Composite image with axial chest CECT (left) and coronal abdomen CECT (right) of a patient with a retroperitoneal lipoleiomyoma shows a large, lobulated right $atrial mass \overleftrightarrow{D}$ that represents intravascular extension of a retroperitoneal mass via the inferior vena cava 🔁 into the heart.





(Left) T1WI C+ FS short-axis MR of a patient with metastatic sarcoma shows a centrally necrotic, enhancing metastasis \supseteq of the inferolateral left ventricular wall and a large malignant pericardial effusion. (Right) Composite image with axial T2WI MR (top) and fused axial FDG PET/CT (bottom) of a patient with lung cancer shows a heterogeneous metastasis \implies in the right ventricular myocardium, which is hyperintense relative to normal myocardium and FDGavid \bowtie on PET/CT.





(Left) Axial CECT of a patient with metastatic non-small cell lung cancer shows a large, low-attenuation metastasis \supseteq centered in the right ventricle with extension into the pericardial space. (Right) Axial CECT of a patient with lung cancer shows a left lower lobe mass 🛃 that invades the pericardium and a lowattenuation metastasis 🌫 arising from the interventricular septum. Lung cancer may affect the heart and pericardium via lymphatic spread, intravascular spread, &/or direct invasion.

Cardiac Myxoma

KEY FACTS

TERMINOLOGY

• Most common primary cardiac neoplasm

IMAGING

- Intracavitary mass originating from interatrial septum near fossa ovalis
- ~ 85% in left atrium, followed by right atrium
- CT
 - Typically low-attenuation intracavitary mass
 - Calcification in ~ 50% of right atrial myxomas
- MR
 - Heterogeneous signal and enhancement
 - May change position during cardiac cycle
 - Stalk visualization; tumor may prolapse through or obstruct atrioventricular valve
 - Cine SSFP to evaluate mobility, valvular obstruction, and flow acceleration

TOP DIFFERENTIAL DIAGNOSES

- Intracardiac thrombus
- Cardiac metastases
- Cardiac lipoma
- Primary cardiac malignancy
- Papillary fibroelastoma

CLINICAL ISSUES

- ~ 60% of affected patients are women
- Symptoms: Valvular obstruction (40%), constitutional symptoms (30%)
- Treated with surgical resection; 3-year survival > 95%

DIAGNOSTIC CHECKLIST

- Consider cardiac myxoma in patient with well-defined noninvasive atrial mass
- Stalk-like connection to interatrial septum may be evident on cross-sectional imaging

(Left) Graphic shows typical morphologic features of a cardiac myxoma with a thin short stalk \bowtie connecting the heterogeneous left atrial mass to the interatrial septum. Large lesions may obstruct the mitral valve during systole. (Right) Composite image with PA (right) and lateral (left) chest radiographs shows an ovoid right atrial myxoma with peripheral curvilinear calcification 🛃. Although myxomas in general are more common in the left atrium, right atrial myxomas are more likely to exhibit calcification.





(Left) Axial cardiac-gated CECT of a patient with cardiac myxoma shows an irregular left atrial mass 🔁 Although irregular in morphology, its location and association with the interatrial septum suggests the diagnosis. (Right) Composite image of a patient with cardiac myxoma with T2weighted double IR (top) and T1 C+ FS MR (bottom) shows a large, well-circumscribed, enhancing right atrial mass *⊡*. Intrinsic T2 hyperintensity reflects myxomatous matrix, while enhancement distinguishes this neoplasm from thrombus.





Cardiac Myxoma

TERMINOLOGY

Definitions

- Most common primary cardiac neoplasm
- ~ 50% of primary benign cardiac neoplasms

IMAGING

General Features

- Best diagnostic clue
 - Intracavitary left atrial mass with stalk-like attachment to interatrial septum near fossa ovalis
- Location
 - **~ 85% in left atrium**, followed by right atrium
 - Rare sites: Ventricle, inferior vena cava, valve
- Size
 - o 1- to 15-cm diameter
- Morphology
 - o Usually solitary; may be multiple in familial forms
 - o Ovoid lesion with lobulated or smooth contours
 - ~ 2/3 are smooth surfaced
 - ~ 1/3 are villous
 - Villous myxomas more likely to produce embolic complications

Radiographic Findings

- Chest radiographs may be normal
- Abnormalities are typically nonspecific
 - Findings may mimic atrioventricular valve stenosis
 - Mitral obstruction: Enlarged left atrium, pulmonary vascular congestion
 - o Pulmonary edema due to elevated left atrial pressure
- Calcification rarely visible; typically right atrial myxomas

CT Findings

- NECT
 - Tumor may not be visible without intravenous contrast
 - Low-attenuation intracavitary mass
 - Occasionally cystic
 - May change position during cardiac cycle
 - Calcification

- Approximately 50% of right atrial myxomas

- Rare in left atrial myxomas
- Secondary to repeated episodes of hemorrhage
- Head NECT for detection of complications
 - Infarction due to embolization
 - Metastatic disease (rare)
- CECT
 - o May exhibit heterogeneous contrast enhancemento No lymphadenopathy or pericardial effusion
- Cardiac gated CTA
 - Best modality for assessment of morphologic features of cardiac tumors
 - Improved detection and localization of calcification compared to non-gated CT
 - Retrospectively gated studies may show mobility when stalk-like attachment is present

MR Findings

- T1WI
 - o Iso- or hypointense

- T2WI
- Usually hyperintense
 T2* GRE
- Calcification may result in blooming
- T1WIC+
 - Heterogeneous enhancement
 - Iterative inversion recovery times up to 600 ms:
 Progressive hypointensity of thrombus vs. tumor (which demonstrates intermediate signal)
- MR cine

Cine SSFP images

- Best sequence for morphologic and functional evaluation
- Mobility due to stalk-like attachment of tumor to chamber surface
- Valve obstruction, typically mitral valve
- Flow acceleration around tumor

Majority heterogeneous on MR

- Brain MR for detection of complications
 - Infarction due to embolization
 - Metastatic disease (rare)

Echocardiographic Findings

- Generally initial imaging modality
- Tumor typically hyperechoic
- Assessment of tumor mobility and cardiac physiology
 - Assessment of hemodynamic degree of obstruction/prolapse

Nuclear Medicine Findings

- PET/CT
 - o Myxomas may be mildly FDG-avid
 - Consider malignancy with increasing FDG avidity

Imaging Recommendations

- Best imaging tool
 - Echocardiography often initial imaging modality for detection of myxoma
 - Cardiac MR: Optimal imaging modality for evaluation of myxoma
 - Cardiac-gated CT may aid in identification of calcification and fine anatomic detail

DIFFERENTIAL DIAGNOSIS

Intracardiac Thrombus

- Exclusion of thrombus is important first step in imaging evaluation of cardiac masses
- Common; usually in posterolateral atrium or appendage
- Associated with atrial fibrillation and mitral valve disease
- Acute thrombus does not enhance; chronic thrombus may exhibit slight peripheral enhancement

Cardiac Metastasis

- Often multiple and enhancing
- Associated with pericardial effusion, lymphadenopathy, or other metastases
- Most common primary sites: Lung, breast, melanoma

Cardiac Lipoma

- Often in interatrial septum
- Fat attenuation on CT; fat signal on MR

Primary Cardiac Malignancy

- Most often angiosarcoma
- Associated pericardial effusion, metastases

Cardiac Lymphoma

- Typically increased FDG uptake on PET imaging
- Other areas of involvement: Lung, mediastinum
- Broad-based septal attachment; no stalk

Pericardial Metastases

- Often associated with pericardial effusion
- Often extend beyond left atrial wall
- Most common primary sites: Lung, breast, melanoma

Cardiac Sarcoidosis

- May rarely produce cardiac masses
- Associated lung or mediastinal disease typical of sarcoidosis

Granulomatosis With Polyangiitis

- Very rarely produces cardiac masses
- Cavitary lung nodules/masses

Papillary Fibroelastoma

- Most common tumor of valvular epithelium
- Usually solitary; aortic or mitral valve origin
- Most have a stalk
- May embolize and produce stroke

PATHOLOGY

General Features

- Etiology
 - Unknown cell of origin
 - Probably primitive mesenchymal cell
- Genetics

90% sporadic

- Carney complex
 - Myxomas of heart and skin, skin hyperpigmentation (lentiginosis), and endocrine overactivity
 - < 10% of all myxomas associated with Carney complex
- Associated abnormalities
 - o Intracranial aneurysms from tumor emboli
 - Ischemic changes from peripheral emboli
 - o Pulmonary tumor emboli from right heart myxomas

Gross Pathologic & Surgical Features

- Soft gelatinous or friable frond-like tumor
- Hemorrhage, thrombus, hemosiderin (80% of cases)
- Calcification common in right-sided myxomas (50%)

Microscopic Features

- Most common: Rings and syncytial chains of myxoma cells embedded in myxomatous matrix
- May contain hematopoietic, glandular, mesenchymal, and endocrine elements
 - o Rarely thymic tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Symptoms of valvular obstruction (40%)
 Left atrium: Orthopnea, dyspnea

- Right atrium: Symptoms of right heart failure (peripheral edema, hepatic congestion, ascites)
- o Constitutional symptoms (30%)
- Fatigue, weight loss, fever
- May mimic infective endocarditis
- Arrhythmias or other electrocardiographic changes
- Peripheral embolization
 - Distribution depends on neoplasm location
 - Left atrium: Systemic circulation → brain (infarction), extremities
- May be associated with auscultation abnormalities
 - Mimics mitral valve disease
 - Tumor plop in ~ 15%
- o Asymptomatic (20%)
- Other signs/symptoms
 - o ~70% express interleukin-6 (IL-6)
 - May lead to symptoms similar to connective tissue disease
 - Elevated erythrocyte sedimentation rate
 - May be associated with electrocardiographic abnormalities
 - Typically signs of left atrial hypertrophy
 - Arrhythmias rare
 - Transient heart block

Demographics

- Age
 - Mean age at presentation: 50 years
 - Range: 1 month to 82 years
 - Relatively infrequent in children
- Sex
 - ~ 60% of affected patients are women

Natural History & Prognosis

- Very slow growth, **3-year survival > 95%**
- May become infected; fever, weight loss, septic emboli

Treatment

- Surgical resection, traditionally via sternotomy
 Recurrent tumor in 5% of cases
- New promising minimally invasive techniques

DIAGNOSTIC CHECKLIST

Consider

 Cardiac myxoma in patients with well-defined noninvasive atrial mass

Image Interpretation Pearls

• Stalk-like connection to interatrial septum may be evident on cross-sectional imaging

- 1. Lichtenberger JP 3rd et al: Cardiac neoplasms: radiologic-pathologic correlation. Radiol Clin North Am. 59(2):231-42, 2021
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- Abbas A et al: Cardiac MR assessment of cardiac myxomas. Br J Radiol. 88(1045):20140599, 2015

Cardiac Myxoma





(Left) Four-chamber view coronary CTA in systole shows a well-marginated spherical left atrial myxoma with a small stalk 🛃 connecting it to the interatrial septum. Note the high level of image noise due to EKG tube modulation. (Right) Four-chamber view coronary CTA of the same patient in diastole shows a better signal:noise ratio, prolapse of the myxoma through the mitral valve annulus 🛃, and a stalk 🗷 connecting the tumor to the interatrial septum.





(Left) Axial CECT of a 60-yearold woman demonstrates a hypoattenuating mass 🔁 in the left atrium adjacent to the interatrial septum, consistent with the classic imaging appearance of a myxoma. (Right) Composite image with 4-chamber cine SSFP in systole (top) and diastole (bottom) shows a large left atrial myxoma attached to the interatrial septum. The myxoma prolapses through the mitral valve \square during diastole, a characteristic feature.





(Left) Four-chamber T2weighted DIR with STIR shows intrinsic T2 hyperintensity of a left atrial myxoma \supseteq with a characteristic attachment to the interatrial septum. (Right) Axial image from an inversion recovery scout taken at 600ms inversion time of the same patient shows intermediate , signal intensity of the left atrial myxoma 🔁. Thrombus will progressively lose signal at higher inversion recovery times, resulting in progressive hypointensity. Exclusion of thrombus is an important first step in the MR evaluation of intracardiac masses.

Cardiac Sarcoma

KEY FACTS

TERMINOLOGY

- Most common primary cardiac malignancy
- Restricted to heart and pericardium

IMAGING

- Best diagnostic clue: Mass involving cardiac wall &/or chamber
- Radiography: Normal or may show cardiomegaly
- CECT
 - Discrete hypodense mass involving cardiac wall &/or chambers
 - o Infiltration/invasion: Pericardium, myocardium, mediastinum
 - Pulmonary metastases
- MR
 - o T1: Heterogeneous; necrosis and hemorrhage
 - T2: Heterogeneously hyperintense
 - T1 C+: Heterogeneous enhancement

TOP DIFFERENTIAL DIAGNOSES

- Cardiac metastases
- Lymphoma
- Cardiac myxoma
- Thrombus

PATHOLOGY

- Most common histologic type: Angiosarcoma (37%)
- Metastases in 66-89% of patients at presentation

CLINICAL ISSUES

- Dyspnea is most common symptom
- Poor prognosis
 - Mean survival: 3 months to 4 years
 - Recurrence and metastases within 1 year
- Treatment
 - Surgery: Palliative, may prolong survival
 - Palliative radiation and chemotherapy

(Left) Graphic demonstrates the morphologic features of cardiac sarcomas, which are infiltrative and locally invasive cardiac neoplasms \implies that often affect the atria and may involve the heart wall &/or chambers. (Right) Axial CECT of a patient who presented with chest pain shows a myxoid cardiac sarcoma that manifests as a lobulated hypodense mass that involves the left atrium \supseteq and the mitral valve 🖂, and extends into the left ventricle 🔁. This is one of the most common imaging manifestations of cardiac sarcoma.





(Left) Axial CECT of a patient with angiosarcoma demonstrates a large, infiltrative soft tissue mass 🔁 that involves the right heart and its adjacent tissues and partially encases portions of the great vessels. Angiosarcomas typically originate in the right heart. (Right) Axial fused FDG PET/CT of a patient with synovial sarcoma shows a large FDG-avid mass 🔁 arising from the roof of the left atrium. Synovial sarcomas most commonly involve the right heart but may affect the left heart and pericardium.





Definitions

- Most common primary cardiac malignancy
- Restricted to heart and pericardium

IMAGING

General Features

- Best diagnostic clue
 Mass involving cardiac wall &/or chambers
- Location
 - Angiosarcomas: Right atrium > left atrium
 - Involvement of ventricles and interventricular septum much less common
 - Other sarcomas: Left atrium > right atrium

Radiographic Findings

- Radiography
 - Chest radiography may be normal
 - Cardiomegaly is most common abnormality
 - Pericardial effusion
 - o Mass
 - o Consolidation
 - Pulmonary edema
 - Pulmonary metastases

CT Findings

- CECT
 - Discrete hypodense mass involving cardiac wall and chambers
 - Angiosarcomas are highly vascular
 - Mineralization may occur in primary osteosarcoma
 - o Diffusely infiltrative cardiac mass
 - Pericardial involvement
 - Pericardial thickening and nodularity
 - Disruption of normal pericardium
 - Pericardial effusion; may be hemorrhagic
 - Myocardial invasion
 - Invasion of interatrial septum in primary osteosarcoma
 - Mediastinal invasion
 - Pulmonary vein invasion
 - Pulmonary metastases
- Cardiac gated CTA
 - Involvement of cardiac valve

MR Findings

- T1WI
 - Heterogeneous
 - Hypointense: Necrosis
 - Intermediate: Viable tumor
 - Hyperintense: Hemorrhage
- T2WI
 - Heterogeneously hyperintense
- T1WIC+
 - Heterogeneous enhancement
 - Marked surface enhancement and central necrosis
 - o Sunray appearance
 - Linear enhancement along vascular spaces

Imaging Recommendations

- Best imaging tool
 - Cardiac-gated MR

DIFFERENTIAL DIAGNOSIS

Cardiac Metastases

- 20-40x more common than primary sarcoma
- Lung, breast, and esophageal cancer, melanoma

Lymphoma

- More common in immunocompromised patients
- Right > left heart involvement

Cardiac Myxoma

• Endoluminal lesion without mural involvement

Thrombus

- Tumor more likely to enhance
- Acute thrombus may enhance

PATHOLOGY

Staging, Grading, & Classification

Metastases in 66-89% of patients at presentation
 Lungs > lymph nodes, bone, liver

Gross Pathologic & Surgical Features

• Invasive mass or diffuse infiltration

Microscopic Features

• Most common histologic type: Angiosarcoma (37%)

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea
- Other signs/symptoms
 Chest pain, arrhythmia, tamponade, and sudden death

Natural History & Prognosis

- Poor prognosis; mean survival: 3 months to 4 years
- Better prognosis
 - Left atrial involvement
 - o Absence of metastases at diagnosis
- Recurrence and metastases within 1 year

Treatment

- Surgery: Palliative, may prolong survival
- Palliative radiation and chemotherapy

DIAGNOSTIC CHECKLIST

Consider

• Primary cardiac sarcoma in patient with locally invasive mass involving cardiac wall and chambers

- Edquist M et al: Computed tomography imaging characteristics of primary atrial intimal sarcoma. Clin Imaging. 54:112-5, 2019
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KEY FACTS

TERMINOLOGY

- Pulmonary artery (PA)
- Most common primary PA malignancy

IMAGING

• Best diagnostic clue: Large filling defect in PA refractory to anticoagulation

• Radiography

- Normal if intraluminal with no PA dilatation
- PA dilatation: Hilar mass
- Distal oligemia, pulmonary infarction, and extraluminal extension possible
- **CECT**: Filling defect in PA; may exhibit contrast enhancement
- MR: Distinction between tumor and thrombus
 - Tumor more likely to enhance
 - Acute thrombus and tumor thrombus may enhance
- Cine MR for pulmonic valve assessment
- FDG PET/CT: FDG uptake within tumor

TOP DIFFERENTIAL DIAGNOSES

- Pulmonary embolism
- Metastatic disease

PATHOLOGY

• Leiomyosarcoma most common histologic type

CLINICAL ISSUES

- Symptoms: Dyspnea, chest pain, hemoptysis
- Median age: 50 years
- Poor prognosis; mean survival: 12 months
- Treatment
 - Tumor resection
 - Chemoradiation
- Palliative stenting

DIAGNOSTIC CHECKLIST

• Consider PA sarcoma in patient with large PA filling defect refractory to anticoagulation

(Left) Graphic shows the morphologic features of pulmonary artery sarcoma. A soft tissue mass fills the pulmonary trunk lumen and extends into the proximal right pulmonary artery. (Right) Axial CECT of a patient who presented with chest pain demonstrates a heterogeneous mass \boxtimes in the right pulmonary artery that represented a pulmonary artery sarcoma. Note invasion into the adjacent mediastinum 🔁 and a small right pleural $effusion \supseteq$ secondary to metastatic disease.





(Left) Axial CTPA shows a soft tissue mass \supseteq in the pulmonary trunk that extends into the proximal right pulmonary artery. Biopsy revealed a pulmonary artery sarcoma, which typically manifests on CT as a filling defect that occupies the entire vascular luminal diameter. Contrast enhancement, extraluminal extension, and pulmonary artery dilatation may also be present. (Right) Fused axial FDG PET/CT of the same patient demonstrates marked FDG avidity in the tumor ⊡.





- Abbreviations
- Pulmonary artery (PA)

Definitions

• Most common primary PA malignancy

IMAGING

General Features

- Best diagnostic clue
 Large filling defect in PA
 - Refractory to anticoagulation
- Location
 - Central PA > peripheral PA

Radiographic Findings

- Intraluminal PA sarcoma
 - Normal chest radiograph if PA is not dilated
 - Hilar mass if PA is dilated
- Distal pulmonary oligemia
 Hyperlucent lung
- Peripheral subpleural basilar consolidations; pulmonary infarcts
- Mass extends outside PA
- Large central mass; mimics lung cancer
- Multifocal lung nodules; **metastases**

CT Findings

• CECT

• Filling defect in PA

- May occupy entire luminal diameter
- PA dilatation ± extraluminal extension
- May exhibit contrast enhancement
- o Mosaic lung perfusion/attenuation reported
- Pulmonary metastases

MR Findings

- May allow differentiation between tumor and thrombus • **Tumor more likely to enhance**
 - Acute thrombus and tumor thrombus may enhance
- Cine MR to identify pulmonic valve involvement

Angiographic Findings

- Polypoid filling defect in PA
- Tumor and thrombus may be indistinguishable
 Lesion movement with cardiac cycle suggests malignancy

Echocardiographic Findings

- Characterization of tumor morphology
- Identification of pulmonic valve involvement

Nuclear Medicine Findings

- PET/CT
- FDG uptake within tumor

Imaging Recommendations

- Best imaging tool
 - CTA for identification of filling defect in PA
 - Contrast-enhanced MR; differentiation between tumor and thrombus

DIFFERENTIAL DIAGNOSIS

Pulmonary Embolism

- Does not occupy entire luminal diameter
- Less commonly dilates PA
- No enhancement on CECT
- Enhancement on MR less common than in tumor
 Acute thrombus and tumor thrombus may enhance

Metastatic Disease

- More common than primary malignancy
- Renal cell and breast cancers, melanoma

PATHOLOGY

General Features

- Etiology
 - Etiology unknown in most cases
 - Prior radiation to mediastinum

Gross Pathologic & Surgical Features

• Tumor adherent to PA

Microscopic Features

- Leiomyosarcoma most common histologic type
- Undifferentiated
- Malignant fibrous histiocytoma

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Mimics pulmonary embolism
 - Dyspnea, chest pain, and hemoptysis
 - o Superior vena cava syndrome
 - Dilated superficial veins, edema, headache, neck swelling
 - o Involvement of pulmonary veins: Left heart failure

Demographics

- Age
 - o Median: 50 years

Natural History & Prognosis

• Poor prognosis; mean survival: 12 months

Treatment

- Tumor resection
 - Vessel wall reconstruction or conduit placement
 - Proximal lesions may require pneumonectomy
- Chemotherapy ± radiation therapy
- Palliative vascular stenting

DIAGNOSTIC CHECKLIST

Consider

• PA sarcoma in patient with large expansile PA filling defect refractory to anticoagulation

- Han Y et al: Surgical treatment of primary pulmonary artery sarcoma. Gen Thorac Cardiovasc Surg. 69(4):638-45, 2021
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Aortic Sarcoma

KEY FACTS

TERMINOLOGY

- Primary malignant tumors of aorta (PMTA)
- Very rare, highly aggressive class of sarcomas that arise from aortic wall or intima and carry poor prognosis

IMAGING

- Radiography
 - Lobulated mediastinal contour
 - Aortic enlargement
- CT
 - Polypoid, enhancing soft tissue mass arising from aortic wall, within aortic lumen, or along &/or around aorta
 - Aortic aneurysm due to weakening of aortic wall by infiltrating mass and flow disturbance
 - Stenosis of aortic lumen from intra- or extraluminal mass
 - Occlusion of aortic branches by bland or tumor emboli
- MR
 - Enhancement and distinction from mural plaque

TOP DIFFERENTIAL DIAGNOSES

- Aortic aneurysm
- Severe atherosclerosis or ulcerated plaque

PATHOLOGY

- Intima: Angiosarcoma, intimal sarcoma
- Mural: Leiomyosarcoma, fibrosarcoma

CLINICAL ISSUES

- Progressive pain; embolic events
- May mimic aortic aneurysm ± rupture
- Treatment: En bloc resection, chemoradiation, endovascular stent graft

DIAGNOSTIC CHECKLIST

- Consider PMTA in patients with enhancing soft tissue masses in or around aorta without atherosclerosis
- Exclusion of metastases to bone, lung, liver, skin, or kidneys in patients with PMTA

(Left) Axial CTA shows an enhancing periaortic mass 🖂 with luminal surface irregularity and focal ulceration \bowtie and bilateral pleural effusions. Aortic sarcomas may be intraluminal or periaortic, and are distinguished from atherosclerosis by absence of intimal calcification. (Right) Axial CTA of the same patient shows anterior displacement and narrowing of the thoracic aorta 🔁 due to extrinsic compression by the periaortic mass 🔁. Note intratumoral hyperattenuating thrombus \Rightarrow





(Left) Axial CTA shows a lobulated endoluminal soft tissue mass \supseteq in the descending thoracic aorta with internal enhancing components 🔁. Enhancement is an important finding in aortic sarcomas that helps differentiate them from thrombus. (Right) Sagittal oblique CTA of the same patient shows the longitudinal extent of the endoluminal aortic sarcoma \supseteq . The tumor also extends caudally along the aortic wall 🔁. Bland and tumor emboli may lead to peripheral symptoms and endorgan infarctions.





Synonyms

• Primary malignant tumors of aorta (PMTA)

Definitions

• Very rare, highly aggressive class of sarcomas that arise from aortic wall or intima and carry poor prognosis

IMAGING

General Features

- Best diagnostic clue
 - Enhancing soft tissue mass arising from aortic wall
- May be entirely within aortic lumen or surround aortaLocation
 - **Descending thoracic aorta** > abdominal aorta > thoracoabdominal aorta > aortic arch

Radiographic Findings

- Abnormal lobulated mediastinal contour
- Aortic enlargement

CT Findings

- NECT
- Hyperattenuating regions on NECT suggest thrombus
- CECT
 - Polypoid, enhancing soft tissue mass arising from aortic wall, within lumen, along &/or around aorta
 - Aortic aneurysm due to weakening of aortic wall by infiltrating mass and flow dynamic changes
 - May exhibit extraluminal contrast suggesting rupture
 - Growing periaortic soft tissue mass; may mimic expanding aneurysm
 - o Stenosis of aortic lumen by intra- or extraluminal effects
 - Associated thrombus may be indistinguishable from mass
 - Occlusion of aortic branch vessels or distal arteries by bland or tumor emboli
 - Renal or splenic infarcts
 - o Metastases to liver, lungs, bone, brain, skin

MR Findings

- Endoluminal or periaortic soft tissue mass
- Enhancement more easily detected on MR than CT
- Enhancement allows differentiation from more prevalent, nonenhancing, aortic mural plaques or thrombi

Imaging Recommendations

- Best imaging tool
 - o MRA
 - Superior to CT in distinguishing tumor from aortic wall plaque or thrombus

Nuclear Medicine Findings

- PET
 - Hypermetabolic foci in or around aortic wall
 - Staging; detection of unsuspected metastases

DIFFERENTIAL DIAGNOSIS

Severe Atherosclerosis With Plaque or Thrombus

• Consider PMTA in absence of atherosclerotic calcification

Aortic Aneurysm

- Consider PMTA if enhancing soft tissue adjacent to aneurysm or progressive/rapid aneurysm growth after stent placement
- Consider PMTA with evidence of metastases

PATHOLOGY

Staging, Grading, & Classification

- Intimal origin (more common): Angiosarcoma (from endothelial cells), intimal sarcoma/malignant fibrous histiocytoma (undifferentiated high-grade tumor)
- Mural origin: Leiomyosarcoma, fibrosarcoma
- Accurate histologic diagnosis requires immunohistochemical stains

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Progressive chest and abdominal pain
 - Embolic events (lower extremities, abdomen)
- Other signs/symptoms
 - Aortic aneurysm ± rupture, claudication
- Clinical profile
 - Aortic graft prostheses implicated as predisposing factors in small percentage of cases

Demographics

- Age
 - o Mean: 60 years
 - Sex
 - Males > females
 - < 200 reported cases in literature

Natural History & Prognosis

- Median survival: 11 months
- Main predictor of prognosis: Distant metastases, emboli
- Aortic arch tumors associated with brain metastases

Treatment

- First line: En bloc tumor resection and graft interposition, chemotherapy, and radiation therapy
- Alternatives
 - Endarterectomy or vascular bypass
 - Chemotherapy, radiation
 - Endovascular stent graft for palliation

DIAGNOSTIC CHECKLIST

Consider

• PMTA in soft tissue masses in or around aorta without evidence of atherosclerosis

Image Interpretation Pearls

• Exclusion of metastases to bone, lung, liver, skin, or kidneys in patients with PMTA

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Introduction

Accidents rank third among the most common causes of death in the United States after diseases of the heart and malignant neoplasms. Motor vehicle collisions (MVC) are a frequent cause of accidents in patients who present to emergency departments and are a leading cause of morbidity and mortality worldwide. Thoracic injuries are common and may be blunt or penetrating. Blunt injuries are caused by impact or shear forces and include deceleration injuries, such as those sustained during MVCs or falls from height. Penetrating injuries occur when the body is pierced by an object and include low- and high-velocity types. In low-velocity penetrating trauma, such as knife wounds, injured organs are located along the path of the penetrating object. Gunshot wounds represent high-velocity penetrating injuries in which the projectile injures tissues located both along and outside its path through pressure waves that damage surrounding tissues and vascular structures that may be forcefully displaced from their normal anatomic locations. As several organ systems may be simultaneously affected by lifethreatening injuries, evaluation of the traumatized patient requires a rapid comprehensive assessment of the head, neck, thorax, abdomen, and extremities to determine the most significant injuries, appropriately triage patients, and initiate treatment.

Initial imaging evaluation of traumatized patients typically includes supine **portable chest radiography**. Overlying artifacts are frequent and include extraneous monitoring and support devices, metallic portions of the patient's clothing, radiopaque components of the trauma board, and, in some cases, foreign bodies. Portable chest radiography expeditiously provides valuable information regarding the integrity of the regions and organs of the thorax, including identification of fractures, pneumothorax, pleural effusion, lung contusion &/or laceration, mediastinal widening from traumatic vascular injury, and traumatic diaphragmatic rupture. Radiography also allows expeditious evaluation of life-support devices for documentation of appropriate positioning and identification of metallic foreign bodies.

Multidetector CT (MDCT) and **CT angiography** (CTA) have revolutionized the evaluation and management of traumatized patients, are routinely employed for early diagnosis of life-threatening conditions, and are valuable for planning endovascular interventional procedures and surgical therapies. Direct visualization of the chest wall, pleura, lung, mediastinum, airways, and diaphragm with CT is reported to disclose up to 30% additional unsuspected injuries (compared to radiography) that impact patient management.

Ultrasound is increasingly performed in the emergency department for the prompt diagnosis of hemoperitoneum. Echocardiography is useful for evaluating the pericardium. Thoracic ultrasound can be employed for the emergent assessment of the pleura to exclude hemothorax and pneumothorax. Transesophageal ultrasonography may also be employed to assess cardiac and aortic injuries.

With the advent of MDCT, there has been a decrease in the use of **angiography** to evaluate traumatic vascular injuries. However, angiography is consistently used to guide endovascular stent placement and embolotherapy for the control of hemorrhage. **Magnetic resonance** (MR) imaging is not routinely employed in the assessment of acutely traumatized patients but may be useful in the evaluation of hemodynamically stable patients in whom intravenous contrast is contraindicated.

Systematic Assessment of the Thorax

Interpretation of radiography and CT of traumatized patients requires a high index of suspicion and a systematic assessment of all the anatomic regions of the thorax for a comprehensive evaluation of a patient's injuries, although significant abnormalities may be obscured by motion and low lung volume.

Chest wall: Soft tissue gas may indicate penetrating lung &/or gastrointestinal injuries. Rib fracture fragments may puncture the lung with resultant pneumothorax. First and second rib fractures are associated with an increased risk of vascular injury. Inferior rib fractures are associated with injuries to abdominal viscera. Five contiguous rib fractures or three contiguous segmental rib fractures are associated with flail chest. Fractures of the sternum and spine and sternoclavicular dislocations correlate with severity of trauma and may be associated with life-threatening vascular injury.

Pleura: Pneumothorax may manifest with the deep sulcus sign on supine radiography. Tension pneumothorax is a clinical diagnosis and may produce mass effect on mediastinal structures. Pleural effusion in the setting of trauma is often a hemothorax and when large may be associated with hemodynamic compromise and may require surgical evacuation and repair or embolization of injured vessels.

Lung and airways: Airspace disease in the traumatized patient may represent pulmonary contusion or laceration, but aspiration, infection, and atelectasis from mucus plugs or aspirated foreign bodies may also occur. Airway injuries are rare but should be suspected in patients with intractable pneumothorax or pneumomediastinum. The fallen lung sign is a specific but unusual radiographic finding in bronchial rupture. Although chest CT may identify the site of airway injury, bronchoscopy is the study of choice for definitive diagnosis.

Mediastinum: Mediastinal widening and loss of normal landmarks on radiography should always raise suspicion for traumatic vascular injury. CTA allows direct visualization of traumatic aortic injuries with high sensitivity and specificity. Hemopericardium manifests with an enlarged cardiac silhouette on radiography and is readily confirmed with echocardiography or CT. Pneumomediastinum is often secondary to alveolar rupture but may also indicate traumatic aerodigestive tract disruption.

Diaphragm: Traumatic diaphragmatic rupture typically occurs posteriorly. Left-sided tears are more common, but right-sided injuries may be easily overlooked. Elevation and indistinctness of the hemidiaphragm and herniation of abdominal organs into the thorax on radiography should prompt further evaluation with CT for early diagnosis.

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Radiography of Lung, Pleura, and Chest Wall Trauma



Radiography of Support Devices



(Left) AP portable chest radiograph of a patient status post fall from a 40-foot height shows overlying monitoring devices and trauma board artifacts \supseteq but is diagnostic of left tension pneumothorax, right pulmonary contusion, and traumatic thoracic spine fracture dislocation \blacksquare . (Right) AP chest radiograph of the same patient after chest tube placement shows decreased left pneumothorax and left lung reexpansion, right pulmonary contusion, and malpositioned endotracheal tube tip ⊉ in the subglottic trachea.

CT of Traumatic Chest Wall Injury

CT of Pulmonary Contusion and Laceration



Radiography of Traumatic Aortic Injury



(Left) Coronal CECT of the same patient shows discontinuity of the thoracic spine \blacksquare due to severe vertebral fracture dislocation and subcutaneous gas 🛃 in the right supraclavicular region. (Right) CECT of the same patient allowed exclusion of traumatic vascular injury but demonstrated bilateral pulmonary contusions 🔁 with intrinsic lucencies 🔁 characteristic of pulmonary lacerations. Multidetector CT in the setting of trauma shows unsuspected significant injuries in 30% of cases.



CT of Traumatic Aortic Injury



(Left) AP chest radiograph of a motor vehicle collision victim shows trauma board artifacts that compromise image quality but allow identification of a right basilar pneumothorax \supseteq and an abnormal left superior mediastinal contour \square , concerning for traumatic vascular injury. (Right) Composite image of the same patient with axial (left) and coronal (right) CECT shows a mediastinal hematoma 🔁 surrounding the normal aortic arch and traumatic injury \blacksquare of the descending aorta with a characteristic intimal flap \supseteq .

KEY FACTS

TERMINOLOGY

• Traumatic disruption of trachea or bronchi following blunt or penetrating injury

IMAGING

- Radiography
 - Pneumothorax, pneumomediastinum, subcutaneous gas; persists or progresses after chest tube placement
 - Up to 80% of patients have 1st rib fracture
 - Fallen lung sign
 - Endotracheal tube (ETT) cuff distention beyond expected location of tracheal walls; ETT cuff displacement out of trachea into neck or mediastinum
- CT
 - Direct identification of injury site in most cases
 - Chronic airway injury
 - Airway stricture ± atelectasis
 - o Optimal modality for assessment of other injuries

TOP DIFFERENTIAL DIAGNOSES

- Pneumomediastinum
- Pneumothorax
- Esophageal rupture
- Esophageal intubation

CLINICAL ISSUES

- Signs and symptoms
 - Respiratory distress
 - Continuous air leak despite chest tube drainage
 - Extensive subcutaneous gas
- 30% of affected patients die; 50% of fatalities occur within 1 hour after trauma
- Delayed diagnosis common: 70% not identified in first 24 hours, 40% delayed > 1 month
 - o Airway stenosis, atelectasis, mediastinitis, sepsis
- Diagnosis confirmed with bronchoscopy
- Treatment: Prompt surgical repair

(Left) AP chest radiograph of a patient with tracheal laceration after a neck stab wound shows pneumomediastinum, extensive subcutaneous gas, a large right pneumothorax, and atelectatic lung withdownward displacement (fallen lung sign). (Right) AP chest radiograph of a patient with tracheobronchial injury after chest trauma shows a large right pneumothorax and the atelectatic right lung \blacksquare "falling away" from the mediastinum secondary to a right mainstem bronchus laceration.





(Left) Axial CECT of a 50-yearold woman involved in a motor vehicle collision shows a laceration \blacksquare of the posterior trachea proximal to the carina, pneumomediastinum \square , and subcutaneous gas \supseteq . Tracheal injuries typically occur at the junction of the membranous and cartilaginous trachea. (Right) Axial CECT (bone window) of the same patient shows a comminuted fracture \blacksquare of the thyroid cartilage, subcutaneous gas \triangleright , and gas tracking up the neck and around the carotid arteries and jugular veins.





Synonyms

• Bronchial fracture

Definitions

• Traumatic disruption of trachea or bronchi following blunt or penetrating injury

IMAGING

General Features

- Best diagnostic clue
 - **Pneumothorax** &/or **pneumomediastinum**; persists or progresses after chest tube placement
- Location
 - Most occur within 2.5 cm of tracheal carina, where airway is fixed and subject to shearing injury
- Size

• Range: Partial thickness tear to complete disruption

Radiographic Findings

- Radiography
 - Site of injury rarely visualized
 - Subcutaneous gas; often massive and progressive
 - **Pneumomediastinum**; large and progressive
 - **Pneumothorax**, often with tension; may not resolve after chest tube placement
 - Up to 80% of affected patients have 1st rib fracture
 - Fallen lung sign
 - Lung falls away from hilum into gravitationally dependent position; hardly ever seen as patients rarely imaged in erect position
 - Endotracheal tube (ETT)
 - Cuff distention beyond expected location of tracheal walls or cuff displacement out of trachea into neck or mediastinum

CT Findings

- CECT
 - Direct identification of site of injury in majority of cases
 - Chronic airway injury: Airway stricture ± associated lobar collapse
 - CT fallen sign: Lung "falls" toward posterior dependent hemithorax
- CTA
 - Assessment of associated life-threatening injuries, especially traumatic aortic injury

Imaging Recommendations

- Best imaging tool
 - CT is optimal modality for identification of site of airway injury and detection of additional injuries
- Protocol advice
 - IV contrast for imaging trauma patients

DIFFERENTIAL DIAGNOSIS

Pneumomediastinum

• Multiple etiologies; rarely airway injury

Pneumothorax

• Common with trauma; often associated with rib fractures

Esophageal Rupture

- Emetic injury, blunt/penetrating trauma
- Pneumomediastinum and pneumothorax

Esophageal Intubation

- Frontal radiograph: ETT cuff overinflation superimposed on tracheal air column ± gaseous distention of stomach
- Lateral radiograph: ETT posterior to trachea

PATHOLOGY

General Features

- Etiology
 - Direct airway compression between sternum and spine
 - o Sudden deceleration of lung with fixed trachea
 - Forced expiration against closed glottis
 - Penetrating trauma: Gunshot and stab wounds
- Iatrogenic; traumatic ETT placement
- Associated abnormalities
 - Aortic injury, esophageal injury, rib and vertebral fractures

Gross Pathologic & Surgical Features

 Tracheobronchial tears commonly occur at junction of membranous airway with cartilage rings

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Respiratory distress
 - Air leak/pneumothorax despite chest tube
 - Extensive subcutaneous gas

Demographics

- Epidemiology
 - Uncommon; 3% of patients who die from blunt chest trauma
 - Delayed diagnosis common: 70% not identified in first 24 hours, 40% delayed > 1 month

Natural History & Prognosis

- 30% of affected patients die; 50% of fatalities within 1 hour after trauma
- Delayed diagnosis
 - Airway stenosis
 - Atelectasis
 - Mediastinitis, sepsis

Treatment

- Diagnosis confirmed with **bronchoscopy**
- Prompt surgical repair

DIAGNOSTIC CHECKLIST

Consider

• Careful evaluation of entire thorax in trauma patients for detection of other life-threatening injuries

- Bagga B et al: Traumatic airway injuries: role of imaging. Curr Probl Diagn Radiol. 49(1):48-53, 2020
- Moser JB et al: Imaging evaluation of tracheobronchial injuries. Radiographics. 40(2):515-28, 2020

Lung Trauma

KEY FACTS

TERMINOLOGY

- Injury to lung parenchyma secondary to **blunt** or **penetrating** trauma
- **Blast** injuries require special consideration as energy deposition is much greater
- Contusion: Torn capillaries and small blood vessels without disruption of alveolar architecture
- Laceration: Architectural disruption leading to elastic parenchymal retraction

IMAGING

- **Contusion**: Patchy ground-glass opacity (mild) → diffuse consolidation (severe)
 - o Typically clears within 7-14 days of injury
- Laceration: Parenchymal cysts ± air-fluid levels; surrounded by contusion and hemorrhage
 - Typically conforms to path of penetrating object
- **CT**: Modality of choice for initial injury assessment
- Radiography usually sufficient for follow-up

TOP DIFFERENTIAL DIAGNOSES

- Aspiration
- Pneumonia
- Fat embolism
- Lung abscess

PATHOLOGY

- Torn capillaries from energy deposition or shear
- Direct lung compression or impalement

CLINICAL ISSUES

- Symptoms: Dyspnea, chest pain, hemoptysis
- Young adult men most commonly affected

DIAGNOSTIC CHECKLIST

- CT more sensitive than radiography in detecting pulmonary contusion and laceration
- CT allows expeditious assessment of coexisting chest wall and mediastinal injuries

(Left) AP supine chest radiograph of a 16-year-old boy who sustained blunt chest trauma shows a peripheral air space opacity \blacksquare in the right lower lung. Adjacent right basilar hyperlucency \supseteq is consistent with pneumothorax. Note right chest wall gas \supseteq adjacent to acute right rib fractures. (Right) Coronal CECT of the same patient confirms right lung pulmonary contusionsand a small right pneumothorax. Gas 🔁 is also seen dissecting along right lower lobe bronchovascular bundles.





(Left) AP chest radiograph of a 24-year-old man who sustained a gunshot injury to the left chest shows left lung heterogeneous consolidation and a small left pleural effusion. Note left chest wall bullet fragment and subcutaneous gas. (Right) Axial CECT of the same patient shows the missile tract coursing through the left upper lobe resulting in lung laceration 🖂, adjacent contusion Ξ , and hemopneumothorax. The bullet \supseteq is located in the posterolateral left chest wall soft tissues.





Abbreviations

• Acute respiratory distress syndrome (ARDS)

Definitions

- Lung injury secondary to blunt or penetrating trauma
- Often hemorrhage + contusion + laceration
- Blast injuries: High-energy forces after explosion
 Spallation: Bursting phenomenon when pressure waves deposit energy at alveolar liquid-gas interfaces
- Contusion: Alveolar hemorrhage without disruption of alveolar architecture
 - Marker of severe kinetic energy absorption; not simply "lung bruise"
- **Laceration**: Alveolar disruption resulting in parenchymal retraction
 - Blunt trauma or blast injury: Linear tear produces ovoid lung defect
 - **Penetrating trauma**: Laceration conforms to path of penetrating object, commonly bullets and knives
 - $\circ~$ Defect fills with variable amounts of air \pm blood
 - Pneumatocele: Air-filled laceration
 - Parenchymal hematoma: Blood-filled laceration

IMAGING

General Features

- Best diagnostic clue
 - **Contusion**: Peripheral airspace opacity with adjacent acute rib fractures
 - Nonanatomical distribution
 - Crosses segmental and fissural boundaries
 - **Laceration**: Irregular cystic space ± layering hemorrhage with adjacent parenchymal contusion
- Location
 - Contusion occurs at point of energy absorption
 - Commonly peripheral lower lung, away from overlying chest wall musculature
 - Bilateral; contralateral paramediastinal/paravertebral ± contrecoup contusion
 - **Laceration** occurs in 4 distinct locations depending on mechanism of injury
 - Conforms to track of penetrating object
 - Peripheral location from rib fracture penetration
 - Central location from spallation or rapid parenchymal compression against closed glottis
 - Paravertebral location: Shearing injuries
 - Lung compressed over spine
- Size

• Contusion

- Small (< 1 cm) to massive (whole lung) depending on extent of injury
- Laceration: Variable size; from < 1 cm up to 20 cm
- Can be multiple and bilateral after blunt trauma
 Morphology
 - Contusion: Typically peripheral with rim-like distribution
 - Decrease in size and density in days following injury

- Laceration appearance dependent on mechanism
 - Blunt or blast: Irregular cystic defects ± layering blood products
 - Penetrating: Typically linear with adjacent hemorrhage

Radiographic Findings

- Radiography
 - Contusions and lacerations may be obscured by chest wall hematoma, atelectasis, pneumothorax, hemothorax
 - Become more conspicuous as other confounding abnormalities clear
 - **Contusion**: Variable radiographic appearance
 - Patchy airspace opacities or consolidations (mild)
 - Diffuse extensive consolidation (severe)
 - Perihilar vascular indistinctness and increased interstitial opacity
 - Edema and hemorrhage in bronchovascular interstitium
 - Worsened by spallation in blast injuries
 - Contusion progression follows predictable temporal pattern
 - \square May be "normal" \leq 6 hours following injury
 - □ Peak at 24-72 hours; resolution in 7-14 days
 - Persistence > 14 days should prompt further investigation
 - Laceration present at time of initial injury
 - Often initially obscured by adjacent contusion
 - Appearance may change over days to weeks: Initially air-filled but becomes blood-filled or vice versa
 - Heals over several weeks with resultant minimal fibrosis
 - Hematomas may appear as spiculated lung masses as they heal (vanishing lung tumor)

CT Findings

- CECT
 - Most sensitive for characterization of pulmonary parenchymal injuries and coexisting thoracic injuries
 - **Contusion**: Findings range from patchy ground-glass opacity (mild) to diffuse consolidation (severe)
 - **Laceration**: Irregular cystic space ± air-fluid levels; surrounded by contusion and hemorrhage

Hematoma: Blood-filled laceration

- Slightly increased attenuation centrally
- □ Enhancing rim as hematoma "organizes"
- □ May be confused with lung nodule or mass

Imaging Recommendations

- Best imaging tool
 - CT is imaging modality of choice for initial assessment of lung injury in trauma
 - Chest radiography usually sufficient to follow course of blunt trauma
- Protocol advice
 - Arterial-phase CECT useful in assessment of mediastinal and vascular injuries

DIFFERENTIAL DIAGNOSIS

Aspiration

• May be superimposed on contusion

Lung Trauma

• Bronchocentric distribution; dependent and perihilar predominant rather than subpleural and peripheral

Pneumonia

- May mimic contusion radiographically; develops later in hospital course
- Radiographically worsening contusion ≥ 72 hours warrants further evaluation for superimposed infection
- Lacerations rarely become secondarily infected; should not be confused with lung abscess

Fat Embolism

- Embolized fat globules result in ↑ alveolar capillary permeability → alveolar edema/hemorrhage
- Peripheral ground-glass opacity ± consolidation
- Occurs in > 90% of patients with traumatic long bone injury;
 ≤ 5% develop fat embolism syndrome

Lung Abscess

• Nontraumatic clinical scenario

PATHOLOGY

General Features

- Etiology
 - Disruption of alveolar capillary network: Hemorrhage and congestive edema
 - Direct (blunt) or indirect (blast) compression or impalement (penetrating)

Staging, Grading, & Classification

- Lung lacerations
 - **Type 1** (compression rupture): Central location; shearing forces between lung and central airways (**most common**)
 - Type 2 (compression shear): Lung compressed against vertebral bodies; lower lobes more susceptible due to ↑ mobility
 - **Type 3** (penetration): Small, round, peripherally located; usually adjacent to rib fracture
 - **Type 4** (adhesion tear): Shear forces tear parenchyma from pleural adhesions

Gross Pathologic & Surgical Features

• Airspaces filled with blood

Microscopic Features

• Disruption of alveolar capillary network resulting in hemorrhage and edema in alveolus and interstitium

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonspecific dyspnea, chest pain
- Other signs/symptoms
 - Hemoptysis
 - Respiratory distress, hemodynamic instability

Demographics

- Age
 - Young adult men suffer blunt chest trauma more frequently than other demographic groups

- Children more susceptible due to ↑ chest wall compliance
 - Results in ↑ compressive and shear force on lung
- Sex
 - 0 M>F
- Epidemiology
 - Contusion: Most common pulmonary injury
 30-70% of blunt chest trauma

Natural History & Prognosis

- Contusions typically clear within 10-14 days unless complicated by ARDS or infection
- Lacerations take longer to clear (several weeks) and often leave residual scar
 - Complications (rare): Pneumothorax, infection ± abscess, bronchopleural fistula
- Extent of parenchymal injuries plays pivotal role in determining mortality
 - Severe contusions: Vascular shunting and inflammatory mediator release → impact non-contused parenchyma and ↑ risk for ARDS development
 - > 20% of pulmonary contusions at initial evaluation can be predicted to progress to ARDS with 90% specificity

Treatment

- Supportive therapy, surveillance for other major organ injuries or complications
- Severe contusions result in poor pulmonary compliance and lead to profound hypoxia
 - o Mechanical ventilation for respiratory failure
 - Concurrent injuries of chest wall and pleura may require prolonged ventilatory support
- Surgical resection may be required for severe lacerations with vascular injury and massive hemorrhage
 - Open thoracotomy or video-assisted thoracoscopic surgery
 - Pulmonary vein laceration: Potential for systemic air embolism

DIAGNOSTIC CHECKLIST

Consider

• Contusions and lacerations are common injuries following chest trauma

Image Interpretation Pearls

- CT more sensitive than radiography for detecting contusion and laceration
- CTA allows expeditious assessment of coexisting chest wall and mediastinal injuries

Reporting Tips

 Query possibility of superimposed infection, fat embolism, or ARDS if radiographic findings progress ≥ 3 days after injury

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- Požgain Z et al: Pulmonary contusions after blunt chest trauma: clinical significance and evaluation of patient management. Eur J Trauma Emerg Surg. 44(5):773-7, 2018
- 3. Dennis BM et al: Thoracic trauma. Surg Clin North Am. 97(5):1047-64, 2017

Lung Trauma





(Left) AP chest radiograph of a 27-year-old man who sustained a stab wound to the medial right hemithorax shows right lung heterogeneous airspace disease and a nodular opacity \blacksquare projecting over the right hilum. (Right) Axial CECT of the same patient shows an enhancing focal right upper lobe nodule \blacksquare , consistent with traumatic right lung laceration and pulmonary artery injury with pseudoaneurysm formation. Note right hemothorax \supseteq and right anterior chest wall soft tissue gas 🄁.





(Left) AP chest radiograph of a 50-year-old man involved in a high-speed motor vehicle collision shows diffuse right lung airspace disease, a large pneumomediastinum, and extensive bilateral chest wall soft tissue gas. (Right) Axial CECT of the same patient shows extensive right lung $consolidations \supseteq and ground$ glass opacities \supseteq , consistent with pulmonary contusions, which may initially obscure underlying lacerations. Note associated right hemopneumothorax treated with a chest tube and diffuse chest wall soft tissue gas.





(Left) Coronal oblique CECT of a 33-year-old man involved in a motorcycle collision shows the characteristic appearance of traumatic lung injury with irregularly shaped, thin-walled cysts and adjacent groundglass opacities, consistent with pulmonary lacerations and surrounding pulmonary contusion. (Right) Sagittal oblique CECT of the same patient demonstrates multiple air-fluid levels with layering blood products within the pulmonary lacerations, also known as traumatic pneumatoceles.

Pneumomediastinum

KEY FACTS

TERMINOLOGY

- Air within mediastinum
 - Spontaneous: Alveolar rupture and air dissection from pulmonary interstitium
 - Traumatic: Tracheobronchial/esophageal tear

IMAGING

• Radiography

- Air anterior and posterior to heart
- Air surrounds/outlines mediastinal structures
- Air dissects superiorly into neck subcutaneous tissues
- Usually more conspicuous on lateral radiograph
- CT
 - More sensitive than radiography
 - Direct visualization of mediastinal air
 - Evaluation of tracheobronchial/esophageal rupture
 - Exclusion of tension pneumomediastinum

TOP DIFFERENTIAL DIAGNOSES

- Pneumothorax
- Pneumopericardium
- Artifact
- Air-distended esophagus
- Paratracheal air cyst
- Mediastinitis

PATHOLOGY

- High intrathoracic pressures
- Trauma; occurs in 10% of blunt chest trauma

CLINICAL ISSUES

- Signs/symptoms
 - Chest &/or neck pain (50-90%)
 - Cough &/or dyspnea
- Pneumomediastinum is typically benign; review of clinical history for exclusion of occult disease/injury

(Left) PA chest radiograph of a patient with spontaneous pneumomediastinum shows streaky lucencies outlining mediastinal structures and extending into the soft tissues of the neck \blacksquare and a subtle linear lucency beneath the heart \boxtimes , the so-called continuous diaphragm sign. (Right) Lateral chest radiograph of the same patient shows streaky lucencies anterior to the heart and great vessels 🔁 and air outlining the posterior heart $rac{1}{2}$ and hilar structures.





(Left) Axial CECT of the same patient shows air ≥ extending into the soft tissues of the neck, outlining the trachea, esophagus, and vascular structures. Bilateral extrapleural gas ≥ produces apical air caps. (Right) Coronal CECT of the same patient shows air ≥ throughout the mediastinum with extension into the soft tissues of the neck and chest wall ≥.





Definitions

- Air within mediastinum
 - Spontaneous: Usually secondary to Macklin effect
 - Alveolar rupture leads to air dissection along axial interstitium and into mediastinum
 - Traumatic: Tracheobronchial/esophageal tear

IMAGING

General Features

- Best diagnostic clue
 - Air outlining heart and mediastinal structures associated with supraclavicular subcutaneous air
 - Usually more conspicuous on lateral radiography
- Location
 - o Spontaneous: Mediastinal air usually cephalad to carina
 - Esophageal tear: Mediastinal air usually in lower paraesophageal location near diaphragm
- Size
 - Progressive pneumomediastinum suggests visceral injury to trachea or esophagus
- Morphology
 - Thin, linear air streaks within mediastinum

Radiographic Findings

- Air surrounds/outlines mediastinal structures
 - Aorta and major arteries
 - Trachea and central airways
 - Mediastinal parietal pleura may manifest as "pleural line"
- Air dissects superiorly into neck and subcutaneous tissues, inferiorly into retroperitoneum/peritoneum
 - Air in neck soft tissues often easier to detect than air in mediastinum
- Pulmonary interstitial emphysema (**PIE**)
- Septal air, subtle, often unrecognized
- Intrapulmonary or subpleural air cysts; usually < 5 mm but may also be large
- Air cysts increase risk of pneumothorax
- Linear nonbranching and mottled lucencies
- o Perivascular lucent halos
- Signs of pneumomediastinum

• Interstitial air

- Double bronchial wall; air on both sides of airway wall
- o Perivascular air
 - **Ring around artery sign**; air surrounding artery or vein seen en face
 - Tubular artery sign; air surrounding vessel along its length
- o Subcutaneous air in neck &/or chest wall
- **Continuous diaphragm sign**: Air outlining inferior aspect of heart above diaphragm
 - May mimic pneumoperitoneum
- Naclerio V sign
 - Paravertebral air adjacent to left hemidiaphragm and descending aorta, suspicious for esophageal tear
- Spinnaker sail sign
 - Elevation of thymic lobes in pediatric patients
- Signs suggestive of tracheobronchial or esophageal rupture • Persistent or progressive pneumomediastinum

- Pleural effusions, rare with spontaneous pneumomediastinum
- Esophageal tear; air preferentially collects around esophagus near diaphragm

CT Findings

- CT more sensitive than chest radiography
- Direct visualization of mediastinal air
- Pneumomediastinum
 - Air within mediastinal fat and in connective tissue sheaths around tubular structures: Trachea, pulmonary arteries, other central arteries, veins
 - Dominant paraesophageal gas at gastroesophageal junction suggests esophageal tear
- PIE
 - Air within pulmonary interstitium
 - Air surrounding arteries, veins, &/or airways
- Tracheobronchial or esophageal rupture site may not be visible
- Tension pneumopericardium or pneumomediastinum
 - o Compression of superior vena cava, right ventricle
 - o Dilatation of inferior vena cava &/or hepatic veins

Imaging Recommendations

- Best imaging tool
 - Chest radiography is usually diagnostic
 - Lateral radiograph usually more sensitive than frontal radiograph
 - CT is more sensitive than radiography
 - Evaluation of suspected tracheobronchial or esophageal tear
- Protocol advice
 - Consider esophagram to exclude clinically suspected esophageal perforation
 - Decubitus radiography: Pneumomediastinum air does not shift to nondependent position unlike air in pneumothorax or pneumopericardium

DIFFERENTIAL DIAGNOSIS

Pneumothorax

- Air in pleural space; shifts on decubitus position
- Thin pleural line; irregular pleural line in pneumomediastinum due to fascial tethering
- Apical air cap
 - Usually unilateral in pneumothorax
 - Pneumomediastinum; air may dissect extrapleurally over lung apex
 - Apical air caps from pneumomediastinum may be bilateral

Pneumopericardium

- Less common but similar pathophysiology; air tracks along pulmonary vessels into pericardium
- More common in infants than adults
- In adults, etiology is usually trauma
 - Penetrating injury, surgery, esophageal fistula, barotrauma
- Tension pneumopericardium may cause decreased cardiac output
- Key features of pneumopericardium
 Air outlining left ventricle &/or right atrium

- Air in pericardial space; may shift on decubitus position
- Air does not extend above mid ascending aorta
- Hydropneumopericardium may occur with concomitant pericardial effusion
- o Small heart sign

Artifact

- Mach band
 - Definition: Perceived lucency at interface of soft tissue density and air density
 - Due to retinal inhibition at contrasting density interface
- Common at heart borders and paraesophageal stripe • Skin fold
 - Soft tissue fold may cause soft tissue edge with lucent Mach line and opposite faded margin
 - Nonanatomic course is clue

Air-Distended Esophagus

- Can mimic extraluminal mediastinal air
- Mimics of mediastinal or pericardial air o Achalasia, colonic interposition, hiatal hernia

Paratracheal Air Cyst

- Single or clustered small rounded air-filled cysts in right paratracheal region at thoracic inlet
- Usually not visible on radiography, but well-described appearance on CT

Mediastinitis

- Fever associated with mediastinal air raises suspicion for mediastinitis
- Low-grade fever may be present in pneumomediastinum

PATHOLOGY

General Features

- Etiology
 - High intrathoracic pressures
 - Mechanisms
 - □ Obstructive lung disease
 - Sustained Valsalva maneuver
 - □ Cough, vomiting, straining, weight lifting
 - □ Inhalational drug use
 - Complicates 1-5% of asthma cases
 - Mucous plugs and increased intra-alveolar pressure Traumatic
 - Blunt chest trauma leads to pulmonary laceration and alveolar rupture
 - < 2% of cases secondary to tracheobronchial fracture
 - Esophageal rupture
 - Mechanical ventilation
 - Extrathoracic causes
 - Dental extraction, other head and neck surgeries
 - Sinus fracture
 - Pneumoperitoneum with extension into mediastinum; duodenal ulcer, diverticulitis
 - o Barotrauma
 - May occur in up to 15% of patients with pulmonary fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest &/or neck pain (50-90%)
 - Cough &/or dyspnea
 - Subcutaneous air; palpable crepitus
 - o Dysphagia
 - Hamman sign: Precordial systolic crepitations, diminished heart sounds
 - Mill wheel murmur (bruit de moulin): Succussion splash with metallic tinkle from pneumopericardium
- Other signs/symptoms
 - Decreased cardiac output may occur in tension pneumomediastinum or pneumopericardium (rare)

Demographics

- Age
- Peak incidence; 20-40 years
- Sex
 - Slight male predominance
- Epidemiology
 - o Blunt chest trauma, 10% have pneumomediastinum
 - 1 in 30,000 emergency department visits

Natural History & Prognosis

- **Benign course**; usually resolves in 7 days (4-14 days)
- Mortality rate > 50% in esophageal rupture following vomiting (Boerhaave syndrome)
- Pneumomediastinum and PIE can lead to pneumothorax • Pneumothorax does not lead to PIE or pneumomediastinum

Treatment

- Spontaneous pneumomediastinum: Observation for tension or pneumothorax
- Bronchoscopy or esophagram may be required if visceral injury suspected

DIAGNOSTIC CHECKLIST

Consider

- Inhalational drug use in patients with unexplained spontaneous pneumomediastinum
- Obstructive airway disease if pneumomediastinum • associated with hyperinflated lungs
- Pneumomediastinum is typically benign; clinical history important to exclude occult condition

Image Interpretation Pearls

 Lateral radiography is more sensitive than frontal radiography for visualization of pneumomediastinum

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- 3 Lee SY et al: Hamman syndrome: spontaneous postpartum pneumomediastinum. Intern Med J. 49(1):130-1, 2019

Pneumomediastinum





(Left) AP chest radiograph of a patient with esophageal rupture status post esophageal dilatation for chronic stricture shows linear lucencies \supseteq along the right heart border and gas Ξ within the soft tissues of the neck. Gas in the supraclavicular region is an important clue for suspecting subtle pneumomediastinum. (Right) Axial NECT of the same patient shows esophageal rupture *⊡* and a pneumomediastinum 🔁. The esophageal defect is rarely visible on CT in patients with esophageal rupture.





(Left) Axial CECT of a patient with lymphoma shows a right paratracheal mass that erodes into the trachea 🛃, a pneumomediastinum 🛃, and a left axillary mass 🛃. (Right) Composite image with AP chest radiograph (left) and esophagram (right) of a patient with Boerhaave syndrome shows a pneumomediastinum manifesting with a linear lucency \blacksquare in the left superior mediastinum and retrocardiac gas 乏. Esophagram confirms contrast leak 🔁 and esophageal perforation.





(Left) Composite image with PA (left) and lateral (right) chest radiographs of a patient with a pneumomediastinum demonstrates lucency \supseteq along the inferior mediastinum, known as the continuous diaphragm sign. The lateral radiograph shows gas surrounding the heart and anterior to the trachea \boxtimes . (Right) Axial CECT of the same patient confirms a pneumomediastinum \supseteq . Alveolar rupture leads to air dissection along the bronchovascular interstitium \blacksquare and into the mediastinum, known as the Macklin effect.

Traumatic Aortic Injury

KEY FACTS

TERMINOLOGY

- Acute traumatic aortic injury (ATAI), blunt traumatic aortic injury (BTAI), blunt aortic trauma (BAT), blunt aortic injury (BAI)
- Disruption of aortic wall, usually from high-velocity blunt injury, less commonly from penetrating trauma

IMAGING

- Radiography
 - Wide mediastinum, Aortic contour abnormality
 - 1st rib fracture: Indicates severe trauma, possible TAI
 - Most specific signs: Left apical cap (65%) downward deviation of left mainstem bronchus (65%), and obscuration of descending thoracic aorta (67%)
- CTA: Imaging modality of choice
 - o Aortic isthmus 90%; commonly on medial aspect
 - o Irregular aortic contour; sudden caliber change
 - Aortic wall disruption or pseudoaneurysm
 - o Sensitivity (98%), specificity (80%)

TOP DIFFERENTIAL DIAGNOSES

- Wide mediastinum of other etiology
- Ductus diverticulum (type III ductus)
- Fusiform enlargement proximal descending aorta
- Aortic spindle
- Atherosclerotic ulceration

CLINICAL ISSUES

- Urgent diagnosis; 50% die within 24 hours if untreated
- Cause of death in 20% of high-speed MVC
- Treatment
 - Adequate blood pressure control paramount in all aortic injuries
 - − Reduces rupture risk from $12\% \rightarrow 1.5\%$
 - **TEVAR over open repair** recommended for **all age groups** with suitable anatomy
 - May require stent coverage of left subclavian artery
 - Open surgical repair: Only if patient's anatomy precludes TEVAR; increased risk of cord ischemia and death

(Left) AP chest radiograph of a 27-year-old man involved in a high-speed motor vehicle collision shows rightward shift of the upper trachea 🔁, a contour abnormality and widening of the upper mediastinum 🛃, a large left hemothorax 🔁 and associated left apical cap, wide left intercostal spaces, and rightward mediastinal shift. (Right) Coronal CECT of the same patient shows the underlying traumatic aortic injury characterized by an intimomedial flap, contour irregularity, and a large contained rupture 🔁.











Abbreviations

• Traumatic aortic injury (TAI)

Synonyms

- Acute traumatic aortic injury (ATAI)
- Blunt traumatic aortic injury (BTAI)
- Aortic transection
- Blunt aortic injury (BAI)
- Traumatic aortic pseudoaneurysm

Definitions

- Aortic wall disruption: Ranges from intimomedial injury to transection
 - Most commonly from blunt, rapid deceleration injury: Motor vehicle collision (MVC), fall from height > 10 feet
 - Less commonly: Penetrating trauma
- Minimal aortic injury: Subcentimeter intimomedial abnormality, no external contour deformity
- Traumatic aortic pseudoaneurysm: Saccular outpouching contained **only** by adventitia

IMAGING

General Features

- Best diagnostic clue
 AD diagnostic clue
 - Wide mediastinum on AP chest radiography
 Intimomedial flap or pseudoaneurysm on CTA
- Location
 - Locations that allow differential deceleration of "mobile" and "fixed" aortic segments resulting in vascular shear
 - Aortic isthmus (90%); distal aortic arch at ligamentum arteriosum
 - Aortic root (5-14%); rare survival
 - Diaphragmatic hiatus (1-12%); may be associated with diaphragmatic injury
 - Multifocal aortic injury uncommon

Radiographic Findings

- Radiography
 - o Normal chest radiograph exceedingly rare
 - Negative predictive value of 98%
 - **Indirect signs** of mediastinal hemorrhage in 30-70% of patients: Sensitive but not specific
 - Mediastinal widening (> 8 cm or > 25% of transthoracic diameter)
 - Aortic contour abnormality; obscuration of AP window
 - Right tracheal/ETT or enteric tube deviation
 - Left apical cap
 - Wide paravertebral or paratracheal stripe
 - Inferior displacement of left mainstem bronchus
 - 1st rib fracture indicates severe trauma and possibility of TAI
 - Considerable force required to fracture 1st rib; protected by clavicle and scapula
 - o Chronic pseudoaneurysm (2% of survivors)
 - Peripherally calcified mass at aorticopulmonary window

CT Findings

• NECT

- ± mediastinal or periaortic hematoma
- CTA
 - Imaging modality of choice: Sensitivity (98%); specificity (80%)
 - Direct signs of aortic injury
 - Intimomedial flap
 - Pseudoaneurysm or "contained" rupture
 - Irregular aortic contour; abrupt caliber change
 - Rarely aortic dissection or active extravasation
 - Indirect signs
 - Periaortic or mediastinal hemorrhage
 - Minimal aortic injury: 10% of ATAI
 - Small intimal tear, polypoid intraluminal clot, lowdensity filling defect

MR Findings

 MR generally has no role in evaluation of acute trauma
 May be used to identify or follow intramural hematoma in stable patients

Echocardiographic Findings

- Transesophageal echocardiography
 - Demonstration of intimal tear, transection, hemopericardium
 - May be technically difficult in severely injured patients
 - Most commonly used intraoperatively when CT cannot be performed

Angiographic Findings

- Angiography: Previous gold standard; now used for endovascular repair
 - Small risk of rupture

Imaging Recommendations

- Best imaging tool
 - CTA is imaging modality of choice
 - Morphologically normal aorta with no mediastinal hematoma = 100% negative predictive value for exclusion of TAI
- Protocol advice
 - CTA with thin-section reconstructions for diagnosis and treatment planning
 - Cannot overstate value of multiplanar reformations for characterization and differentiation of injury from mimics
 - Rapid-acquisition MDCT (high pitch) or cardiac gating may be helpful in cases with equivocal findings (pulsatility/motion artifacts) or follow-up

DIFFERENTIAL DIAGNOSIS

Wide Mediastinum

• False-positives: Rotation, supine positioning, expiratory imaging, mediastinal fat, tortuous great vessels

Ductus Diverticulum (Type III Ductus)

- Anteromedial outpouching of aortic isthmus
- Smooth, gently sloping shoulders; no intimomedial flap
Normal Variant: Fusiform Enlargement of Proximal Descending Aorta

• Similar to ductus diverticulum, no intimomedial flap

Aortic Spindle

• Congenital narrowing at ligamentum arteriosum

Atherosclerotic Ulceration

 Irregular or ulcerated plaque; more common in older patients

Infundibulum of Bronchial-Intercostal Trunk

• Takeoff may show bump in aortic contour

PATHOLOGY

General Features

- Postulated mechanisms of pathogenesis
 - Rapid differential deceleration injury with resultant shear greatest at levels of aortic immobility: Ligamentum arteriosum, aortic root, diaphragmatic hiatus
 - Osseous pinch: Aortic isthmus compressed between sternum and spine
 - Water hammer effect: Sudden ↑ in intraaortic pressure during traumatic extrinsic compression
 - Viscous response: Velocity of extrinsic compression determining factor of internal injury
- Multivariate hypothesis likely: Shearing, torsion, stretching, hydrostatic forces

Staging, Grading, & Classification

- Society of Vascular Surgery Classification
 - Based on anatomical layers of aortic wall
 - Grade I: Intimal injury (minimal aortic injury)
 - Grade II: Intramural hematoma
 - Grade III: Pseudoaneurysm
 - Grade IV: Rupture
- Newer classification systems (Vancouver, Harborview) support restructuring → combine grades I and II

Gross Pathologic & Surgical Features

- 90% at aortic isthmus
 - From origin of left subclavian artery to ligamentum arteriosum, often anteromedially
- 7-8% ascending aorta; 2% descending aorta at diaphragmatic hiatus
- Ascending aortic tear: 20% of autopsy cases; rarely survive to reach hospital
- Transverse tears: Segmental (55%) or circumferential (45%); partial (65%) or transmural (35%)
- Noncircumferential tears more common posteriorly
- Concurrent **dissection** infrequent (11%); may be seen in patients with baseline hypertension

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - No specific or sensitive signs or symptoms until hemodynamic instability ensues
 - May have chest pain or dyspnea
- Multiple associated injuries: Diaphragm rupture, lung contusion, rib fractures, head injury

Demographics

Epidemiology
 Cause of death in 20% of high-speed MVC

Natural History & Prognosis

- 85% die at site of trauma (MVC)
- Urgent diagnosis; 50% expire within 24 hours if untreated
- 22% die during resuscitation
- 28% die during or shortly after repair
- 2% long-term survival
- Survival depends on time from injury to intervention

Treatment

- Adequate blood pressure control paramount in management of all injuries
 - Reduces rupture risk from $12\% \rightarrow 1.5\%$
 - Specific concurrent injuries (brain, spinal cord) may preclude aggressive blood pressure control
- **Conservative, nonoperative management**: Anti-impulse control (IV beta-blocker)
 - Grade I injuries only; growing support for inclusion of grade II and select grade III
 - Goal systolic blood pressure ≤ 100 mm Hg, mean arterial pressure ≤ 80 mm Hg, heart rate ≤ 100 bpm
 - 85-90% of minimal aortic injuries **heal spontaneously** within 4-8 weeks
- Thoracic endovascular aortic repair (TEVAR)
 - All grade II-IV injuries
 - Recommended over open repair for **all age groups** with suitable anatomy
 - Feasible in patients with multiple comorbid injuries
 - Urgent (< 24 hours) repair recommended
 - Emerging data suggests delayed (> 24 hours) repair may decrease mortality
 - Allows management of concurrent injuries and patient optimization
 - May require stent coverage of left subclavian artery
 - No detrimental impact on mental or physical outcomes; no compromise of function
- Open surgical repair: Only if anatomy precludes TEVAR
 o Increased risk of cord ischemia and death
 - 14% develop paraplegia; related to cross-clamp time
 - 20% overall mortality

DIAGNOSTIC CHECKLIST

Consider

• Careful evaluation of chest radiograph in trauma for indirect signs of aortic injury

Image Interpretation Pearls

• Consider chronic pseudoaneurysm in any patient with vascular calcification at aorticopulmonary window

Reporting Tips

 Aortic injury with pseudoaneurysm or "contained rupture" should not imply stability

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Traumatic Aortic Injury





(Left) Axial CECT of a 43-yearold woman involved in a motor vehicle collision shows an intimomedial flap 🛃 at the aortic isthmus, associated intramural hematoma , and concurrent left hemothorax. (Right) Parasagittal CECT of the same patient shows the location of the aortic injury at the aortic isthmus with resultant focal outpouching ➡, consistent with pseudoaneurysm formation, which results as the aortic adventitia "contains" the focal aortic disruption, but should not imply stability.





(Left) Sagittal CECT of a 30year-old man who sustained blunt chest trauma shows a contour irregularity and a focal aortic pseudoaneurysm . Adjacent mediastinal hemorrhage helps distinguish injury from branch vessel infundibulum. (Right) Sagittal CECT of a 58-year-old man who sustained blunt chest trauma shows a smooth caliber change 🖘 of the aortic isthmus adjacent to a calcified ligamentum arteriosum **⇒**. Absence of adjacent hemorrhage should prompt consideration of ductus diverticulum.





(Left) Lateral chest radiograph of an asymptomatic 65-yearold man shows a rounded peripherally calcified opacity \blacksquare in the middle mediastinum. (Right) Axial CECT of the same patient shows a focal pseudoaneurysm at the level of the aortic isthmus with peripheral calcification and eccentric intraluminal thrombus, corresponding to the radiographic abnormality. Upon further inquiry, the patient reported a history of trauma due to a high-speed motor vehicle collision 25 years previously.

Esophageal Perforation

KEY FACTS

TERMINOLOGY

- Esophageal laceration/tear
- Boerhaave syndrome: Esophageal rupture after forceful emesis
- Mallory-Weiss tear: Partial-thickness tear after forceful emesis

IMAGING

• Radiography

- Pneumomediastinum and subcutaneous gas (60%)
- V sign of Naclerio: Left costovertebral angle gas
- Bilateral pleural effusions (60%)
- Hydropneumothorax (50%)
- Consolidation or atelectasis adjacent to tear
- CT
 - Extraluminal oral contrast
 - Pneumomediastinum; acute mediastinitis
 - Pleural effusion or hydropneumothorax

TOP DIFFERENTIAL DIAGNOSES

- Mediastinal abscess
- Mediastinal hemorrhage
- Pneumomediastinum

CLINICAL ISSUES

- Signs/symptoms: Sudden substernal/lower thoracic chest pain, dysphagia, hemoptysis, hematemesis
- Treatment: Conservative for small tears; surgical for large tears (within 24 hours)
- Mortality rate related to time between perforation and treatment

DIAGNOSTIC CHECKLIST

- Esophagography is procedure of choice for diagnosis
- Esophageal rupture is often overlooked; diagnosis requires high index of suspicion
- CT is optimal imaging modality for evaluation of mediastinal complications

(Left) AP chest radiograph of a patient with esophageal perforation shows pneumomediastinum 🔁 and extensive subcutaneous gas \bowtie in the supraclavicular regions. Note bilateral pleural effusions and associated relaxation atelectasis. The diagnosis requires a high index of suspicion. (Right) Axial CECT of the same patient shows pneumomediastinum with gas \supseteq surrounding a dilated thickened esophagus. CT may not demonstrate the exact location of the esophageal tear.





(Left) Axial CECT of a patient with chest pain after forceful emesis shows bilateral pleural effusions 🔁 and pneumomediastinum 🖘 surrounding a hiatal hernia *⊡*. (Right) *Esophagram of the* same patient following the CT shows extraluminal contrast ➡, consistent with perforation and leak. Boerhaave syndrome accounts for about 15% of esophageal ruptures. Management is typically surgical, depending on the size and location of the tear, time to diagnosis, and extent of mediastinal involvement.





Synonyms

Esophageal tear

Esophageal laceration

TERMINOLOGY

Definitions

- Boerhaave syndrome: Esophageal rupture after forceful emesis
- Mallory-Weiss tear: Partial-thickness tear after forceful emesis

IMAGING

General Features

- Best diagnostic clue
- High degree of suspicion in appropriate clinical scenarioMorphology
 - Tear usually linear and longitudinal

Radiographic Findings

- Normal early (10%)
- Pneumomediastinum and subcutaneous gas (60%)
 V sign of Naclerio (25%): Extraluminal air localized to
- left costovertebral angleBilateral pleural effusions (60%)
- Hydropneumothorax (50%)
 Mid or upper tear: Right hydropneumothorax (5%)
 Lower tear: Left hydropneumothorax (75%)
- Consolidation or atelectasis adjacent to tear

Fluoroscopic Findings

- **Esophagram**: Detection/localization of esophageal tear
 - Nonionic water-soluble contrast: False-negative rate of 20%
 - Barium: Improved detection of small leaks
 - Gastrografin: Risk of aspiration

CT Findings

- Extraluminal oral contrast: Does not show tear size; may not show tear site
- **Esophageal thickening**: Intramural hematoma, esophageal dissection
- **Pneumomediastinum:** Centered on esophagus (90%)
- Acute mediastinitis: Periesophageal fluid/gas, abscess
- Pleural effusion/hydropneumothorax: May progress
- CT esophagography may be equivalent to fluoroscopy

Imaging Recommendations

- Protocol advice
 - Esophagography (fluoroscopic or CT) is diagnostic procedure of choice
 - Initial assessment with nonionic water-soluble contrast
 - If no leak detected, barium esophagram
 - Barium may detect small leaks not initially visualized

DIFFERENTIAL DIAGNOSIS

Mediastinal Abscess

• Perforated esophageal neoplasm (carcinoma, lymphoma), esophagitis, foreign body, postsurgical

Mediastinal Hemorrhage

• Aortic dissection, aortic transection, blunt or penetrating trauma

Pneumomediastinum

• Bronchial fracture, esophageal fistula, asthma

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Sudden onset of substernal/lower thoracic chest pain
 - May mimic acute myocardial infarction, aortic dissection, perforated peptic ulcer
 - Boerhaave syndrome: Follows drinking and eating binge
 Mackler triad: Vomiting, severe chest pain,
 - Mackier triad: vomiting, severe subcutaneous gas (50%)
 - o Dysphagia, hemoptysis, hematemesis (50%)

Demographics

- Epidemiology
 - o latrogenic following endoscopic procedures
 - Esophagoscopy: 50%
 - Pneumatic dilatation (achalasia): 2-6%
 - Postsurgical
 - Esophageal surgery, dilatation, biopsy
 - Boerhaave syndrome: 15% of esophageal ruptures
- Esophagitis: Infectious, eosinophilic

Natural History & Prognosis

- Mortality rate directly related to time interval between perforation and treatment initiation
 - Untreated perforation, nearly 100% mortality rate (fulminant mediastinitis)
 - o Intervention after 24 hours; 70% mortality rate

Treatment

- Conservative: Small tears
- Surgical: Large tears (within first 24 hours)
- **Percutaneous drainage**: Mediastinal abscess, fluid collection
- Esophageal stent: Used to bridge esophageal tear

DIAGNOSTIC CHECKLIST

Consider

• Esophageal rupture is often overlooked; must have high index of suspicion

Image Interpretation Pearls

- Radiographic V sign of Naclerio should prompt suspicion of esophageal tear
- CT: Optimal imaging modality for evaluation of mediastinal complications

- Cutaia G et al: Caustic ingestion: CT findings of esophageal injuries and thoracic complications. Emerg Radiol. 28(4):845-56, 2021
- Norton-Gregory AA et al: CT esophagography for evaluation of esophageal perforation. Radiographics. 41(2):447-61, 2021
- Wei CJ et al: Diagnostic utility of CT and fluoroscopic esophagography for suspected esophageal perforation in the emergency department. AJR Am J Roentgenol. 215(3):631-8, 2020

(Left) Axial NECT of a patient with sudden onset of chest pain and esophageal rupture demonstrates extraluminal gas a surrounding the distal esophagus, small bilateral pleural effusions, and a small left loculated

hydropneumothorax D. Left hydropneumothorax suggests a left-sided esophageal tear. (Right) Axial NECT of a patient with chest pain and a sticking sensation of food in the lower chest shows

pneumomediastinum 2 centered on the distal esophagus, consistent with esophageal tear or rupture.





(Left) AP chest radiograph of a patient with esophageal perforation shows a subtle pneumomediastinum ∂ and a linear gas collection ∋ at the right medial

costodiaphragmatic recess. Similar extraluminal gas occurring on the left is known as the V sign of Naclerio. (Right) Esophagram of a patient with an iatrogenic right esophagopleural fistula shows a multiloculated right basilar

hydropneumothorax 2 and extravasated contrast 2 in the dependent right pleural space.





(Left) Axial CECT of the same patient shows a . multiloculated right pneumothorax 🔁, right basilar relaxation atelectasis \blacksquare , and gas outlining a communication between the mediastinum and the right pleural space \implies . (Right) Axial CECT of the same patient shows a right basilar hydropneumothorax with $contrast \ge$ in the dependent right pleural space. CT is the imaging modality of choice for evaluating complications of esophageal perforation, but it may not allow localization of the site of esophageal tear.





Esophageal Perforation





(Left) PA chest radiograph of a patient with esophageal perforation shows a multiloculated right hydropneumothorax with multiple air-fluid levels ₽. (Right) Lateral chest radiograph of the same patient shows a small left pleural effusion and multiple air-fluid levels 🛃 associated with a multiloculated right hydropneumothorax. The findings suggest empyema with bronchopleural fistula. The diagnosis of esophageal perforation requires a high index of suspicion and careful review of the patient's history.





(Left) Axial CECT of the same patient demonstrates a loculated right pleural effusion with enteric contrast \mathbf{E} in the right pleural space and extraluminal contrast 🛃 in the mediastinum, consistent with esophageal perforation. (Right) Axial CECT of the same patient shows the large loculated right hydropneumothorax and enteric contrast 😂 in the right pleural space. Pneumomediastinum 🔁 centered about the right distal esophagus is consistent with esophageal perforation.





(Left) Axial CECT of a patient with esophageal rupture shows pneumomediastinum \blacksquare and mural esophageal gas E or pneumatosis in the esophageal wall. (Right) Axial CECT of the same patient shows pneumomediastinum \supseteq and distal esophageal pneumatosis 🖾. There are no , mediastinal fluid collections or pleural effusions. Although this patient had an iatrogenic esophageal tear, she recovered with simple enteric tube drainage. Small esophageal tears may respond to conservative treatment, as in this case.

Thoracic Duct Tear

KEY FACTS

TERMINOLOGY

- **Thoracic duct**: Transports chyle from intestinal lacteals; vertically traverses and crosses visceral mediastinum, drains into left subclavian vein
- Thoracic duct tear: Thoracic duct disruption
 Chylothorax, chylopericardium, chylous ascites

IMAGING

- Radiography
 - Unilateral or bilateral layering effusion; may be large
 - Effusion location depends on anatomic level of thoracic duct tear
- CT
 - o Water attenuation; fat content obscured by high protein content of chylous effusion
- MR
 - T1-hyperintense fluid reflecting proteinaceous content
- Lymphangiography
 - Documentation/localization of duct tear

TOP DIFFERENTIAL DIAGNOSES

- Pleural effusion
- Chylothorax without thoracic duct injury
 Malignancy, lymphangioleiomyomatosis
- Pseudochylothorax or chyliform effusion

PATHOLOGY

- Milky, whitish pleural fluid
- Chylomicrons; ↑ fluid cholesterol and triglycerides

CLINICAL ISSUES

- Dyspnea, malnourishment
- Conservative management: Drainage, low-fat diet
- High output leak: Embolization or surgical ligation

DIAGNOSTIC CHECKLIST

• Consider thoracic duct injury in patient with rapidly accumulating or persistent pleural effusion following trauma or surgery

(Left) Axial CECT of a man who sustained a traumatic fracture of T10 🔁 with associated injury to the cisterna chyli and thoracic duct shows elevation of the right diaphragmatic crus 🔁 and a simple fluid attenuation right chylous pleural effusion. (Right) AP chest radiograph of the same patient obtained 4 days later shows a large right chylous pleural effusion despite catheter drainage 🔁 and low fat diet. Chylous pleural effusions are typically indistinguishable from pleural effusions of other etiologies.





(Left) Coronal NECT MIP reformatted image of a woman who underwent lymphangiography for treatment of chylous effusion after esophagectomy shows the leftward and superior course of the thoracic duct 🛃 in the visceral mediastinum to join the left subclavian vein. (Right) Axial NECT of the same patient shows the right chylous effusion ➡ and radiodense lymphangiography lipiodol contrast within the thoracic duct *⊡*. Note the immediate proximity of the thoracic duct to the esophagus.





Definitions

- **Thoracic duct**: Transports chyle from intestinal lacteals; vertically traverses and crosses visceral mediastinum, drains into left subclavian vein
- Thoracic duct tear: Thoracic duct disruption • Chylothorax, chylopericardium, chylous ascites

IMAGING

General Features

- Best diagnostic clue
 - Chylous pleural effusion on thoracentesis
 - Recent trauma or surgical intervention
 - Often accumulates quickly despite indwelling catheter
- Location
 - Pleural effusion laterality depends on anatomic level of thoracic duct tear: Duct crosses midline in region of T6
 - Right (most common): Tear in right mediastinum below T6 vertebra
 - Left: Tear in left mediastinum above T6 vertebra
 - Bilateral: Tear as duct crosses midline from right to left at T6 vertebra

Radiographic Findings

- Unilateral or bilateral free pleural effusion
 - Blunt costophrenic angles, hemidiaphragm obscuration
 Ipsilateral atelectasis; opaque hemithorax if large

CT Findings

- Often indistinguishable from nonchylous pleural effusion
 - Typically water attenuation; fat attenuation obscured by hemorrhagic or proteinaceous fluid
 - May be hypoattenuating due to fat content of lymph

MR Findings

- T1-hyperintense fluid reflecting proteinaceous content
- Signal suppression on opposed-phase chemical shift imaging due to presence of microscopic intravoxel fat

Nonvascular Interventions

- Lymphangiography: Localization of duct tear
 - Fluoroscopic guided percutaneous embolization
 - Identification of exact tear location not always necessary; manipulation in itself can incite closure

Imaging Recommendations

- Best imaging tool
 - **Lymphangiography**: Tear documentation/localization – Allows percutaneous embolization or sclerosis
 - CT useful for assessing effusion size and loculation

DIFFERENTIAL DIAGNOSIS

Pleural Effusion

• Imaging features indistinguishable from chylothorax

Chylothorax Without Thoracic Duct Injury

- Malignancy: Lymphoma, metastatic carcinoma
- Lymphangioleiomyomatosis: Diffuse thin-walled lung cysts
- Diffuse pulmonary lymphangiomatosis: Diffuse thickening of bronchovascular interstitium and septa

Pseudochylothorax or Chyliform Effusion

- Chronic pleural effusion or pleurisy; tuberculosis, rheumatoid pleuritis
 - Accumulation of cholesterol crystals; absence of chylomicrons

PATHOLOGY

General Features

- Etiology
 - Traumatic thoracic duct injury: 25% of chylothoraces
 - Surgical injury most common
 Complication of up to 4% of esophagectomies
 - Any surgical manipulation of visceral mediastinum
 - Cardiac or aortic surgery, pleuropulmonary resection/transplant, mediastinoscopy
 - Nonsurgical: Blunt or penetrating trauma, childbirth, emesis
 - Thoracic duct obstruction resulting in rupture

Gross Pathologic & Surgical Features

Milky, whitish pleural fluid

Microscopic Features

- Chylomicrons present; absent in nonchylous effusions
- Elevated triglyceride level (> 110 mg/dL; 1.24 mmol/L); may be elevated in any exudative pleural effusion

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Clinical profile
 - Malnourishment as result of altered fat metabolism
 - Low serum albumin reflects nutritional deficiencyReduced protein and lymphocytes can result in

Natural History & Prognosis

• Up to 50% mortality if untreated

immunosuppression

Treatment

- Conservative management: Percutaneous drainage; can be self limiting/heal spontaneously
 - Decrease lymphatic fluid production via low fat diet and parenteral nutrition
- High output or persistent leak (> 7 days)
 - Percutaneous embolization or sclerosis
 - o Surgical ligation; pleuroperitoneal shunt creation

DIAGNOSTIC CHECKLIST

Consider

 Thoracic duct injury in patient with rapidly accumulating or persistent pleural effusion after surgery or trauma

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KEY FACTS

TERMINOLOGY

- Pneumothorax (PTX)
- Air in pleural space following blunt or penetrating trauma

IMAGING

- Radiography
 - Thin (< 1-mm) visceral pleural line without peripheral lung markings
 - Parallels chest wall
 - Supine radiography least sensitive, underestimates size
 - Deep sulcus sign: Nondependent pleural air results in hyperlucent basilar hemithorax with inferior displacement of costophrenic sulcus
 - Tension PTX: Contralateral mediastinal shift, flattened hemidiaphragm, hemodynamic compromise
- CT
 - o Assessment of associated life-threatening injuries
 - Distinction of PTX from bullae

TOP DIFFERENTIAL DIAGNOSES

- Skin fold, scapula, hair, superimposed monitoring/support devices
- Bullous emphysema
- Pneumomediastinum
- Primary or secondary spontaneous PTX

CLINICAL ISSUES

- Chest pain, sudden dyspnea
- Tension PTX: Respiratory failure and hemodynamic instability
- Observation and supplemental oxygen for small PTX
- Chest tube drainage for large/symptomatic PTX
- Size of PTX less important than patient's physiologic status

DIAGNOSTIC CHECKLIST

• Report location and size/amount of pleural separation in cases of traumatic PTX

(Left) AP chest radiograph of a 28-year-old man involved in a motor vehicle collision who had a left pneumothorax that required emergent chest tube placement shows a right basilar pneumothorax that produces the deep sulcus sign *⊡*. Note right basilar hyperlucency, asymmetric hyperexpansion of the right hemithorax, right intercostal space widening, and mild leftward mediastinal shift. (Right) Coronal CECT of the same patient shows a right basilar pneumothorax \supseteq and the anatomic basis for the deep sulcus sign.





(Left) AP chest radiograph of a young man who sustained blunt chest trauma in a motor vehicle collision shows a right pneumothorax \rightarrow , pneumomediastinum 🖂, and diffuse bilateral subcutaneous gas. The right lung consolidation is attributed to diffuse right pulmonary contusion. (Right) Axial CECT of the same patient shows the right pneumothorax \square pneumomediastinum \square , and diffuse bilateral subcutaneous gas. Note right basilar consolidation \supseteq with intrinsic lucencies, consistent with lung contusion and laceration.





- Abbreviations
- Pneumothorax (PTX)

Definitions

• Air in pleural space following blunt or penetrating trauma

IMAGING

General Features

- Best diagnostic clue
 - Visualization of thin (< 1-mm) visceral pleural line without peripheral lung markings in traumatized patient
- Location
 - Upright chest radiograph: Apical
 - Decubitus chest radiograph: Nondependent
 - Supine chest radiograph: Basilar/nondependent
- Size
 - Small < 2-cm pleural separation
 - Large > 2-cm pleural separation

Radiographic Findings

- Visceral pleural line usually **parallels** adjacent chest wall
- Supine radiography; least sensitive, underestimates size
 - **Deep sulcus sign**: Nondependent pleural air, hyperlucent basilar hemithorax, inferiorly displaced costophrenic sulcus
 - Basilar hemithorax hyperlucency
 - Sharp mediastinal and diaphragmatic margins
- Decubitus chest radiography
 - More sensitive than upright and supine techniques
- Expiratory chest radiography
 Equally sensitive as full inspiratory chest radiography
- Tension PTX: Hemodynamic compromise
 Contralateral mediastinal shift, hyperexpanded
 - hemithorax, hemidiaphragm flattening

CT Findings

- High sensitivity for PTX
- Distinction from bulla or emphysema
 - Important differentiation prior to chest tube placement to avoid iatrogenic bronchopleural fistula
- Assessment of associated life-threatening injuries

Ultrasonographic Findings

• Absence of visceral pleural "gliding" during respiration

Imaging Recommendations

- Best imaging tool
- AP chest radiograph usually sufficient for diagnosis
- Protocol advice
 - CT: Assessment of traumatic chest injuries, identification of appropriately positioned support devices, distinction of bulla from PTX

DIFFERENTIAL DIAGNOSIS

Skin Fold, Scapula, Hair, Superimposed Monitoring or Support Devices

- Often extend outside thoracic cavity
- Edge rather than line: Mach effect
 - Thick black line rather than thin visceral pleural line

Bullous Emphysema

- Concave/acute margins with chest wall
- Basilar displacement of bronchovascular structures

Pneumomediastinum

• Can mimic medially located PTX

Primary or Secondary Spontaneous Pneumothorax

• Acute onset, absence of trauma

PATHOLOGY

General Features

- Etiology
 - **Penetrating** trauma: **Laceration** of visceral pleura allows air to enter pleural space
 - Penetrating injury produces PTX in > 80% of cases
 - Blunt trauma: 1 alveolar pressure and rupture of air into pleural space (Macklin effect)
 - Displaced rib fracture may lacerate visceral pleura
 - latrogenic injury
 - Transthoracic > transbronchial lung biopsy
 - Thoracentesis
 - Line placement: Central venous catheter (subclavian > internal jugular), pacemaker, enteric tube

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain, sudden dyspnea
 - o Tension PTX: Severe dyspnea, cyanosis, tachycardia

Natural History & Prognosis

- Resorption of pleural gas: 1.5% per day on room air (50-75 mL/day)
- Time for full re-expansion: ~ 3 weeks

Treatment

- Observation for small PTX
- Supplemental oxygen increases rate of resorption of pleural air by factor of 4
- Needle decompression/chest tube drainage for large or symptomatic PTX
 - Size of PTX less important than patient's physiologic status
- Complications: Prolonged air leak, bronchopleural fistula

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- CT assessment of associated life-threatening injuries
 - Distinguish bullous or cystic lung disease from PTX
 - Identification of chest tube malposition

Reporting Tips

• Report location and size/amount of pleural separation

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- Durso AM et al: Penetrating thoracic injury. Radiol Clin North Am. 53(4):675-93, vii-viii, 2015

Traumatic Hemothorax

KEY FACTS

TERMINOLOGY

• Blood in pleural space following blunt or penetrating trauma

IMAGING

- Rarely isolated: ± rib fracture, contusion, pneumothorax
- Radiography
 - Blunt costophrenic angle (upright), increased hemithorax opacification (supine)
 - Large hemothorax may produce contralateral mediastinal shift and "**tension hemothorax**"
- CT/CTA
 - Pleural fluid attenuation > 30 HU
 - Layered high-attenuation pleural fluid; "hematocrit effect"
 - Exclusion of life-threatening traumatic vascular injury
- Angiography
 - Selective catheterization for identification/embolization of intercostal/internal mammary arterial injury

TOP DIFFERENTIAL DIAGNOSES

- Exudative pleural effusion
- Extrapleural hematoma
- Thoracic duct tear
- Esophageal rupture

CLINICAL ISSUES

- Signs and symptoms
 - Pleuritic chest pain and dyspnea
 - Hemorrhagic shock and respiratory failure when large
- Treatment
 - Tube thoracostomy
 - Hemothorax evacuation via VATS or thoracotomy
 - Embolization of intercostal/internal mammary arterial injury

DIAGNOSTIC CHECKLIST

• Consider hemothorax in traumatized patient with pleural effusion; careful assessment for traumatic vascular injury

(Left) Axial CECT of a patient status post penetrating right chest trauma shows an intermediate-attenuation right pleural effusion \blacksquare with layering high-attenuation fluid *▶*, the so-called hematocrit effect, consistent with acute hemorrhage. (Right) Composite image with axial CECT (left) and MIP reformatted image (right) of a patient with chest trauma shows a left hemothorax \square , and an anterior rib fracture 🖂 with adjacent contrast blush \square from an intercostal artery pseudoaneurysm 🖾, more conspicuous on MIP image.





(Left) AP chest radiograph of an 80-year-old woman with chest pain and dyspnea after a fall shows large right and small left pleural effusions. Pleural effusion in the setting of trauma should prompt consideration of hemothorax. (Right) Axial CECT of the same patient shows a large right pleural effusion with areas of high attenuation \square , consistent with hemothorax, in contradistinction to the water-attenuation small left transudative pleural effusion \square related to underlying heart failure. Note complete right lung atelectasis.





Definitions

• Blood in pleural space following blunt or penetrating trauma

IMAGING

General Features

- Best diagnostic clue
 Pleural effusion in setting of blunt or penetrating injury
- Location
 - Upright radiography: Basilar pleural fluid
 - o Supine radiography: Layers posteriorly or laterally
- Size
- Variable; may be massive
- **Rarely isolated**: ± rib fracture, contusion, pneumothorax

Radiographic Findings

- Acute findings
 - Pleural effusion: Blunt costophrenic angle (upright), ↑ hemithorax opacification (supine)
 - Large volume: Ipsilateral atelectasis, opaque hemithorax
 ± contralateral mediastinal shift, tension hemothorax
- Subacute findings: Loculated pleural effusion; empyema
- Chronic findings
 - Organized hemothorax; pleural thickening ± calcification
 - o Fibrothorax and ipsilateral volume loss

CT Findings

- NECT
 - High-attenuation pleural fluid (> 30 HU)
 - Heterogeneous fluid, layering high attenuation ("hematocrit effect")
- CTA
 - o Assessment of traumatic arterial injury as source

Angiographic Findings

• Selective catheterization for identification/embolization of intercostal/internal mammary arterial injury

Ultrasonographic Findings

• Rapid estimation of pleural fluid volume in trauma cases

Imaging Recommendations

- Best imaging tool
 - o Radiography typically adequate for diagnosis
 - CT more sensitive for detection
- Protocol advice
 - CT angiography for evaluation of life-threatening traumatic vascular injury

DIFFERENTIAL DIAGNOSIS

Exudative Pleural Effusion

• Proteinaceous pleural fluid due to ↑ pleural permeability

Extrapleural Hematoma

• Peripheral high-attenuation pleural mass, displaced subpleural fat (extrapleural fat sign)

Thoracic Duct Tear

• Water-attenuation fluid; traumatic chylothorax

Esophageal Rupture

• ± hemothorax or hemopneumothorax

PATHOLOGY

General Features

- Etiology
 - Blunt and penetrating thoracic trauma
 - 30-50% of blunt injuries
 - Motor vehicle collision **most common etiology**
 - o Laceration of intercostal/internal mammary vessels
 - o latrogenic injury, following emergent line placement

Microscopic Features

• Pleural fluid hematocrit > 50% of serum hematocrit

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Pleuritic chest pain and dyspnea
- Clinical profile
- Absent/diminished breath sounds, dullness to percussion
- Hemorrhagic shock and respiratory failure when large
 - Rapid bleeding from systemic vessel laceration
 - Low-pressure bleeding from lung usually self-limited
- Auscultation and percussion: Rare detection of hemothorax < 500 mL

Natural History & Prognosis

- Inadequate evacuation and organization with resultant fibrothorax
- Bacterial contamination with resultant empyema

Treatment

- Tube thoracostomy
 - 36-42 F thoracostomy tube in 6th or 7th intercostal space
 - $\circ~$ Intrapleural fibrinolytic agents to $\downarrow~$ need for surgical intervention
 - Tube removal with drainage < 100 mL/day and lung reexpansion
- VATS for evacuation of residual hemothorax; within 7 days of trauma
- Thoracotomy: Massive output (> 1 L), hemodynamic instability, empyema
- Catheter angiography directed embolization of intercostal/internal mammary arterial injury

DIAGNOSTIC CHECKLIST

Consider

• Hemothorax in traumatized patient with pleural effusion

Image Interpretation Pearls

- Careful assessment for traumatic vascular injury
- Important distinction from extrapleural hematoma, for which thoracostomy tube placement is not required

SELECTED REFERENCES

 Marro A et al: Blunt chest trauma: classification and management. Emerg Radiol. 26(5):557-66, 2019

Thoracic Splenosis

KEY FACTS

TERMINOLOGY

• Pleural autotransplantation of splenic tissue after injury

IMAGING

- Multiple pleural nodules/masses almost exclusively on left in patient with remote history of trauma
- Predilection for posterior inferior hemithorax
- Radiography
 - Incomplete border sign; obtuse angles with pleura
 - Most exhibit sharp borders, < 3 cm in diameter
 - Signs of remote trauma
- CT
 - o Multiple left basilar pleural nodules; absence of spleen
 - May exhibit contrast enhancement
 - Similar lesions may occur in abdomen and subcutaneous tissue

• Nuclear Medicine

DRBC-tagged heat damaged red blood cell scintigraphy
 Gold standard; uptake specific for splenic tissue

TOP DIFFERENTIAL DIAGNOSES

- Pleural metastases
- Asbestos-related pleural disease
- Invasive thymoma with drop metastases
- Malignant mesothelioma
- Localized fibrous tumor of pleura

PATHOLOGY

- Transdiaphragmatic pleural dissemination following thoracoabdominal trauma
- Diaphragmatic defect often not identified at surgery

CLINICAL ISSUES

• Asymptomatic; incidentally discovered on imaging

Treatment: None DIAGNOSTIC CHECKLIST

• Consider splenosis in any patient with multiple left pleural nodules and absence of intact spleen

(Left) Axial CECT of a patient with left thoracic splenosis shows multiple small left pleural nodules \implies and retained bullet fragments 🔁 from remote gunshot injury. Thoracic splenosis almost exclusively involves the left hemithorax. (Right) Graphic shows the typical features of thoracic splenosis. Multiple implants of splenic tissue 🔁 on the left inferior pleural surface are the result of prior trauma, splenic injury, and ipsilateral diaphragmatic rupture 🔁.





(Left) Axial CECT of a patient with prior gunshot wound to the abdomen shows multifocal left basilar pleural masses and nodules 🛃, consistent with splenosis. Splenectomy had been performed at the time of injury following hemodynamic instability due to splenic rupture. (Right) Axial CECT of a patient with prior blunt traumatic injury and resultant thoracic splenosis shows multiple smoothly marginated, noncalcified left pleural nodules 🔁. Thoracic splenosis may mimic unilateral solid pleural metastases.





Definitions

• Autotransplantation of splenic tissue following traumatic or surgical disruption of spleen

IMAGING

General Features

- Best diagnostic clue
 - Smoothly marginated left pleural nodules or masses in patient with history of trauma
 - Prior splenic rupture; absence of intact intraabdominal spleen
- Location
 - Thoracic splenosis; inferior posterior left pleural space
 Abdominal splenosis; typically left upper quadrant
- Size
 - Typically < 3 cm in diameter

Radiographic Findings

- Radiographic features of pleural lesion
 - **Incomplete border sign**: Combination of sharp and indistinct margins
 - Sharp margin in profile; Indistinct margin en face
 - o Obtuse angles with adjacent pleura
- Thoracic splenosis
 - Single or multiple left posterior basilar pleural nodules/masses
 - Most exhibit sharp borders, < 3 cm in diameter
 - Signs of remote trauma

CT Findings

- Multiple left basilar pleural nodules/masses
- Predilection for posterior inferior hemithorax along paraspinal and costophrenic pleura
- Noncalcified; may exhibit contrast enhancement
- Absence of spleen
- Similar lesions may occur in abdomen and subcutaneous tissue
 - Lesions may seed prior thoracostomy tube tract

Nuclear Medicine Findings

- Tc-99m sulfur colloid
 - Reticuloendothelial uptake in liver and **splenic** tissue
- Tc-99m labeled red cell scintigraphy
 - DRBC-tagged heat damaged red blood cell scintigraphy
 - Gold standard; uptake specific for splenic tissue
 - More sensitive than Tc-99m sulfur colloid scan; may be used when sulfur colloid fails to identify splenic tissue

MR Findings

- Signal characteristics and enhancement comparable to normal spleen
- Feruxomide-enhanced MR: Iron oxide cleared by reticuloendothelial system

DIFFERENTIAL DIAGNOSIS

Pleural Metastases

• Multiple pleural masses, nodular pleural thickening ± circumferential; frequent associated pleural effusion

Asbestos-Related Pleural Disease

Bilateral discontinuous nodular pleural thickening; ± calcification

Invasive Thymoma

- Prevascular mediastinal mass
- Unilateral or bilateral drop pleural metastases; rarely associated with pleural effusion

Malignant Mesothelioma

• Unilateral circumferential pleural thickening; often involves mediastinal pleura

Localized Fibrous Tumor of Pleura

 Solitary pleural nodule or mass; heterogeneous enhancement

PATHOLOGY

General Features

- Etiology
 - Follows thoracoabdominal trauma; **penetrating most common**
 - Transdiaphragmatic pleural dissemination via traumatic or congenital defect, diaphragmatic hiatus

Gross Pathologic & Surgical Features

- Pleural and abdominal implants: Serosal surfaces of solid viscera; peritoneum, omentum, subcutaneous tissue
- Diaphragmatic defect often not found at surgery

CLINICAL ISSUES

Presentation

• Asymptomatic; incidentally discovered on imaging

Demographics

- Epidemiology
 - Up to 15% of patients with splenic trauma and diaphragmatic laceration

Natural History & Prognosis

 Variable interval between splenic rupture and splenosis; months to years

Treatment

• None; differentiation from neoplastic process

DIAGNOSTIC CHECKLIST

Consider

• Splenosis in patient with prior splenic/diaphragmatic trauma and multiple left pleural nodules/masses

Image Interpretation Pearls

• Determine presence or absence of spleen in any patient with multiple left pleural nodules/masses

Reporting Tips

 Consideration of thoracic splenosis may preclude unnecessary thoracic intervention

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Rib Fractures and Flail Chest

KEY FACTS

TERMINOLOGY

- Rib fracture: Displaced or non-displaced cortical break
- Flail chest: ≥ 3 segmental (≥ 2 fractures in same rib) or > 5 adjacent rib fractures
- Flail segment shows paradoxical motion with respiration

IMAGING

- Radiography (specific but not sensitive)
 - Cortical break and step-off
 - Ribs 4-9 most commonly fractured
 - Fractures are usually multiple
 - Dedicated rib series for fracture documentation
 - Fracture visualization with healing and callus formation
 - Flail chest (up to 20% of patients with major trauma)
- **CT**: Evaluation of underlying visceral injury
 - Frequent associated extrapleural hematoma
 - Costochondral fractures
 - Marker of increased severity of trauma and higher mortality

TOP DIFFERENTIAL DIAGNOSES

- Pathologic rib fracture
- Thoracostomy tube

CLINICAL ISSUES

- Most common thoracic injury in blunt chest trauma
- Rib fractures common after CPR (anterior)
- Cough-induced rib fractures primarily affect women
- Rib fractures in children denote significant trauma
- Treatment
 - Symptomatic pain management
 - Intubation and mechanical ventilation for flail chest

DIAGNOSTIC CHECKLIST

- Pneumothorax and contusion more significant injuries than fractured ribs
- Lower rib fractures: Markers for abdominal visceral injury
- Rib series without chest radiography may miss associated pneumothorax

(Left) Graphic shows the morphologic features of flail chest. There are three consecutive left rib fractures *▶* with resultant ipsilateral pneumothorax 🔁 hemothorax 🔁, and pulmonary contusion 🔁. The rib fractures should alert the radiologist to look for signs of associated injuries in patients with chest trauma. (Right) AP chest radiograph of a patient with multiple posterior left rib fractures shows three contiguous rib fractures 🔁, a moderate left pneumothorax *⊠*, and left chest wall subcutaneous gas 🖂.





(Left) AP chest radiograph of a young patient who sustained blunt chest trauma shows fifth and sixth right rib fractures 🔁 and a deep sulcus sign 🔁 from a moderate to large right pneumothorax. It is not uncommon for pneumothoraces to not exhibit a discrete pleural line. Thus, one must look for subtle findings such as the deep sulcus sign. (Right) Axial CECT of the same patient confirms the presence of a large right pneumothorax 🔁 and optimally demonstrates the rib fractures 🔁.





Definitions

- **Rib fracture**: Displaced or non-displaced cortical break
- Flail chest: ≥ 3 segmental (≥ 2 fractures in same rib) or > 5 adjacent rib fractures
 - Flail segment shows **paradoxical motion with respiration**

IMAGING

General Features

- Best diagnostic clue
 Cortical break and step-off
- Location
 - Dependent on site of energy absorption
- Morphology
 - Traumatic rib fractures; often multiple and in anatomic alignment
 - Multiple fractures of contiguous ribs are typically vertically aligned

Radiographic Findings

- Radiographs are specific but not sensitive
 - Fractures are **usually multiple**
 - Ribs 4-9 most commonly fractured
 - Role of chest radiograph is to identify complications: Pneumothorax, pleural effusion (i.e., hemothorax)
 - 30% sensitivity for non-displaced fractures (rib fractures often missed)
- Dedicated rib series may be helpful, especially when fracture documentation is important
 - o Medical-legal cases
 - Should not substitute for chest radiography
- Fractures may only become evident with healing and callus formation
 - Initial radiographs often do not show non-displaced fractures
 - Repeat radiography 4 or more days after injury usually reveals fractures
 - Early treatment for uncomplicated rib fractures identical to treatment for bruised ribs; diagnosis delay does not hinder treatment
- Flail chest (up to 20% of patients with major trauma)
 - Segmental fractures of ≥ 3 adjacent ribs or fractures or > 5 adjacent ribs
 - Costal hook sign: Elephant trunk-shaped ribs (rotation of segmental fracture fragments)
- Traumatic 1st rib fracture, marker of high-energy chest trauma
 - 1st rib protected by clavicle and scapula
 - Aortic transection in 10%, bronchial tear in 2%
 - Non-traumatic 1st rib fracture: Very low incidence of major vascular injury
- Children with nonaccidental trauma
 - o 5-25% of all skeletal injuries in abused children
 - Typically fractures at costovertebral and costochondral junctions
 - Shaken baby: Fractures typically posterior near costovertebral junctions
 - o 1st rib fracture virtually diagnostic of abuse

CT Findings

- More sensitive than radiography
 Assessment of underlying visceral injuries
- Frequent associated extrapleural hematoma
 - Crescentic or biconvex soft tissue between fractured rib and parietal pleura
 - Differentiation from hemothorax
 Internally displaced chest wall fat
- Costochondral fractures
 - Marker of increased severity of trauma and higher mortality
 - Often difficult to identify on axial images
 - Costochondral junction step-off
 - Maximum intensity projection (MIP) reformatted images help demonstrate lucent lines across cartilage
 - Ancillary findings
 - Adjacent soft tissue and fat stranding
 - Extrapleural hematoma

Ultrasonographic Findings

- Ultrasound may detect rib fractures
 - Does not significantly increase detection rate
 - Too time consuming to justify routine use

Nuclear Medicine Findings

• Bone scintigraphy sensitive for identification of stress fractures, bone metastases, and fractures in suspected child abuse

Imaging Recommendations

- Best imaging tool
 - Chest radiography usually sufficient for clinically important decisions
 - Exclusion of pneumothorax, pleural effusion, pulmonary contusion
- Protocol advice
 - Routine radiographic follow-up of fractures not recommended
 - CT volume-rendered images significantly reduce interpretation time for identification of rib fractures

DIFFERENTIAL DIAGNOSIS

Pathologic Rib Fracture

- Typically not aligned or adjacent to each other
- Uncommon contiguous fractures
- Skeletal lesion at fracture site
- May result from minimal trauma
- Does not manifest with comorbidities, such as pneumothorax

Thoracostomy Tube

• Thoracostomy tubes may mimic ribs &/or displaced rib fractures on CT

PATHOLOGY

General Features

- Etiology
 - Rib stability
 - Maximal chest wall weakness at 60° rotation from sternum; flatter less supported ribs

- Anterior-posterior compression: Ribs typically fracture in 2 places: 60° from sternum, and posteriorly
- **Trauma**: Direct blow from motor vehicle collision, fall, assault, contact sports
- Severe coughing
- Stress rib fractures uncommon
 - Locations: Anterolateral 1st rib, lateral 4th-9th ribs, posteromedial upper ribs
 - Golfers (duffer's fracture), canoeists, rowers, swimmers, weightlifters, ballet dancers
- Isolated 1st rib fracture
 - May represent avulsion injury, especially from throwing motion, rowing, or related to whiplash
 - Avulsion from scalene muscle attachment

Gross Pathologic & Surgical Features

- Paradoxical flail segment motion (pendelluft breathing)
 - Segment moves inward with inspiration and outward with expiration

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Physical exam sensitive but not specific
 - Chest wall pain, pain with deep breathing, sneezing, or coughing
 - o Severe local rib tenderness, swelling, &/or crepitus
- Other signs/symptoms
 - Flail chest
 - May not be clinically evident in 1/3 of cases
 - Clinical findings masked by positive pressure ventilation; delayed diagnosis
 - Traumatic extrathoracic intercostal lung herniation; rare extraordinary associated injury

Demographics

- Age
 - More common with advancing age
 - Longer duration of pain
 - Admission of older patients for observation and treatment of isolated rib fractures is both justified and beneficial
 - Overall trauma-related mortality higher in older patients with multiple rib fractures than in younger patients
- Epidemiology
 - Most common thoracic injury in blunt chest trauma (10%)
 - Rib fractures ominous in children and older adults
 - Ribs difficult to fracture in children due to plasticity; fractured ribs signify significant trauma
 - Rib fractures more common in older adults due to osteoporosis and decreased muscle mass; increased morbidity and mortality
 - Rib fractures common following cardiopulmonary resuscitation (CPR); typically anterior rib fractures
 - Typically underreported, occur in up to 30%
 - Cough-induced rib fractures occur primarily in women with chronic cough
 - Middle ribs along lateral rib cage most commonly affected
 - Pertussis infection, post-nasal drip

o Flail chest: Level 1 trauma center 1-2 cases/month

Natural History & Prognosis

- Typically heal with callus
 Desclusion and ecoudoacted
- Rarely non-union and pseudoarthrosis
 Multiple bilateral healed rib fractures common in alcoholics
- Mortality and morbidity increase with number of fractured ribs and age (> 65 years)
- Location
 - Right-sided rib fractures below 8th rib: 20-50% probability of liver injury
 - Left-sided rib fractures below 8th rib: 25% probability of splenic injury
 - 1st and 2nd rib fractures not indication for investigating aortic injury in absence of other findings of aortic transection
- Flail chest
 - Acutely, associated with mortality rates of 10-20%
 - Chronically, 25-50% have long-term disability, including chronic chest wall pain and exertional dyspnea

Treatment

- Options, risks, complications
 - Atelectasis: Common sequela of rib fractures, predisposes to pneumonia
 - Often complicated by lung contusion, laceration, pneumothorax, hemothorax
 - Rarely, sharp edges of extremely displaced rib fractures may puncture or lacerate viscera
 - Diaphragm
 - Aorta
 - Airway
 - Heart
- Symptomatic pain management
 - o Oral analgesia
 - Epidural analgesia, especially for flail chest, associated with decreased nosocomial pneumonia and shorter duration of mechanical ventilation
- Observation for development of delayed hemothorax
- Surgical fixation rarely necessary
- Intubation and mechanical ventilation
 - Need determined by underlying cardiopulmonary status, not presence or absence of flail segments

DIAGNOSTIC CHECKLIST

Consider

• Pneumothorax and contusion are clinically more significant injuries than rib fractures

Image Interpretation Pearls

- Lower rib fractures: Markers for abdominal visceral injury
- Dedicated rib radiographs without chest radiography may miss associated pneumothorax

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Rib Fractures and Flail Chest





(Left) Coned-down PA chest radiograph shows multiple right segmental rib fractures suggestive of flail chest, a right clavicle fracture \square , and a tiny right apical pneumothorax. Multifocal rib fractures are common in blunt . chest trauma, particularly severe motor vehicle collisions. (Right) 3D reformatted image from NECT shows multiple segmental rib fractures 🛃, concerning for flail chest. Flail chest is a clinical diagnosis characterized by local paradoxical motion of the chest wall but can be suspected on imaging.





(Left) PA chest radiograph of a patient with blunt chest trauma shows a lentiform $opacity \ge along the$ peripheral right mid and upper hemithorax that exhibits the incomplete border sign. (Right) Axial NECT of the same patient shows an extrapleural hematoma that manifests as a lentiform high-attenuation $collection \rightarrow that displaces$ subpleural fat 🖂, a small right hemothorax \square , and a posterior rib fracture 🔁. Differentiation of hemothorax from extrapleural hematoma is critical, as evacuation of the latter is rarely required.





(Left) Composite image with axial CECT of a patient who sustained blunt chest trauma shows costochondral fractures that exhibit cartilaginous stepoff \square of two left costal cartilages, one with intrinsic air 🔁 from associated pneumothorax. (Right) Coronal CECT MIP image of the same patient shows costochondral fractures that manifest with cartilaginous discontinuity \supseteq and intrinsic air across a displaced costochondral fracture 🖂 Costochondral fractures are markers of increased mortality.

Spinal Fracture

KEY FACTS

IMAGING

- Anterior compression fracture
 - Almost always involves superior endplate
 - < 40-50% height loss with normal bone density; greater loss of height suggests Chance fracture
- Burst fracture
 - Vertebral compression on lateral radiograph
 - Wide interpedicular distance on frontal radiograph
- Flexion-distraction (Chance) fracture
 - o > 40-50% vertebral body height loss
 - Focal kyphosis; separation of facet joints and increased interspinous distance
- Fracture-dislocation
- Gross malalignment
- CT for emergent evaluation of skeletal injury and alignment
- MR for evaluation of soft tissue injury and cord contusion
- **CT** is imaging modality of choice in initial evaluation of skeletal injury and alignment

TOP DIFFERENTIAL DIAGNOSES

- Spinal abscess
- Spinal metastasis

PATHOLOGY

- 3-column model of Davis
 - Anterior column: Anterior 2/3 of vertebral body
 - Middle column: Posterior 1/3 of vertebral body
 - Posterior column: Posterior elements
- Spinal instability if more than 2-column failure

CLINICAL ISSUES

- Signs and symptoms
 - Hypotension without tachycardia; priapism

DIAGNOSTIC CHECKLIST

• Widened interpedicular distance suggests burst fracture and vertebral instability

(Left) Graphic shows the morphologic features of thoracolumbar fracture dislocation, a common location for spinal fractures due to flexion forces in blunt trauma. (Right) Composite image with axial NECT (left) and sagittal volume-rendered 3D reformation (right) shows a T12 anterior column fracture ➡. Sagittal image shows the superior endplate T12 fracture without evidence of thoracolumbar malalignment. Given isolated single column involvement, the fracture is considered stable and is managed conservatively.

(Left) Composite image with axial (left) and sagittal (right) CECT shows a T5 burst fracture \square , which involves the posterior aspect of the vertebral body with a small fragment displaced into the spinal canal 🔁. Burst fractures are often unstable and can be associated with spinal cord trauma. (Right) Composite image with axial (left) and sagittal (right) CECT shows a T7 Chance fracture *→* with extensive comminution extending into the spinal canal ightarrow 2 and a fracture of the posterior elements 🔁.









IMAGING

General Features

- Best diagnostic clue
 - Compression fracture
 - Most common thoracic spine fracture due to blunt trauma
 - Wedge-shaped vertebral body deformity
 - **Burst fracture**: Compressed thoracic vertebral body with fractured endplates and widened pedicles
 - Flexion-distraction (Chance) fracture: Anterior compression deformity with posterior distraction
 - Fracture-dislocation: Gross vertebral malalignment + fracture(s)
- Location
 - Thoracolumbar junction most vulnerable site

Radiographic Findings

- Anterior compression fracture
 - Paraspinal hematoma and kyphosis
 - Almost always involves superior endplate
 - o < 40-50% loss of height with normal bone density; if greater loss of height, probably Chance fracture
- Burst fracture
 - Widened interpedicular distance on AP radiograph; wedge-shaped vertebral body on lateral radiograph
 Possible malalignment
- Flexion-distraction (Chance) fracture
 - o Usually > 40-50% vertebral body height loss
 - Focal kyphosis; separation of facet joints and increased interspinous distance
- Fracture-dislocation: Gross malalignment

CT Findings

- Bone CT
 - Anterior compression fracture
 - Mild anterior wedging with associated fracture
 - Absence of posterior cortical displacement and posterior element fractures
 - Burst fracture
 - Stellate fracture pattern
 - Flexion-distraction (Chance) fracture
 - Fractured vertebral body, often comminuted
 - Separation of facet joints and increased interspinous distance

• Fracture-dislocation

- Widened, comminuted neural arch
- Fracture through facet joints
- Overlapping or uncovered articulating processes on axial imaging
- Vertebral body comminution; retropulsed fracture fragments in spinal canal

MR Findings

- Burst fracture
 - May be associated with cord contusion
- Flexion-distraction (Chance) fracture
 - T2WI: Disruption of posterior longitudinal ligament, interspinous ligaments
 - Anterior longitudinal ligament usually intact but may be stripped from vertebra inferior to fracture

- Fracture-dislocation
 - o Cord edema/compression, skeletal distraction

Imaging Recommendations

- Best imaging tool
 - CT is imaging modality of choice in initial evaluation of skeletal injury and alignment
 - o MR for evaluation of soft tissue injury and cord contusion

DIFFERENTIAL DIAGNOSIS

Spinal Abscess

- Marrow edema in facet articular processes and adjacent laminae on MR
- Surrounding soft tissue edema/enhancement; direct visualization of abscess

Spinal Metastasis

- More likely to involve inferior cortex of vertebral body
- Involvement of posterior elements and vertebral body

PATHOLOGY

General Features

- 3-column model of Davis
 - Anterior column: Anterior 2/3 of vertebral body
 - Middle column: Posterior 1/3 of vertebral body
 Posterior column: Posterior elements
- Spinal instability if more than 2-column failure

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Pain, point tenderness
 - Hypotension without tachycardia
 - o Priapism

Demographics

- Epidemiology
 - 2% incidence in blunt chest trauma
 - o 15% have fractures at multiple levels

Treatment

• Surgical fixation of thoracic spine fractures ± canal decompression

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Widened interpedicular distance suggests burst fracture and vertebral body instability
- Severe compression fracture in patient with normal bone density suggests Chance fracture
- Compression fracture of inferior endplate with normal superior endplate suspicious for pathologic fracture

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Sternal Fracture

KEY FACTS

IMAGING

- Best diagnostic clue
 - Anterior chest wall trauma; sternal tenderness
 - Direct visualization of cortical discontinuity
- Radiography
 - Lateral: Visualization of fracture line
 - Frontal: Difficult fracture visualization
 - ± abnormal superior mediastinum on frontal radiography: Mediastinal hemorrhage
- CT
 - Direct visualization of sternal fracture
 - Increased sensitivity with multiplanar imaging
 - Evaluation of associated injuries
- MR
 - Useful in diagnosis of sternal stress fractures
 - o T1WI: Intermediate signal intensity
 - o T2-weighted fat-suppressed images: High signal intensity

TOP DIFFERENTIAL DIAGNOSES

- Pathologic fracture
- Osteomyelitis
- Pectus excavatum
- Ossification centers

CLINICAL ISSUES

- Mechanism of injury: Motor vehicle collision (68%)
- Symptoms
 - o Localized sternal pain (98%)
 - Palpable mass with point tenderness
 - o Ecchymosis (50%)
- Mortality rate (25-45%); associated with serious intrathoracic injury

DIAGNOSTIC CHECKLIST

- MDCT is imaging modality of choice
- Lateral radiography is useful for demonstrating fracture and degree of sternal displacement

(Left) Lateral chest radiograph of an older patient who sustained chest trauma shows displaced comminuted fractures of the sternal body 🔁, manubrium 🖾, and thoracic spine 🖂. Lateral radiography is superior to frontal radiography for detecting sternal fractures. (Right) Sagittal CECT of the same patient shows sternal fractures 🔁, associated callus formation \blacksquare , and multiple thoracic spine fractures 🖂 CECT allows exclusion of retrosternal hematoma &/or traumatic aortic injury.





(Left) Axial CECT of an older patient involved in a motor vehicle collision shows a comminuted displaced sternal fracture with presternal \triangleright and retrosternal ightarrowhematoma. Note the absence of mediastinal hemorrhage or traumatic vascular injury. (Right) Axial CECT shows a comminuted sternal fracture *▶*, a small displaced fracture fragment 🔁 in the prevascular mediastinum, and a small traumatic aortic pseudoaneurysm ₽.





IMAGING

General Features

- Best diagnostic clue
 - o Direct visualization of sternal cortical discontinuityo Anterior chest wall trauma; sternal point tenderness
- Location
 Mid sternal body, most common location
- Morphology
 - Usually transverse and nondisplaced

Radiographic Findings

- Radiography
 - Lateral radiography
 - Direct visualization of sternal fracture
 - Transverse mid body (60% nondisplaced)
 Association with thoracic spine fracture
 - Association with thoracic spine fracture
 Frontal radiography: Typically not visualized
 - ± abnormal superior mediastinum

CT Findings

- Direct visualization and assessment of sternal fractures
- Associated injuries
 - **Retrosternal hematoma**: Smooth, elongated, or rounded soft tissue
 - Mediastinal hematoma: Hemorrhage of sufficient magnitude; not always related to vascular injury
 - Aortic injury: Irregular aortic contour, aortic wall disruption/pseudoaneurysm, mediastinal hematoma
 - Myocardial contusion, hemopneumothorax, lung contusion/laceration
 - Manubriosternal dislocation (rare)

MR Findings

- Useful in diagnosis of sternal **stress fractures**
 - o T1WI: Intermediate signal intensity
 - o T2-weighted fat-suppressed images: High signal intensity
- Imaging Recommendations
- Best imaging tool
 - Lateral radiography; optimal projection
 - MDCT with multiplanar reformatted and MIP images improves diagnostic sensitivity
- Protocol advice
 - Sagittal and coronal reformatted images and 3D reformations improve diagnostic accuracy

DIFFERENTIAL DIAGNOSIS

Pathologic Fracture

- Underlying neoplastic lesions with bone destruction
- History of malignancy

Osteomyelitis

- Associated soft tissue mass
- Constitutional symptoms: Fever, chills, malaise
- Skeletal scintigraphy for early diagnosis

Pectus Excavatum

No cortical discontinuity

Ossification Centers

• Nonunited ossification centers may simulate fracture

PATHOLOGY

General Features

- Etiology
 - o Deceleration injury or direct anterior chest wall trauma
 - Motor vehicle collision (seat belt injury)
 - Cardiopulmonary resuscitation (CPR)
 - Stress fractures: Golfers; weight lifters; women with osteoporosis, vitamin D deficiency, kyphotic thoracic spine
- Associated abnormalities
 - o Peristernal hematoma, mediastinal hematoma
 - Thoracic aortic/vascular injury
 - Pulmonary or myocardial contusion
 - o Vertebral fractures in 1.4%; rib fractures

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Localized sternal pain (98%)
 - Palpable mass with point tenderness
 - Ecchymosis (50%)
 - o Dyspnea (15-20%); painful respiration

Demographics

- Sex
- Older patients and women most commonly affected
- Epidemiology
 - Most common mechanism of injury: Motor vehicle collision (68%)

Natural History & Prognosis

 Mortality rate (25-45%); serious intrathoracic injury
 Myocardial contusion (8%), thoracic aortic injury (4%), heart laceration (2.5%)

Treatment

- Directed toward associated injuries, monitor for cardiac injury
- Analgesia with appropriate opiates or nonsteroidal antiinflammatory drugs
- Surgical fixation: Nonunion, severe pain, respiratory regurgitation, sternal instability

DIAGNOSTIC CHECKLIST

Consider

 Evaluation of patients with sternal fracture to exclude associated serious intrathoracic injury

Image Interpretation Pearls

• No established relationship between sternal fracture and cardiac or aortic injury

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Diaphragmatic Rupture

KEY FACTS

TERMINOLOGY

- Traumatic hemidiaphragm laceration
 - May result in intrathoracic herniation of abdominal organs

IMAGING

- Left visceral herniation in 70-90% of cases
- Radiography
 - Low sensitivity: 50% for left-sided and 20% for rightsided tears
 - Abnormal diaphragmatic contour
 - Intrathoracic air-filled bowel/enteric tube
- CT
 - Direct visualization of diaphragmatic discontinuity
 - Collar sign: Focal constriction of bowel or liver by torn diaphragm edges
 - Dependent viscera sign: Herniated abdominal contents abut posterior ribs

TOP DIFFERENTIAL DIAGNOSES

- Diaphragmatic eventration
- Bochdalek hernia
- Diaphragmatic paralysis
- Pleural effusion: Subpulmonic/loculated

PATHOLOGY

- High-energy blunt thoracoabdominal trauma
 - Sudden rise in intraabdominal pressure ruptures diaphragm
 - o Lateral impact distorts chest wall and shears diaphragm

CLINICAL ISSUES

- Nonspecific signs and symptoms
- Latent: May manifest late in hospital course

DIAGNOSTIC CHECKLIST

• Diagnosis requires high index of suspicion and careful evaluation of multiplanar reformatted images

(Left) Graphic demonstrates a ruptured left hemidiaphragm and intrathoracic herniation of the gastric fundus through a small diaphragmatic defect. The nasogastric tube courses normally through the esophagogastric junction \blacksquare , but the tip 🔁 is in the intrathoracic gastric fundus. (Right) Coronal CECT of a patient with left diaphragmatic rupture shows gastric herniation into the thorax through a ruptured left hemidiaphragm. Note the nasogastric tube tip 🛃 in the *intrathoracic gastric fundus* and bilateral chest tubes 🕰.





(Left) AP chest radiograph of a patient status post severe thoracoabdominal blunt trauma shows poor visualization of the left hemidiaphragm and increased opacity in the left inferior hemithorax. Basilar airspace disease and pleural effusion may also obscure diaphragmatic visualization. (Right) Axial CECT shows intrathoracic location of the stomach, omentum, and bowel. The stomach abuts the left posterior ribs 🔁 (dependent viscera sign), confirming left diaphragmatic rupture.





Synonyms

• Diaphragmatic tear or laceration

Definitions

- Traumatic diaphragmatic laceration
 - o More common with blunt than penetrating traumao May result in intrathoracic herniation of abdominal
 - organs

IMAGING

General Features

- Best diagnostic clue
 - Air-filled bowel above hemidiaphragm
 - Increased accuracy with supradiaphragmatic enteric tube
- Location
 - Right and left sides likely equally affected
 - Visceral herniation more common on left (70-90%)
 - Liver less likely to herniate through right-sided lacerations
- Size
 - o Variable
 - Small in penetrating trauma
 - Large in blunt trauma
 - Prevalence of visceral herniation increases with larger tears
- Morphology
 - Blunt: Linear or radial tears typically at hemidiaphragm dome where tendon is thinnest
 - Most commonly extend posterolaterally along embryonic closure of pleuroperitoneal membrane

Radiographic Findings

- Abnormal in 90% of cases; sensitivity 50% for left-sided tears and 20% for right-sided tears
 - Often nonspecific due to associated lower lobe atelectasis or contusion
- Abnormal diaphragmatic contour
 - Hemidiaphragm elevation > 7 cm
 - o Positional change of hemidiaphragm contour/shape
- Intrathoracic air-filled bowel
- Intrathoracic enteric tube
 - Tear usually spares esophageal hiatus
 - Enteric tube courses into abdomen and then into hemithorax
- Contralateral mediastinal shift: Mass effect from visceral herniation
- Bowel strangulation
 - o Pleural effusion suggests strangulation
 - With open communication, pleural fluid may not accumulate in pleural space
 - Omental fat may simulate pleural effusion; may layer on decubitus imaging

Upper Gastrointestinal Series

- Visualization of herniated bowel
- Approximation and narrowing of afferent/efferent bowel loops (pinched limbs) through diaphragmatic defect (collar sign, kissing birds sign)

CT Findings

- **Dependent viscera sign**: Herniated bowel or viscera no longer supported posteriorly by diaphragm
 - Right: Upper 1/3 of liver in contact with posterior ribs
 - Left: Stomach or bowel contact with posterior ribs
 Stomach or bowel posterior to spleen
- **Direct visualization** of diaphragmatic discontinuity • Segmental absence of hemidiaphragm
 - Potential false-positive: Normal posterolateral diaphragmatic defects in 5% of cases
 - Diagnosis should not be based on this sign alone
- **Collar sign**: Visceral herniation with focal constriction of bowel or liver by torn diaphragm edges
- Diaphragmatic thickening
 - Muscle retraction vs. muscular hematoma
 - Subjective finding; high proportion of false-positives
 Normal crural thickness variation with age and sex
- Blunt trauma
 - Left diaphragmatic tear: Sensitivity 71-90%; specificity 98-100%
 - Right diaphragmatic tear: Sensitivity 70-80%; specificity 100%
 - Coronal and sagittal reformatted images may increase diagnostic confidence
- Penetrating trauma
 - Same as blunt trauma but includes
 - Trajectory of missile or penetrating instrument (sensitivity 35%; specificity 100%)
 - Active extravasation of contrast (sensitivity < 10%)

MR Findings

• Similar to CT; difficult to perform in acute trauma setting

Nuclear Medicine Findings

• Liver-spleen scintigraphy for diagnosis of right diaphragmatic tear (scintigraphic collar sign)

Imaging Recommendations

- Best imaging tool
 - Diaphragmatic indistinctness/elevation on radiography should raise index of suspicion
 - CT is imaging modality of choice for global evaluation in polytrauma
- Protocol advice
 - Reformatted images increase sensitivity for diaphragmatic tears: Sagittal > coronal > axial

DIFFERENTIAL DIAGNOSIS

Diaphragmatic Eventration

- Intact hemidiaphragm
- No associated injuries, dependent viscera sign, or bowel loop approximation
- Difficult evaluation if preexistent condition in setting of recent blunt trauma

Bochdalek Hernia

- Herniated abdominal content through normal remnant of pleuroperitoneal canal
- Posterior; more common on left
- Normal aging process, more common with emphysema

Diaphragmatic Paralysis

• Paradoxical motion on fluoroscopic sniff test

Pleural Effusion: Subpulmonic/Loculated

- May mimic hemidiaphragm elevation
- No abnormally positioned air-filled bowel
- Intact diaphragm and diaphragmatic crus

Paraesophageal Hernia

- Large hernia may preferentially extend to right or left hemithorax
- Diaphragmatic contour typically intact

Esophageal Rupture

• Tear rare at esophageal hiatus

Subphrenic Abscess

- Diaphragm intact, separate from bowel
- Clinical presentation of chronic infection

Morgagni Hernia

• Congenital defect of anteromedial diaphragm (sternocostal triangle)

PATHOLOGY

General Features

- Etiology
 - High-energy blunt thoracoabdominal trauma
 - Sudden rise in intraabdominal pressure ruptures diaphragm
 - Lateral impact distorts chest wall and shears diaphragm
 - o Physiology
 - Diaphragm separates abdomen (positive intraabdominal pressure) from thorax (negative intrapleural pressure)
 - 7-20 cm H₂O pressure gradient between abdomen and pleura favors intrathoracic visceral herniation
- Associated abnormalities
 - Rib fractures 90%
 - o Liver or spleen laceration 60%
 - Pelvic fractures 50%
 - Traumatic aortic injury 5%
 - High association with head injury
- Kinetic energy absorption does not respect anatomic borders
 - Multiple simultaneous injuries above and below diaphragm
- Spontaneous healing uncommon; herniated structures prevent approximation of torn edges
- Most frequently herniated organs
 - Left: Stomach > colon > spleen
 - Right: Liver
- Penetrating injuries usually smaller (< 1-cm diameter)

Gross Pathologic & Surgical Features

- Blunt: Radial tear extends from central tendon posterolaterally
 - o > 2 cm long (most > 10 cm long)
- Penetrating: Any location; typically < 1 cm long

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Nonspecific; consider in any patient with blunt thoracoabdominal injury
 - Initially missed in 7-66% of cases; right hemidiaphragm most commonly affected in missed cases
- Other signs/symptoms
 - Thoracic splenosis may rarely occur years after injury
 Rupture with intrapericardial herniation is rare
- Latent: May manifest late in hospital course, especially after weaning from ventilator
 - During normal respiration, pressure gradient exacerbates herniation of abdominal contents
 - Importance of high index of suspicion
- Bowel obstruction
 - Bowel strangulation
 - Strangulation in 85% of cases within 3 years (presentation may be delayed for decades)
 - Obstructive symptoms, fever, chest pain

Demographics

- Age
 - o Adults and children equally affected
 - Most common in young men
- Epidemiology
 - o 0.8-8% in cases of blunt trauma

Natural History & Prognosis

- Diagnosis delayed in 25% of cases
 - o Initial nonspecific signs; injury not considered
 - Affected by changes in pressure
 - Positive pressure ventilation may delay herniation until spontaneous respiration resumes
- Morbidity and mortality higher with strangulation
 - New pleural effusion in patient with herniated bowel heralds onset of strangulation

Treatment

- Immediate surgical repair of other life-threatening injuries, such as traumatic vascular injury
- Surgical repair of torn diaphragm and reduction of herniation

DIAGNOSTIC CHECKLIST

Consider

• Diagnosis requires high index of suspicion and careful evaluation of multiplanar reformatted images

- 1. Fadl SA et al: Core curriculum illustration: blunt traumatic diaphragmatic hernia. Emerg Radiol. 27(2):215-7, 2020
- Hammer MM et al: Traumatic injuries of the diaphragm: overview of imaging findings and diagnosis. Abdom Radiol (NY). 42(4):1020-7, 2017
- Petrone P et al: Diaphragmatic injuries and post-traumatic diaphragmatic hernias. Curr Probl Surg. 54(1):11-32, 2017
- Desir A et al: CT of blunt diaphragmatic rupture. Radiographics. 32(2):477-98, 2012
- Bergin D et al: The "dependent viscera" sign in CT diagnosis of blunt traumatic diaphragmatic rupture. AJR Am J Roentgenol. 177(5):1137-40, 2001

Diaphragmatic Rupture





(Left) Lateral oblique upper GI series of a patient status post blunt trauma shows gastric herniation through a ruptured left hemidiaphragm. The stomach is constricted **₽** by the torn diaphragm edges (the collar sign). (Right) Coronal CECT shows a left diaphragmatic rupture with intrathoracic gastric herniation. The stomach is constricted by the edges of the torn hemidiaphragm 🛃 (the collar sign). Posttraumatic splenic laceration 🔁, hemoperitoneum, and hemothorax are also present.





(Left) Axial CECT of a patient who sustained blunt thoracoabdominal trauma shows that the liver abuts the right posterior ribs (dependent viscera sign), one of which is fractured 🛃. Note the small right hemothorax and chest wall subcutaneous gas. (Right) Coronal CECT of the same patient shows right diaphragmatic rupture and intrathoracic liver herniation with hepatic constriction by the torn diaphragmatic edges ➡ (the collar sign). Multiple fractured ribs **≥**, a common finding in the setting of blunt trauma, were present.





(Left) Axial NECT of a patient with a remote history of blunt thoracoabdominal trauma shows a soft tissue mass 🛃 adjacent to the right hemidiaphragm and an old right posterior rib fracture \blacksquare . (Right) Sagittal NECT of the same patient shows herniation of a small portion of the liver $\stackrel{\cdot}{\blacksquare}$ into the left hemithorax, consistent with a small focal right diaphragmatic tear. The dependent viscera sign is not present due to the small and focal nature of the diaphragmatic defect and the small amount of herniated liver.



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Introduction

A frequent challenge for general and thoracic radiologists is the imaging assessment of the chest in patients who are undergoing or have undergone treatment of thoracic and systemic diseases. Radiographic findings are often unrevealing or nonspecific, and sometimes expected post-treatment findings may simulate pathologic conditions. An important step in the imaging assessment of the treated patient is developing an understanding of the disease process being treated and the specific treatment or treatments used. Some examples include the patient's location (e.g., intensive care unit, inpatient ward, outpatient clinic), the method of treatment (e.g., surgery, ablation procedure, pleurodesis), &/or the type of medical treatment used (e.g., drugs, chemotherapy, immunotherapy, radiotherapy).

The interpreting radiologist is often provided with limited clinical information that typically consists of the indication for the specific imaging study requested. For this reason, it is often helpful to gather additional relevant information via direct communication with the referring physician or other provider or by reviewing relevant entries in the electronic medical record. The patient's history and physical exam typically list prior treatments and surgeries, current therapies, and plans for future management.

The approach to the post-treatment chest includes assessment of various medical and support devices commonly identified on radiography, evaluation of prior surgical or interventional procedures and their potential complications, monitoring response to therapy, and identification of treatment-related complications.

Tubes and Lines

A significant volume of radiographic interpretation in the inpatient setting consists of portable or bedside radiography for assessment of medical devices. These studies are usually performed to document the exact location of the support apparatus and potential complications arising from its placement. Familiarity with normal imaging anatomy allows the radiologist to assess appropriate device position and alert the clinical team regarding device malposition and associated complications. Interpretation of portable radiographs is often challenging, as radiographic technique is limited compared to conventional radiography, and resultant images may be compromised by magnification, motion, improper positioning, large body habitus, and overlying extraneous radiopaque objects.

Common support devices routinely assessed with portable chest radiography include central venous catheters, peripherally inserted central catheters (PICC), pulmonary artery catheters, endotracheal tubes, enteric tubes, intraaortic balloon pumps (IABP), pacemakers/implantable cardioverter-defibrillators (ICD), ventricular assist devices (VAD), and extracorporeal membrane oxygenation (ECMO) devices.

Portable chest radiographs obtained for documentation of medical device position must be carefully interpreted with a high index of suspicion for potential malposition or complications. For example, central line placement is often initially attempted on the right side. Therefore when a leftsided central catheter is identified, even when appropriately positioned, the entire thorax must be scrutinized to exclude contralateral pneumothorax &/or pleural effusion or interval mediastinal widening due to hemorrhage from vascular injury. Such findings typically indicate complications from an attempted contralateral catheter placement. It should be noted that radiographic abnormalities that are easily seen on conventional chest radiography may be more difficult to identify on portable radiographs. For instance, a pneumothorax on supine radiography may manifest with the **deep sulcus sign** or as a hyperlucent hemithorax rather than the apical pleural line seen on upright PA radiography. Likewise, a pleural effusion may manifest as increased haziness over the lung bases rather than the typical **meniscus sign** seen on upright radiography.

Surgical Procedures

A variety of procedures are used in the surgical management of thoracic diseases. These include sublobar resection, lobectomy, pneumonectomy, sternotomy, cardiac transplantation, single- and double-lung transplantation, and esophagectomy. The radiologist must develop familiarity with the postoperative appearance of these procedures as well as with their known complications.

Radiographic interpretation in patients who have undergone thoracic surgical procedures can be challenging. It is usually important to review the clinical chart or consult with the clinical team to establish the nature of the surgical procedure performed. This helps avoid erroneous interpretation of expected postsurgical findings. A good example is the appearance of the pleural space following pleurodesis. Such patients characteristically develop high-attenuation nodular pleural thickening that often exhibits exuberant FDG avidity, but may occasionally develop nodular pleural thickening of soft tissue attenuation that may mimic solid pleural metastases. An awareness of the expected imaging manifestations of prior surgical treatments can prevent unnecessary additional imaging &/or tissue sampling.

Medical Treatment

Medical treatment may also produce a variety of expected imaging manifestations. The medical literature establishes that several drugs can produce pulmonary toxicity. The sheer number of drugs associated with pulmonary toxicity and the variable imaging manifestations of toxicity can be overwhelming. An excellent source available through the internet for public consultation can be found at www.pneumotox.com. This website provides an extensive and thorough evidence-based list of drugs that produce toxicity and the specific pathologic and imaging findings of such drug reactions.

When interpreting chest imaging studies of patients undergoing drug treatment, it is important to assume that drug toxicity may be present. Knowledge of idiosyncratic manifestations, length and timeline of drug therapy, and dosage may be critical in determining whether drug-induced lung disease is more or less likely.

Radiation

Often patients with thoracic malignancies undergo radiation therapy. It is important for radiologists to be familiar with thoracic changes following radiation. Radiation changes include various patterns, such as radiation pneumonitis, fibrosis, and organizing pneumonia. The latter pattern is relatively common and often misinterpreted for progression of disease, as it typically exhibits new multifocal opacities with increased FDG uptake on PET/CT.

Vascular Catheters







(Left) Composite image with PA chest radiographs shows interval mediastinal widening 🔁 due to mediastinal hematoma after left internal jugular catheter placement (right) compared to prior chest radiograph (left) that documented a previously normal mediastinum. (Right) PA chest radiograph shows a moderate left pneumothorax after placement of a left pectoral implantable cardioverter defibrillator. Pneumothorax is a known complication of line placement via subclavian approach.

Radiation-Induced Lung Injury



Pleurodesis



(Left) Axial fused FDG PET/CT of a patient undergoing right lung irradiation shows bilateral FDG-avid consolidations 🛃. Open lung . biopsy demonstrated multifocal organizing pneumonia. (Right) Composite image with axial NECT (left) and FDG PET (right) of a patient with prior talc pleurodesis for malignant pleural effusion shows calcified left pleural nodules \blacksquare . Talc elicits a pleural granulomatous reaction that is often FDG avid ₽.

Lung Transplantation



Chemotherapy

(Left) Composite image with coronal minIP (left) and coronal 3D reformatted image (right) of a patient with bilateral lung transplant shows anastomotic dehiscence manifesting with an air-filled outpouching \boxtimes at the right bronchial anastomosis also seen on the 3D reformatted image 🛃. (Right) Axial NECT of a patient treated with busulfan shows extensive bilateral peribronchovascular heterogeneous airspace disease proven to represent organizing pneumonia on open lung biopsy.

KEY FACTS

IMAGING

- Endotracheal tube (ETT)
 - Neutral position: Tube tip 5-7 cm from carina
 - Tube tip moves distally with cervical flexion
 - Tube tip moves proximally with cervical extension
 - Tube width: Ideally at least 2/3 of tracheal width
 - Complications: Bronchial intubation, esophageal intubation, ventilator-associated pneumonia, tracheal/vocal cord injury, tracheal stenosis, barotrauma

• Tracheostomy tube (TT)

- No mobility with cervical flexion and extension
- Complications: Pneumothorax, pneumomediastinum, mediastinal hemorrhage, false tract

• Gastric tube (GT)

- Air suction in supine position; tube tip in antrum
- Fluid suction in supine position; tube tip in fundus
- Tip ~ 10 cm caudal to gastroesophageal junction; side holes in stomach

• Complications: Coiling, knot formation, tracheobronchial intubation, perforation

• Feeding tube (FT)

- Tip beyond pylorus at ligament of Treitz
- Complications: Coiling in pharynx, esophagus, stomach; tracheobronchial intubation; aspiration
- Radiography always performed after ETT, TT, GT, or FT placement to document position and identify complications

CLINICAL ISSUES

- Critically ill and postoperative patients
- ETT initial malposition in ~ 27% of cases
- Pitfalls: Superimposed extraneous devices, external portions of enteric tubes

DIAGNOSTIC CHECKLIST

• Importance of knowledge of normal and variant imaging anatomy and recognition of malpositioned tubes and associated complications

(Left) AP chest radiograph of a critically-ill patient with head (not shown) in neutral position shows an appropriately positioned endotracheal tube with the tube tip \square approximately 5 cm proximal to the carina \supseteq . (Right) Graphic shows variations in endotracheal tube tip position with neck flexion and extension. The tube tip descends with neck flexion (left) and ascends with neck extension (right). Assessment of endotracheal tube position should take into account the degree of cervical flexion or extension.











Definitions

- Endotracheal tube (ETT): Airway management/protection (intraoperative/postoperative, shock), risk of airway compromise (stroke, overdose, coma), mechanical ventilation/oxygenation, respiratory failure, upper airway obstruction, resuscitation of critically-ill patients
 Dual-lumen ETT: Differential lung ventilation
- Tracheostomy tube (TT): Long-term mechanical ventilation • Surgical stoma in anterior trachea
- Usually placed 1-3 weeks post initial intubation
 Gastric tube (GT): Gastric aspiration/decompression,
- nutritional support, drug administration
- Feeding tube (FT): Enteral nutrition

IMAGING

General Features

- Location
- Nasal or oral placement
- Morphology
 - Thin vertical radiopaque line for optimal visualization
 - Inflatable cuff in ETT
 - Metallic density tip in some GTs; long stiff weighted metallic tip in FTs

Radiographic Findings

- ETT
 - Carina located at T5-T7
 - Neutral head and neck position
 - Tube tip ideally 3-7 cm proximal to carina
 - Approximately at T2-T4
 - Cervical flexion: ETT may descend 2 cm
 - Tip of mandible overlies clavicles
 - Tube tip 3-5 cm proximal to carina
 - Cervical extension: ETT may ascend 2 cm
 - Tip of mandible off radiographic field of view
 - Tube tip 7-9 cm proximal to carina
 - Tube width: At least 2/3 of tracheal width
 - Tube cuff: Should not overly distend trachea
 - Selective bronchial intubation: Dual-lumen ETT allows independent ventilation of each lung
 - May be misinterpreted as inadvertent bronchial intubation
 - Complications
 - Bronchial intubation, R > L
 - More vertical course of right mainstem bronchus; smaller angle of right mainstem bronchus with trachea
 - Atelectasis, ipsilateral hyperinflation, pneumothorax
 - Esophageal intubation: Gastric overdistention
 - Ventilator-associated pneumonia
 - Barotrauma from high peak ventilation pressures
 - Tracheal/vocal cord injury
 - Acquired tracheal stenosis
- 11
 - No mobility with cervical flexion/extension
 - o Tube tip halfway between stoma and carina
 - o Tube width 1/2-2/3 of tracheal width

- Cuff should not distend tracheal wall
- Small pneumomediastinum immediately post placement
- Complications
 - Pneumothorax, subcutaneous gas, pneumomediastinum, mediastinal hemorrhage, false tract
- GT
 - Nasal (nasogastric) or oral (orogastric) placement
 - Suction of fluid in supine position; tube tip in fundus
 - Suction of air in supine position; tube tip in antrum
 - Tip ~ 10 cm caudal to gastroesophageal junction; side holes in stomach
 - o Complications
 - Coiling in pharynx or esophagus, aspiration (side holes in esophagus)
 - Knot formation: Narrow bore tube, excessive tube length in stomach
 - Tracheal/bronchial intubation: Pneumonia, lung contusion/laceration, hydropneumothorax
 - Laryngeal/pharyngeal/esophageal/tracheal perforation

• FT

- Nasal or oral placement
- Tip beyond pylorus at ligament of Treitz
- Complications: Coiling in pharynx, esophagus, stomach; tracheobronchial intubation; aspiration

Imaging Recommendations

- Best imaging tool
 - AP portable chest radiography for initial assessment
- Protocol advice
 - Radiography always performed after ETT, TT, GT, or FT placement to document position and identify complications
 - CT rarely performed for assessment of complications

DIFFERENTIAL DIAGNOSIS

Pitfalls

- Extraneous medical devices on or under patient
- External portions of enteric tubes that overlie thorax may be misinterpreted as tube malposition

CLINICAL ISSUES

Complications

- ETT initial malposition in ~ 27% of cases
- Esophageal intubation in ~ 1-24% of cases

DIAGNOSTIC CHECKLIST

Consider

• Importance of knowledge of normal and variant imaging anatomy and recognition of malpositioned tubes and associated complications

- 1. Ahmed RA et al: Endotracheal Tube 2021
- American College of Radiology: Intensive care unit patients. Revised August 2021. Accessed August 2021. https://acsearch.acr.org/docs/69452/Narrative/
- 3. Sigmon DF et al: Nasogastric Tube 2021

(Left) Composite image with AP chest radiograph (left) and coronal NECT (right) shows an ovoid lucency 🛃 at the thoracic inlet that corresponds to an overinflated endotracheal tube cuff. CT shows the overinflated cuff *⊠*, which is larger than the tracheal diameter \supseteq . (Right) Composite image with coronal NECT in lung (left) and soft tissue (right) window shows focal tracheal narrowing \supseteq and mural thickening 🔁 secondary to postintubation tracheal stenosis. Prolonged intubation is a common cause of acquired tracheal stenosis.





(Left) AP chest radiograph of a patient with an appropriately positioned tracheostomy tube → shows that the tube diameter is > 50% of the diameter of the tracheal air column 🛃. Note the malpositioned right upper extremity PICC 🔁 coursing cephalad and off the field of view. (Right) Composite image with AP chest radiograph (left) and sagittal NECT (right) shows a malpositioned tracheostomy with the tip \supseteq outside the tracheal lumen. CT documents the tracheostomy tube tip 🔁 position in the pretracheal soft tissues.





(Left) Sagittal CECT obtained after a complicated tracheostomy shows the tracheostomy tube tip \supseteq just barely within the tracheal lumen and the overinflated $cuff \ge$ in the pretracheal soft tissues. (Right) AP chest radiograph of the same patient obtained after repositioning the tracheostomy shows the tube $tip \longrightarrow overlying the lower$ trachea. Note subcutaneous gas, pneumomediastinum and left pneumothorax, which were complications of the procedure.







(Left) Coned-down AP chest radiograph obtained after abdominal surgery shows an appropriately positioned gastric tube, which courses caudally 🔁 off the inferior field of view. Note that the side hole \supseteq is well within the gastric lumen. (Right) Coneddown AP chest radiograph of a critically-ill patient status post gastric tube placement shows the tube tip \supseteq located within the stomach and the side hole \supseteq within the distal esophagus. Such placement predisposes the patient to aspiration. Advancement was recommended.





(Left) AP chest radiograph obtained immediately after gastric tube placement shows that the tube coils 🔁 in the upper thoracic esophagus, then courses caudally to terminate 🛃 in the distal esophagus. Radiography is indicated immediately after gastric and endotracheal tube placement. (Right) AP chest radiograph shows a malpositioned enteric tube in the bronchus intermedius 🖂 Right mainstem bronchus intubation is more common than left due to the more vertical course of the right mainstem bronchus.





(Left) AP chest radiograph shows a malpositioned gastric tube, which coils 🔁 in the distal esophagus, courses cephalad and off the field of view, and then courses back caudally into the right mainstem bronchus with tip \square in a right lower lobe bronchus. (Right) AP radiograph shows an appropriately positioned feeding tube 🔁 that terminates at the ligament of Treitz. Note the characteristic stiff metallic density tip that facilitates both placement and visualization.

KEY FACTS

TERMINOLOGY

- Thoracostomy tube (chest tube)
- Flexible hollow tube for pleural drainage
- Mediastinal drain
 - Evacuation of mediastinal collections

IMAGING

Thoracostomy tube

- o Straight, J-shaped, pigtail
- Radiopaque stripe along length; interrupted by holes or fenestrations (side ports) along insertion end
- Pneumothorax evacuation in supine patient: Anterosuperior tube course; tip at apical pleural space
- Hydrothorax evacuation in supine patient:
 Posteroinferior tube course; tip at basilar pleural space

• Mediastinal drain

- Various mediastinal locations
- Often based on surgeon's preference
- Pericardial fluid drainage

- **Radiography**: Always performed after insertion of thoracostomy tubes &/or mediastinal drains to document chest tube/drain position and identify complications
- **CT**: Rarely needed to assess tube/drain position; identification and assessment of complications

Pitfalls

- Extraneous radiopaque devices on or under patient
- Extrathoracic portion of thoracostomy tube/mediastinal drain may be mistaken for malposition
- Chest tube imaged end-on may mimic kink

CLINICAL ISSUES

- Thoracostomy tube complications
 - Complication rate post chest tube placement: 5-10%
 - Angulation, dislodgement, malposition
 - o Bleeding, infection, organ/vessel injury
 - Reexpansion pulmonary edema
- Mediastinal drain complications
 - o Organ/vessel injury, infection

(Left) AP chest radiograph shows a small bore left chest tube 🛃 placed for treatment of a left pneumothorax that developed after percutaneous biopsy of a left upper lobe nodule 🔁. No residual pneumothorax remains. The optimal chest tube position for pneumothorax evacuation is the anterior superior pleural space. (Right) AP chest radiograph of a patient with acute respiratory distress syndrome shows a right pleural pigtail chest tube 🔁 placed for treatment of a right pneumothorax 🔁 secondary to barotrauma.





(Left) AP chest radiograph of a patient status post mitral valve replacement via right thoracotomy shows two right chest tubes and a small right pleural effusion. Note that the chest tube side ports 🔁 are well within the pleural space. (Right) Axial CECT of a patient with a left empyema shows a well-placed left basilar chest tube 🔁 within a dependent loculated left basilar pleural fluid collection with intrinsic air bubbles. Large bore chest tubes may be specifically placed within loculated pleural collections.





Definitions

- **Thoracostomy tube (chest tube)**: Flexible hollow tube placed in pleural space; drains infected collections and those that compromise respiration and cardiovascular function
 - Pneumothorax drainage
 - Pleural fluid drainage (simple fluid, blood, empyema)
 Empyema and hemothorax: Early chest tube drainage
 - Drug administration: Sclerosing agent for pleurodesis, hyperthermic intrathoracic chemotherapy
- Mediastinal drain: Drainage of mediastinal &/or pericardial collections
 - Post cardiac surgery: Prevention of tamponade and subsequent pericarditis
- French (F): Outer diameter (equivalent to 0.333 mm)
- **Bore**: Internal diameter (varies with manufacturer and tube length)

IMAGING

General Features

- Location
 - Large bore chest tube: Placed at mid axillary line
 - Typically placed surgically or via blunt dissectionSmall bore chest tube: Second intercostal space at mid
 - clavicular line – Typically placed with Seldinger technique
 - Chest tubes placed along superior rib margin to avoid intercostal vessel injury
 - Mediastinal drain: Typically subxyphoid approach
- Size
 - Range: 6F to 40F
 - o Large bore: ≥ 20F; small bore: < 20F
 - Small bore chest tubes (≤ 14F and pigtail) for pneumothorax evacuation and patient comfort
 - Size selection depends on pleural fluid viscosity
- Morphology
 - o Straight, J-shaped, pigtail
 - Radiopaque stripe along tube length; interrupted by holes or fenestrations (side ports) along insertion end
 Sentinel side port = most peripheral side port

Radiographic Findings

• Thoracostomy tube

- Pneumothorax evacuation in supine patient: Anterosuperior tube course; tip at apical pleural space
- Hydrothorax evacuation in supine patient:
 Posteroinferior tube course; tip at basilar pleural space
- Chest tube directed toward loculated fluid or air
- Post placement assessment
 - Exclusion of residual effusion/pneumothorax
 - Identification of malposition/complications
- Post removal assessment
 - Exclusion of pneumothorax, pleural effusion
 - Chest tube tract: Tubular radiolucency along previous thoracostomy tube course; may mimic pneumothorax
- Complications
 - Angulation or kink; dislodgement

- Malposition: Interlobar fissure, lung, chest wall soft tissues, mediastinum, abdomen
- Bleeding, clogging, infection, organ/vessel injury
- Reexpansion pulmonary edema

Mediastinal drain

- Usually placed after cardiac surgery; location within mediastinum based on surgeon's preference
- o Various mediastinal locations, including pericardium
- Post placement assessment
 - Evaluation of mediastinum for enlargement/hemorrhage
- Post removal assessment
 - Assessment for mediastinal hemorrhage, residual pericardial effusion, pneumomediastinum
- Complications: Organ/vessel injury, infection
- Nondraining chest tube: Occlusion, malposition

Fluoroscopic Findings

• Fluoroscopic guidance for tube/drain insertion

CT Findings

- Assessment and planning prior to drainage of complex pleural collections
- Identification of soft tissue within chest tube lumen: Blood and debris may produce obstruction
- CT guidance for thoracostomy tube or mediastinal drain placement

Ultrasonographic Findings

• Ultrasound guidance for insertion of thoracostomy tubes and pericardial drains

Imaging Recommendations

- Best imaging tool
 - Chest radiography: Assessment of proper tube/drain placement
 - CT: Rarely needed to assess tube/drain position; assessment of complications
- Protocol advice
 - Radiography always performed after insertion of thoracostomy tubes &/or mediastinal drains to document position and identify complications
 - Daily radiography for thoracostomy tube/mediastinal drain assessment often performed, but no strong data to support this practice

DIFFERENTIAL DIAGNOSIS

Pitfalls

- Extraneous radiopaque devices on or under patient
- Extrathoracic portion of thoracostomy tube/mediastinal drain may be mistaken for tube/drain malposition
- Chest tube imaged end-on may mimic kink

CLINICAL ISSUES

Complications

• Complication rate post chest tube placement: 5-10%

- 1. Ravi C et al: Chest Tube 2021
- Filosso PL et al: Errors and complications in chest tube placement. Thorac Surg Clin. 27(1):57-67, 2017
(Left) AP chest radiograph of a patient who underwent heart transplantation shows bilateral thoracostomy tubes with side ports in the pleural spaces and a mediastinal drain \supseteq coursing vertically along the anterior mediastinum. Mediastinal drains are often placed after cardiac surgery. (Right) AP chest radiograph of a patient who presented with tamponade physiology and underwent pericardiocentesis with catheter insertion shows a small bore pericardial drainage catheter 🔁 coiled in the pericardial space.



(Left) AP chest radiograph of a patient status post right upper lobectomy shows a right thoracostomy tube with tip projecting over the right apex and side port 🔁 well within the right pleural space. (Right) PA chest radiograph of the same patient after right thoracostomy tube removal shows an obliquely oriented peripheral tubular radiolucency \supseteq that is morphologically identical to the course and shape of the removed chest tube and represents a chest tube tract, which is not to be confused with a pneumothorax.





(Left) AP chest radiograph of a patient who sustained chest trauma shows multiple right rib fractures complicated by a right pneumothorax. Note the malpositioned right chest tube with its tip 🔁 barely within the pleural space and its side port \bowtie in the right chest wall soft tissues. (Right) Coronal NECT of a patient with persistent right pneumothorax treated with thoracostomy tube placement shows a malpositioned right chest tube with its tip \Longrightarrow embedded into and obstructed by the right prevascular mediastinal fat.





Chest Tubes and Drains





(Left) AP chest radiograph of a patient who sustained chest trauma with resultant multifocal left rib fractures and left hemopneumothorax and was evaluated for left chest tube malfunction shows a tight kink 🔁 in the distal aspect of the left thoracostomy tube. (Right) Axial CECT of the same patient shows that the kinked left chest tube \supseteq is not within the left pleural space, but is located within the soft tissues of the left chest wall. Note the persistent left pneumothorax 🔁 and left chest wall subcutaneous gas 🖂.



(Left) Coronal CECT of a woman who sustained a gunshot wound to the chest and had persistent bilateral pneumothoraces in spite of bilateral chest tube placement shows a right chest tube 🔁 within the minor fissure and a persistent right pneumothorax →. (Right) Coronal CECT of the same patient shows a left chest tube \supseteq coursing within the left major fissure between the aerated left upper lobe and the atelectatic left lower lobe and a small left pneumothorax 🔁. Fissural placement is a known etiology of chest tube malfunction.





(Left) Axial NECT of a patient with persistent left pneumothorax status post chest tube placement shows an intraparenchymal course of the thoracostomy tube $\overline{\mathbb{A}}$, resultant pulmonary laceration 🖾, and residual left pneumothorax \supseteq . (Right) Composite image with axial (left) and coronal (right) NECT of a patient with a malfunctioning left chest tube shows luminal obstruction of the chest tube due to herniation \supseteq of the adjacent emphysematous lung into the chest tube lumen via several chest tube side ports.

KEY FACTS

TERMINOLOGY

• Vascular catheters and devices: Access to circulation for administration of drugs, resuscitative fluid, and nutrition; emergent venous access; obtaining blood samples; hemodialysis; hemodynamic monitoring/support

IMAGING

- Vascular catheters should follow anatomic course of cannulated vessel; vascular devices in expected anatomic locations
- **Central venous catheter (CVC)**: Tip at superior cavoatrial junction
- Peripherally inserted central catheter (PICC): Tip at superior cavoatrial junction
- Tunneled central vascular catheter: Tip in distal superior vena cava/right atrium
 - Port catheter, tunneled CVC
- **Pulmonary artery catheter**: Tip in right or left pulmonary artery with deflated balloon

- Impella: Coiled tip in left ventricle; distal portion in ascending aorta
- Intra-aortic balloon pump: Marker in proximal descending aorta
- Extracorporeal membrane oxygenation (ECMO)
 - **Veno-venous (VV)**: Wide bore venous catheters in vena cavae/right atrium
 - Veno-arterial (VA): Wide bore venous catheters in central vein and artery/aorta
- **CardioMEMS**: Small radiopaque tubular structure with paired metallic dots at either end
- Radiography always performed after insertion to document position and identify complications

CLINICAL ISSUES

• Complications: Malposition, pneumothorax, infection, bleeding, unintended arterial puncture, vascular injury/thrombosis/stenosis, arrhythmia, catheter fracture

(Left) AP chest radiograph of a critically-ill patient with multiple support devices shows a right internal jugular vein central venous catheter with the tip \blacksquare at the mid superior vena cava. Internal jugular vein central catheters extend caudally from above the ipsilateral clavicle. (Right) AP chest radiograph of a critically-ill patient shows a well-positioned right subclavian central catheter with the tip \square at the superior cavoatrial junction. Subclavian central catheters course along or below the clavicle \supseteq .





(Left) Composite image with PA (left) and lateral (right) chest radiographs shows a malpositioned left internal jugular vein central catheter with the tip \square in the azygos arch. (Right) AP chest radiograph of a patient status post placement of a right internal jugular vein catheter \bowtie shows a large right tension pneumothorax manifesting with a visible pleural line \blacksquare . Malposition and pneumothorax are the first and second most common complications of central catheter placement, respectively.





Definitions

- Vascular catheters and devices: Access to circulation for administration of drugs, resuscitative fluid, and nutrition; emergent venous access; obtaining blood samples; hemodialysis; and hemodynamic monitoring/support
- **Central venous catheter (CVC)**: Short-term drug/fluid administration; venous access
- Peripherally inserted central catheter (PICC): Mid- and long-term central venous access
- Tunneled central catheter
 - o Long-term central venous access: Weeks-months
 - **Port catheter (PC)**: Drug (chemotherapy), nutrition, fluid administration
 - **Hemodialysis catheter (HDC)**: Hemodialysis, nutrition, transfusion, drug administration
- **Pulmonary artery catheter (PAC)**: Measurement of central venous, intracardiac, pulmonary arterial, and pulmonary capillary wedge pressures
 - Pulmonary capillary wedge pressure reflects left atrial and left ventricular end-diastolic volume
- Intra-aortic balloon pump (IAPB)
 - Temporary mechanical hemodynamic support in patients with cardiogenic shock using counterpulsation
 - Aortic balloon inflates in diastole (↑ coronary and peripheral organ perfusion); deflates in systole (↓ afterload)
- Impella heart pump: Transcatheter intracardiac ventricular assist device for short-term mechanical circulatory support (cardiogenic shock; left heart failure)
 - Impella RP: Right or biventricular heart failure
- Extracorporeal membrane oxygenation (ECMO): Modified pulmonary/cardiopulmonary bypass for cardiorespiratory support in severe cardiac/respiratory failure
 - Veno-venous (VV): Primarily for gas exchange
 - Veno-arterial (VA): Gas exchange and hemodynamic support
- CardioMEMS: Ambulatory heart failure monitoring
 - Pulmonary artery pressure and heart rate measurements
 - Daily wireless transmission of pressure readings

IMAGING

General Features

- Best diagnostic clue
 - Vascular catheters along anatomic course of cannulated vessel; vascular devices in expected anatomic locations
- Location
 - Catheter in anatomic course of cannulated vessel; device in expected anatomic location
 - **CVCs**: Tip at superior cavoatrial junction [lower superior vena cava (SVC)/upper right atrium (RA)]
 - Radiographic determination of superior cavoatrial junction location
 - □ Inferior aspect of bronchus intermedius
 - 2 vertebral bodies below carina
 - □ Intersection of SVC interface and upper right cardiac border

- Intersection of bronchus intermedius with upper right heart border
- Catheter above superior cavoatrial junction: Risk of vessel injury, reflux of toxic drugs
- Catheter below superior cavoatrial junction: Risk of cardiac arrhythmia
- Right internal jugular (IJ) vein
 - Vertical course; catheter above clavicle
 - Direct path to SVC and RA; wider and more superficial
- Subclavian vein catheter
 - □ Course along &/or below clavicle
 - □ Accessible in trauma (cervical spine injuries)
- **PICC**: Cephalic, basilic, or brachial vein; tip at superior cavoatrial junction
- **Tunneled central catheter**: Surgically placed catheter travels under skin, proximal aspect away from venous access site with tip at superior cavoatrial junction
 - Subclavian or IJ placement
 - PC; HDC
- **PAC**
 - Placed via femoral, subclavian, or IJ vein
 - Tip in central right or left pulmonary artery (usually right)
- IAPB
 - Placed via femoral or subclavian (typically right) artery approach
 - Along descending thoracic/upper abdominal aorta
 Below aortic arch
 - □ Above celiac, mesenteric, and renal arteries
- Impella heart pump
 - Placed via femoral or axillary artery
 - Extends from left ventricular cavity to aorta
- ECMO
 - VV: Wide bore venous catheters (cannulae); drainage cannula deoxygenated blood, return cannula oxygenated blood
 - Drainage cannula inserted in femoral vein with tip at diaphragm, return cannula inserted at IJ with tip at SVC/RA junction
 - Single cannula dual lumen (drainage and return) inserted at IJ with tip in inferior vena cava (IVC)
 - VA (central): Drainage cannula in RA; return cannula in aorta (ascending) through open sternum
- CardioMEMS: Distal branch of left pulmonary artery
- Morphology
 - **PC**: Single or double subcutaneous port(s); one or two lumina
 - HDC
 - Ends at skin; cuff surrounding catheter
 - Various diameters/access ports
 - Large bore (and volume/flow rates) dual lumen
 - **PAC**
 - IJ or subclavian placement: Via catheter sheath
 - o **IAPB**
 - Long inflatable balloon (23-28 cm); radiopaque markers at either end
 - Impella heart pump
 - Pigtail-shaped catheter tip
 - Blood inlet draws left ventricular blood

- Blood outlet releases blood into ascending aorta
- **CardioMEMS**: Inductor coil and pressure sensitive capacitor (in tubular protective housing)

Radiographic Findings

- CVC
 - Large central vein (IJ or subclavian) course to superior cavoatrial junction
 - IJ vein: Catheter projects above clavicle
 - Subclavian vein: Catheter course along/below clavicle

• PICC

- Thin catheter
- Right or left upper extremity placement
- Catheter course along medial upper extremity, axilla, and along clavicle to superior cavoatrial junction
- Tunneled CVC
 - Large caliber, single lumen, multiple lumina
 - IJ or subclavian placement to reach superior cavoatrial junction
 - PC
 - Visualization of single or double subcutaneous port(s) in upper chest wall
 - □ **CT** designation on PC = port is power injectable
 - One lumen or two lumina
 - Port accessed via needle stick (access needle may be visible)
 - Hemodialysis
 - Large caliber catheter
 - Two or more lumina; ± offset tips
- PAC
 - Subclavian/IJ approach: SVC \rightarrow RA \rightarrow RV \rightarrow pulmonary trunk \rightarrow distal right or left pulmonary artery
 - Courses through catheter sheath
 - Femoral vein approach: IVC → RA → RV → pulmonary trunk → distal right or left pulmonary artery
 - Tip in right or left pulmonary artery (deflated balloon); should not extend > 2 cm distal to ipsilateral hilum
- IAPB
 - Common femoral or right subclavian artery (surgical placement) approach
 - Radiopaque marker at upper descending thoracic aorta; 2 cm below top of aortic arch
 - o Inflated balloon may be visualized
- Impella
 - Left heart placement
 - Pigtail catheter tip in left ventricular apex: blood inlet (draws blood from left ventricle)
 - Blood outlet (delivers blood to ascending aorta)
 - Right heart placement: Impella RP
 - Pigtail catheter tip in pulmonary trunk; blood outlet (delivers blood to pulmonary trunk)
 - Blood inlet in IVC (draws blood from IVC)
- ECMO
 - VV: Wide bore venous cannula(e); SVC/RA and IVC or single cannula coursing from SVC to IVC
 - VA: Wide bore cannulae with venous (RA) and arterial (ascending aorta) limbs
- CardioMEMS
 - Small radiopaque tubular object in left lower lobe pulmonary artery
 - Paired metallic dots at either end

• Easily missed on portable radiography due to small size and low conspicuity

MR Findings

- MR safety
 - IABP and Impella: MR-unsafe
 - CardioMEMS: MR-conditional at 1.5T and 3.0T

Ultrasonographic Findings

• Ultrasound guidance for insertion of vascular catheters

Imaging Recommendations

- Best imaging tool
 - Radiographic assessment of catheter/device position
 - CT rarely needed to assess position or evaluate complications
- Protocol advice
 - Radiography always performed after insertion to document position and identify complications

DIFFERENTIAL DIAGNOSIS

Pitfalls

- Failure to recognize variant vascular anatomy, e.g., persistent left SVC
- External portions of catheters and other devices
- Superimposed extraneous radiopaque medical devices

CLINICAL ISSUES

Complications

- CVCs
 - Most common complication: Malposition (including looping, kinking)
 - Azygos arch/system, IJ vein, internal mammary vein, superior intercostal vein, extravascular
 - Second most common complication: Pneumothorax
 Subclavian vein: Higher risk of pneumothorax than IJ
 - Other: Infection (usually with *Staphylococcus* sp.), bleeding, unintended arterial puncture, vascular injury/thrombosis/stenosis/occlusion, fibrin sheath formation, arrhythmia, catheter fracture
 - Subclavian vein: Low rate of infection/thrombosis
- PAC: Lung infarction, pulmonary artery pseudoaneurysm
 Controversy: Studies have shown no change in mortality or length of hospital stay with use
- IABP: Vessel wall injury, thrombus formation, limb/visceral ischemia
- Impella: Myocardial wall perforation, disruption of mitral apparatus with resultant severe mitral regurgitation
- ECMO: Gas emboli, cerebral ischemia/stroke, hemorrhage
- CardioMEMS: In situ thrombosis, pulmonary artery injury

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(Left) PA chest radiograph shows an appropriately positioned right upper extremity peripherally inserted central catheter with the tip *■* at the superior cavoatrial junction. (Right) AP chest radiograph shows an appropriately positioned tracheostomy
ightarrow and amalpositioned right upper extremity peripherally inserted central catheter 🔁, which courses cephalad into the right internal jugular vein and off the superior field of view. Malposition is the most common complication of central catheter placement.





(Left) AP chest radiography shows a malpositioned left upper extremity peripherally inserted central catheter with the tip \supseteq coiled in the azygos arch. Note the catheter course \square along the medial left upper extremity, below the ipsilateral clavicle and into the superior vena cava. (Right) PA chest radiograph shows an appropriately positioned tunneled right internal jugular vein port catheter with the port 🔁 located in the right anterior mid thorax and the tip \supseteq at the superior cavoatrial junction.





(Left) PA chest radiograph of a patient with advanced lung cancer shows a left subclavian tunneled port catheter with the port in the left anterior chest wall and the tip at the superior cavoatrial junction. The catheter was placed for the administration of systemic chemotherapy. (Right) PA chest radiograph of the same patient coned-down to the left pectoral port shows the letters "CT" 🔁, which signify that this port is power injectable and can be used for administration of contrast during CECT or CT angiography.

(Left) PA chest radiography of a patient with end-stage renal disease shows a right internal jugular vein tunneled dual lumen central venous catheter, in this case a hemodialysis catheter with the $tip \supseteq in the mid right atrium.$ Note the external limbs 🖂 of the catheter, which connect to the dialysis apparatus. (Right) AP chest radiograph of a critically-ill patient shows an appropriately positioned right internal jugular vein pulmonary artery catheter placed via a vascular sheath \supseteq with the tip \supseteq in the distal right pulmonary artery.





(Left) AP chest radiograph shows a pulmonary artery catheter placed via inferior vena cava 乏 approach with tip \supseteq in the right pulmonary artery and an intra-aortic balloon pump marker 🔁 that should ideally be located in the upper descending aorta. (Right) AP chest radiograph shows a malpositioned pulmonary artery catheter with the tip 🔁 in a subsegmental right lower lobe pulmonary artery, which should be retracted by about 10 cm to avoid traumatic pulmonary artery injury and pseudoaneurysm formation.





(Left) AP chest radiograph shows an appropriately positioned intra-aortic balloon pump with the marker 🔁 in the upper descending thoracic aorta, approximately 2 cm below the top of the aortic arch. (Right) AP chest radiograph shows an intraaortic balloon pump placed via right subclavian artery approach with the marker 🔁 near the aortic arch. Note the vertical tubular lucency 🔁 that corresponds to the inflated balloon, which outlines the course of the descending thoracic aorta.









(Left) AP chest radiograph shows a malpositioned right subclavian artery intra-aortic balloon pump marker \supseteq in the brachiocephalic artery. The inflated balloon *is in* the aortic arch and potentially occludes the aortic branch vessels. (Right) AP chest radiograph shows an Impella heart pump with the pigtail tip \supseteq and blood inlet \supseteq in the left ventricle and the blood outlet \ge in the distal ascending thoracic aorta. The Impella device is used for short-term mechanical circulatory support in patients with cardiogenic shock.





(Left) AP chest radiograph of a patient with biventricular failure shows an Impella RP with pigtail tip and blood outlet \supseteq in the pulmonary trunk and blood inlet in the inferior vena cava 🔁. Note the appropriately positioned left heart assist Impella \implies . (Right) AP chest radiograph of a patient with acute respiratory distress syndrome due COVID-19 shows a venovenous extracorporeal membrane oxygenation apparatus with the drainage $cannula \supseteq$ in the inferior vena cava and the return cannula 🔁 in the right atrium.





(Left) AP abdomen radiograph shows a veno-arterial extracorporeal membrane oxygenation apparatus with drainage cannula \supseteq in the right atrium and return $cannula \bowtie$ in the ascending thoracic aorta. (Right) Composite image with PA (left) and lateral (right) chest radiographs shows the typical tubular morphology and paired radiopaque dots at either end of a CardioMEMS 🔁 in the left lower lobe pulmonary artery. The CardioMEMS provides ambulatory heart failure monitoring.

KEY FACTS

TERMINOLOGY

- Implantable cardioverter defibrillator (ICD)
- Right atrium (RA); right ventricle (RV); left atrium (LA); left ventricle (LV)

IMAGING

- Variable lead location
- Temporary pacemaker: Single RV lead
- Temporary epicardial pacing wires: Epimyocardial needlelike leads on RV and RA surfaces
- Single-chamber pacemaker: Single RA or RV lead
- Dual-chamber pacemaker: Leads in RA and RV
- Biventricular pacemaker: Dual-/single-chamber leads; coronary sinus lead
- Leadless pacemaker: Percutaneous transvenous placement in RV
- ICD: Transvenous, subcutaneous
- Remede (Respircardia): Leads near phrenic nerve and in azygos system (near diaphragm)

TOP DIFFERENTIAL DIAGNOSES

- Other implanted devices
 - Implantable loop recorder
 - o Vagus nerve stimulator
 - Deep brain stimulator
 - Abandoned leads from previously removed pacemaker

CLINICAL ISSUES

- Twiddler syndrome: Inadvertent or deliberate pacemaker unit rotation in subcutaneous pocket
- Pacemaker syndrome: Loss of atrioventricular synchrony
- Sudden cardiac arrest due to conduction disturbances related to malposition or malfunction

DIAGNOSTIC CHECKLIST

- PA and lateral chest radiography for initial assessment of lead placement and detection of complications
- Consider lead fracture &/or dislodgement in cases of pacemaker malfunction

(Left) PA chest radiograph shows normal location of a dual-chamber biventricular implantable cardioverter defibrillator (ICD), with leads in the right atrium \supseteq , right ventricle \boxtimes , and a tributary of the coronary sinus \square . The generator unit is in the left anterior chest wall, and the leads exit in a clockwise direction. (Right) Lateral chest radiograph of the same patient shows appropriate lead location in the right atrium \blacksquare , right ventricle \blacksquare , and a tributary of the coronary sinus \square . The coronary sinus lead courses posteriorly.











Abbreviations

- Cardiac implantable electronic devices (CIEDs)
 Implantable cardioverter defibrillator (ICD)
 - Biventricular pacemaker: Cardiac resynchronization therapy (CRT)
- Right atrium (RA); right ventricle (RV); left atrium (LA); left ventricle (LV); atrioventricular (AV)

IMAGING

General Features

- Size
- Variable size of pacemaker units; leads 2-3 mm thickMorphology
 - Leads may exit pacer clockwise or counterclockwise
- Pacemaker components
 - Pacemaker generator
 - Left/right anterior/lateral chest wall soft tissues
 - Variable lead locations: RA, RV, coronary vein via coronary sinus
 - RA: Atrial appendage, sinoatrial node, AV node
 - RV: RV apex, RV outflow tract
 - LV: Variable coronary sinus tributary
- Pacemaker types (management of bradyarrhythmias)
 - o Temporary
 - Emergent placement for complete AV block, sinus node dysfunction, unstable vital signs
 - Transjugular or transfemoral approach
 - Temporary epicardial pacing wires
 - Placed after coronary bypass or open heart surgery
 - Epimyocardial needle-like lead on RV and RA surface
 - Removed ≤ 7 days postop; may be clipped at skin surface and retained
 - o Dual chamber
 - RV paced following each sensed RA event up to programmed maximal RV rate
 - o Leadless
 - Pulse generator and electrode in self-contained unit
 - Percutaneous transvenous implantation in RV
 - Indications: Poor upper extremity venous access, older adult patient with multiple co-morbidities, infrequent pacing requirement
 - His bundle pacing (HBP): Electrical activation of both ventricles, may avoid dyssynchrony
 - Lead tip in vicinity of His bundle: Selective and nonselective His bundle capture
 - Stimulates native His-Purkinje conduction system with physiologic activation of LV and RV
 - Indications: AV block, pacemaker-induced cardiomyopathy, AV nodal ablation, nonresponders to CRT
 - Left bundle branch pacing
 - Lead placed deep in RV septum into left bundle branch area or in mid distal septum: Selective and nonselective
- ICD
 - o Indications: 1ary or 2ary sudden cardiac death prevention
 - Components: Pacing/sensing electrodes, defibrillation electrodes, generator

- Subcutaneous ICD
 - Addresses lead-associated complications of transvenous ICD
 - Purely subcutaneous generator and defibrillator lead
- Management of heart failure
 - o CRT
 - Cardiac contractility modulation (CCM)
- Management of cardiovascular comorbidities
 - Treatment of moderate/severe central sleep apnea
 Remede system (Respircardia): Chest wall subcutaneous battery-powered device; stimulation lead near phrenic nerve, optional sensing lead in azygos system

Radiographic Findings

- **Single-chamber pacemaker**: Single lead: RA near sinoatrial node, RV apex, RV outflow tract
- **Dual-chamber pacemaker**: Leads in RA appendage and RV apex
- Biventricular pacemaker
 - Dual- or single-chamber pacemaker leads + additional lead coursing into coronary sinus
 - Coronary lead on LV surface; lateral or posterolateral cardiac vein; posterior location on lateral radiography

• Epicardial pacemaker

- Generator in abdominal wall; lead on cardiac surface, usually RV
- Used in children and young patients for prevention of long-term venous damage
- Leadless pacemaker: Small device anchored in RV apex
- Temporary epicardial pacing wires: Long thin metallic wires projecting over heart and upper abdomen
- (postoperative period)

• ICD

- Typically 2 leads: Superior vena cava (defibrillator) and RV apex (defibrillator and sensor)
- May be component of biventricular pacemaker
- Leads larger; dense coiled spring appearance compared to pacemaker leads

• Subcutaneous ICD: Vertical parasternal defibrillator coil

• Remede (Respircardia)

- Stimulation lead near phrenic nerve, sensing lead in azygos system (near diaphragm)
- Complications

• Early complications: 4-5%

- Pneumothorax: 1.5% of procedures
- Hemothorax
- Lead-related complications: Perforation (may lead to tamponade), dislodgement (2-3%, usually within 24-48 hours), diaphragmatic stimulation, malposition

Late complications: 3%

- Twiddler syndrome: Subconscious, inadvertent or deliberate pacemaker generator rotation
 - Change in orientation of generator
 - Change in lead direction exiting pacemaker
 - Lead retraction toward pacemaker unit
- □ ↑ number of wire loops around pacemaker unit
- Lead fracture: Difficult visualization if nondisplaced
 - Usually when pinched between clavicle and 1st rib
 - Suspect when pacemaker does not capture in spite of stable lead position

 Retained temporary epicardial pacing wires: Migration, infection

CT Findings

- CECT
 - Detection of chamber perforation
 - Lead tip projecting outside RV myocardium
 - Exact localization may be difficult to determine due to beam-hardening artifact
 - Identification of hemopericardium; uncommonly hemoperitoneum
 - Detection of venous thrombus/stenosis
 - Mediastinal and chest wall venous collaterals

MR Findings

- MR relatively contraindicated in patients with pacemakers
 - Absolute contraindication in pacemaker-dependent patients
 - Can be performed safely in patients with demand pacemakers, particularly exams remote from chest (e.g., brain)
 - Pacemaker should be pre-tested outside MR suite
 - Cardiologist in attendance during procedure
 - Monitor during examination; communicate with patient between sequences
 - Post-test pacemaker outside MR suite
 - Significant change in pacing thresholds in approximately 10%

Ultrasonographic Findings

- Ultrasound for assessment of venous complications or fluid around pacemaker unit
 - Symptomatic venous thrombosis in 5%; risk increases with multiple leads

Imaging Recommendations

- Best imaging tool
 - PA and lateral chest radiography for initial assessment and detection of complications

DIFFERENTIAL DIAGNOSIS

Other Implanted Devices

- Implantable loop recorder: Long-term cardiac monitoring of patients with syncope
- Vagus nerve stimulator: Leads extend into neck, terminate in region of carotid artery
- Deep brain stimulator: Leads continue cephalad
- Abandoned leads from previously removed pacemaker
- Retained temporary epicardial pacer wires

PATHOLOGY

General Features

- Etiology
 - Indications for pacemaker placement
 - Sinus node dysfunction
 - □ Most common indication for pacemaker insertion
 - Long-term therapy for symptomatic bradycardia
 - Neurocardiogenic syncope
 - Hypertrophic obstructive cardiomyopathy
 - Heart failure; CRT

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic with normal pacer function
- Other signs/symptoms
 - **Pacemaker syndrome**: Secondary to loss of AV synchrony with resultant adverse hemodynamics
 - Common symptoms: Malaise, fatigue, dyspnea, orthopnea, cough, dizziness, chest discomfort, throat fullness
 - Less common symptoms: Syncope, near syncope
 - Physical exam: Hypotension, rales, ↑ jugular venous pressure
 - AV block in single-chamber right atrial pacing
 - Sudden cardiac arrest due to conduction disturbances related to malposition or malfunction
 - Pacemaker pocket complications: Hematoma, pain, infection

Demographics

- Epidemiology
 - In use since mid 20th century; continually evolving technology
 - o > 1 million pacemakers implanted annually worldwide

Natural History & Prognosis

- Expected longevity of pacemaker: 5-10 years
- In patients with bacteremia: Risk of infected lead thrombus and subsequent septic pulmonary emboli
- Complications: Lead dislodgement, lead fracture, malfunction, endocarditis, venous occlusion; generator pocket infection, hematoma

Treatment

- Replacement of fractured wires
- Perforation: Lead withdrawal and rescrewing into myocardium
- Surgical replacement of pacemaker unit at battery end-oflife

DIAGNOSTIC CHECKLIST

Consider

• Lead fracture/dislodgement if pacemaker malfunction

Image Interpretation Pearls

- Evaluation of pacemaker should be performed with extraneous superficial leads removed
- Carefully evaluate pacemaker unit to look for change in orientation
- Compare direction of leads exiting pacemaker unit; initial post placement and prior comparison radiographs

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Cardiac Conduction Devices





(Left) PA chest radiograph shows a left pectoral subcutaneous ICD. The generator 🔁 is implanted in the lateral mid axillary line soft tissues. The subcutaneous parasternal lead 🔁 is vertically oriented creating a trans-cardiac vector with the generator. (Right) Lateral chest radiograph of the same patient shows the generator \bowtie implanted in the lateral mid axillary line subcutaneous soft tissues, and the subcutaneous parasternal lead \square , which is vertically oriented creating a trans-cardiac vector with the generator.





(Left) PA chest radiograph of a 55-year-old man with syncope and previously documented appropriately positioned dualchamber biventricular pacer shows migration of the coronary sinus lead into the right ventricle with the lead $tip \square$ in the pulmonary outflow tract. (Right) Lateral chest radiograph of the same patient shows the tip \triangleright of the migrated coronary sinus lead within the right ventricular outflow tract. Chest radiographs must be actively surveilled to detect malpositioned leads.





(Left) PA chest radiograph shows a leadless intracardiac pacemaker 乏 in the right ventricular apex. Leadless pacemakers eliminate several complications associated with transvenous pacemakers and leads (e.g., pocket infection, hematoma, lead *dislodgement, lead fracture)* but lack defibrillation capacity. (Right) Lateral chest radiograph of the same patient shows the leadless intracardiac pacemaker 🔁 in the right ventricular apex.

Pleurodesis

KEY FACTS

TERMINOLOGY

- Definition: Chemical pleural sclerosis to treat refractory malignant pleural effusion and recurrent pneumothorax
- Pleurodesis agents and methods
 - Pure talc (hydrated magnesium silicate)
- o Bleomycin

IMAGING

• Radiography

- o Focal or multifocal diffuse pleural thickeningo Smooth or nodular pleural thickening
- CT
 - Unilateral smooth or nodular pleural thickening; posterior/basilar pleura
 - Smooth or nodular thickening of interlobar fissures
 - Frequent high attenuation
 - Loculated pleural fluid
- FDG PET/CT
 - FDG avidity in talc-related pleural thickening

TOP DIFFERENTIAL DIAGNOSES

- Solid pleural metastases
- Malignant pleural mesothelioma
- Pleural tuberculosis
- Pleural or extrapleural hematoma
- Calcified pleural plaques

CLINICAL ISSUES

- Goal of treatment is to improve respiratory status
- Talc is most effective sclerosant agent available for pleurodesis
- Signs/symptoms: Pain and fever
- Overall success rate (50-90%)
 - Complete drainage of pleural fluid
 - Ability of collapsed lung to reexpand

DIAGNOSTIC CHECKLIST

• High-attenuation nodular pleural thickening post intervention should suggest pleurodesis

(Left) Axial NECT of a patient with prior talc pleurodesis shows heterogeneous linear and lenticular high attenuation of the right basilar pleura \blacksquare . Talc is among the most effective pleurodesis agents, has intrinsic high attenuation, and may manifest as curvilinear or nodular high attenuation. (Right) Composite image with axial CECT of a patient with lung cancer (not shown) status post pleurodesis shows areas of high attenuation along the right posterior pleura 🔁 and adjacent multiloculated right pleural fluid 🔁.





(Left) Composite image with CECT (left) and FDG PET (right) of a patient who had talc pleurodesis shows hyperattenuating material 🖂 in the right posterior costophrenic sulcus that demonstrates FDG avidity. FDG uptake can persist for months or years after pleurodesis. (Right) Coronal fused FDG PET/CT shows increased FDG uptake in multifocal circumferential bilateral pleural nodules and masses 🔁. Talc pleurodesis may result in chronic nodular pleural thickening, which may exhibit increased FDG uptake.





Synonyms

- Pleural sclerosis
- Talc poudrage

Definitions

- Chemical pleural sclerosis to treat refractory malignant pleural effusion and recurrent pneumothorax
- Other indications
 - Recurrent benign pleural effusions: Heart failure, ascites, systemic lupus erythematosus
 - Recurrent pneumothorax: Chronic obstructive pulmonary disease, lymphangioleiomyomatosis, catamenial
 - o Chylothorax: Postsurgical, post-traumatic
- Contraindications
 - Infection, advanced heart disease, coagulation disorders, planned lung transplant
- Pleurodesis agents and methods
 - Pure **talc** (hydrated magnesium silicate)
 - Most used/most effective sclerosant agent
 - Highest success rate for malignant pleural effusion
 - 4-8% risk of respiratory failure after talc exposure
 - Bleomycin
 - Readily available
 - More expensive; must be used immediately
 - Physical pleural abrasion

IMAGING

General Features

- Best diagnostic clue
- High-attenuation often nodular pleural thickeningLocation
 - Basilar (dependent) pleura, posterior costophrenic sulci
- Morphology
 - o Lentiform
 - Variable attenuation: Soft tissue, fluid, calcification

Radiographic Findings

- Talc pleurodesis
 - Focal or multifocal diffuse pleural thickening
 - Smooth or nodular pleural thickening
 - Pleural mass/talcoma, often years after procedure

CT Findings

- Unilateral smooth or nodular pleural thickening; posterior/basilar pleura
- Fissural pleural thickening
- Frequent high attenuation
- Loculated pleural fluid

Nuclear Medicine Findings

- PET/CT
 - FDG avidity in talc-related pleural thickening

Imaging Recommendations

- Best imaging tool
 - Chest CT for assessment of pleural abnormality and detection/characterization of high attenuation

DIFFERENTIAL DIAGNOSIS

Solid Pleural Metastases

• Circumferential nodular thickening; unilateral or bilateral

Malignant Pleural Mesothelioma

• Unilateral nodular thickening; often circumferential

Empyema

• Unilateral noncalcified loculated pleural effusion

Pleural Tuberculosis

• Unilateral, thick pleural rind; dense calcification

Pleural or Extrapleural Hematoma

• Unilateral pleural thickening; calcification

Calcified Pleural Plaques

• Bilateral, multifocal, discontinuous ± calcification

PATHOLOGY

Gross Pathologic & Surgical Features

• Dense pleural fibrosis; loculated fluid

Microscopic Features

- Dense fibrosis from damage to mesothelium
- Talc crystals under polarized microscopy

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - **Pain and fever**; fever may indicate robust inflammatory response and increased success rate

Demographics

- Age
 - > 40 years; patients affected by malignancy
- Sex
 - \circ M = F

Natural History & Prognosis

- Treatment goal is improved respiratory status
- Overall success rate (50-90%)
 - Optimal results
 - Complete drainage of pleural fluid
 - Reexpansion of collapsed lung
 - Decreased success/failure
 - Lung entrapment or long-term atelectasis
 - Steroids, NSAIDs

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

 High-attenuation nodular pleural thickening post intervention should suggest pleurodesis

SELECTED REFERENCES

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Sublobar Resection

KEY FACTS

TERMINOLOGY

- Anatomic sublobar resection (segmentectomy): Excision of 1 or more segments and dissection of artery, vein, and bronchi
- Nonanatomic sublobar resection (wedge): Nonanatomic peripheral pulmonary excision without involving hilar lobar structures

IMAGING

- Radiography
 - Staple line: Radiopaque (metallic)
 - Findings of volume loss &/or thoracotomy
- CT
 - Staple line: May mimic calcified granulomas on axial imaging; linear on multiplanar and MIP reformations
 - Adjacent pleural thickening (postsurgical reaction)
 - Soft tissue adjacent to staple line (common)
 - When nodular or bulky, underlying locoregional recurrence is of concern

TOP DIFFERENTIAL DIAGNOSES

• Calcified granuloma

CLINICAL ISSUES

- Sublobar resection vs. lobectomy
 - Lobectomy is gold standard treatment for early nonsmall cell lung cancer
 - Similar short-term mortality for both
 - o Sublobar resection: \downarrow morbidity and \downarrow length of stay
 - No statistically significant difference in overall survival between sublobar (anatomic or nonanatomic) resection and lobectomy
- Sublobar resection
 - Specific clinical scenarios in lung cancer
 - Anatomic sublobar resection
 - Nonanatomic sublobar resection
 - Peripheral typical carcinoid tumor
 - o Metastasectomy

(Left) AP chest radiograph obtained on postoperative day 1 after a lingular sublobar resection shows a peripheral nodular airspace opacity 🔁 around the thin metallic staple line. (Right) AP chest radiograph of the same patient obtained 2 days later shows marked improvement of the nodular opacity about the staple line 🔁 and residual linear atelectasis, consistent with resolving parenchymal hematoma and atelectasis, which are common findings following nonanatomic sublobar resection.





(Left) Composite image with axial CECT (bone window) (left) and sagittal oblique MIP reformatted image (right) of the same patient shows the staple line as a small dense nodule \supseteq on axial imaging and as a linear structure 🖂 on the MIP reformation. (Right) Composite image with axial NECT before (left) and after (center) right upper lobe lung cancer recurrence and FDG *PET/CT (right) of the same* patient shows a new solid nodule 🔁 at the staple line 🔁 of a sublobar resection that exhibits intense FDG avidity





Synonyms

- Wedge resection (nonanatomic sublobar resection)
- Segmentectomy (anatomic sublobar resection)

Definitions

• Anatomic sublobar resection (segmentectomy): Excision of 1 or more lung segments and accompanying lymph nodes; requires dissection of corresponding artery, vein, and bronchi

o Basilar segmentectomy: All lower lobe basilar segments

• Nonanatomic sublobar resection (wedge): Nonanatomic excision of peripheral pulmonary lesion with clear margins and without involving hilar structures

IMAGING

Radiographic Findings

- Radiography
 - Staple line: Radiopaque (i.e., metallic), may mimic calcified granulomas
 - Volume loss (e.g., hemidiaphragm elevation, mediastinal displacement)
 - Findings of thoracotomy (e.g., rib fracture/deformity)
 - Immediate postoperative complications
 - Pneumothorax ± pleural effusion/hemorrhage
 - Parenchymal hemorrhage/hematoma = opacity adjacent to staple line ↓ over time

CT Findings

- Staple line
 - May simulate calcified granulomas on axial imaging
 - Linear on multiplanar images (i.e., sagittal and coronal);
 MIP reformations depict staple line in great detail
 - Adjacent pleural thickening (postsurgical reaction)
- Problem solving of immediate postoperative complications
 Parenchymal hemorrhage/hematoma along staple line
 - Perioperative infection adjacent to staple line
 - Bronchopleural fistula; less common in sublobar than in more extensive resections
- Soft tissue adjacent to staple line (common)
 - Typically atelectasis &/or focal fibrosis/scarring
 - Concern for nodular or bulky locoregional recurrence: Interval growth on CT, ↑ FDG uptake on PET/CT

DIFFERENTIAL DIAGNOSIS

Calcified Granulomas

• Nodular in cross section and multiplanar reformations

CLINICAL ISSUES

Natural History & Prognosis

 Sublobar resection associated with ↓ morbidity and ↓ length of stay compared to more extensive resection; increasing number of indications for sublobar resection

Treatment

- Options, risks, complications
 - **Perioperative complications**: Prolonged air leak (> 5 days after surgery), bleeding, empyema, pneumonia, atrial fibrillation, pain

- Ablation or radiotherapy are alternative treatments
- Sublobar resection performed by open thoracotomy or video-assisted thoracoscopic surgery (VATS)
 - Sublobar resection for **nonmalignant conditions**
 - Diagnosis of interstitial lung disease and other diffuse lung diseases
 - Treatment of recurrent pneumothorax (blebectomy)
 - Presumed benign tumors
 - Lung volume reduction surgery for advanced emphysema (bullectomy)

• Sublobar resection vs. lobectomy

- Lobectomy is gold standard treatment for early nonsmall cell lung cancer due to ↑ risk of locoregional recurrence and cancer-related death in sublobar resection
 - Sublobar resection increasingly considered in high risk patients
 - Similar short-term mortality for both
 - No statistically significant difference in overall survival between sublobar resection and lobectomy
 - Lobectomy associated with better outcomes in lung adenocarcinoma with tumor spread through air spaces
- Anatomic sublobar resection in lung cancer
 - Prior solid malignancy in which intraoperative frozen section does not differentiate primary cancer from metastasis
 - Prior pulmonary resection with 2nd primary malignancy
 - High-risk patients for lobectomy (e.g., respiratory disease, ↑ age)
 - Peripheral early lung cancer < 2 cm or suspicion of invasive mucinous adenocarcinoma
- Nonanatomic sublobar resection in lung cancer
 - Mandatory parenchymal preservation (i.e., limited pulmonary reserve)
 - Preoperative histology not verified
 - Diagnostic dilemma (e.g., nodular lung disease due to tuberculosis, sarcoidosis, or rheumatoid arthritis with dominant nodule suspicious for lung cancer)
 - Comorbidities necessitating rapid procedure time and shortened duration of general anesthesia
- Carcinoid: Lobectomy is gold standard
 - Growing evidence supporting sublobar resection for peripheral **typical carcinoid**; similar long-term survival
- Metastasectomy for pulmonary metastases
 - o Resection may improve survival in certain histologies
 - Offered to patients with technically feasible resection and locoregional control of primary tumor; absence of widespread metastatic disease, poor pulmonary reserve, other medical contraindications for surgery
 - Favorable prognostic factors: Long disease-free interval, few metastases, small size of dominant lesion

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KEY FACTS

TERMINOLOGY

- Lung volume reduction surgery (LVRS)
 - Treatment of severe emphysema by removing approximately 20-35% of peripheral, emphysematous parenchyma from each lung
 - Decreases lung volume and improves elastic recoil of remaining lung

IMAGING

- Radiography
 - Reduced apical lung volume
 - Apical metallic staple line
 - Evaluation of postoperative complications

• CT pre-LVRS

- Used for patient selection and surgical planning
- Evaluation of distribution of emphysema and fissural integrity
- Confirmation of emphysema as principal cause of hyperinflation

- CT post-LVRS
 - Direct visualization of surgical site and staple line
 - May show increase in functional lung volume
- Nuclear scintigraphy
 - Evaluation of regional blood flow, which reflects distribution of emphysema for surgical planning
- Combination of CT and perfusion scintigraphy superior to either study in preoperative evaluation

TOP DIFFERENTIAL DIAGNOSES

- Bronchoscopic lung volume reduction
- Sublobar resection or biopsy

CLINICAL ISSUES

- Best candidates for LVRS: Disabling upper lobe predominant emphysema refractory to medical therapy
- LVRS: Overall survival advantage over best medical therapy in carefully selected patients

(Left) PA chest radiograph of a patient who had bilateral lung volume reduction surgery through a median sternotomy shows faint visualization of bilateral apical staple lines ➡. (Right) Axial NECT of a patient status post lung volume reduction surgery shows bilateral staple lines ➡ along the medial aspects of the bilateral upper lobes and severe confluent upper lobe predominant emphysema.





(Left) Frontal chest radiograph shows a placement of multiple endobronchial valves in left lower lobe segmental bronchi, which manifest as multiple thin branching metallic densities 🔁. (Right) Coronal CECT of a patient with severe upper lobe emphysema who underwent a lung volume reduction procedure shows bronchoscopically placed 1way metallic valves 😂 in right upper lobe segmental bronchi, associated right upper lobe volume loss, and mediastinal shift to the right.





Abbreviations

• Lung volume reduction surgery (LVRS)

Definitions

- **Treatment of severe emphysema** by removing approximately 20-35% of peripheral, emphysematous parenchyma from each lung
- Decreases lung volume
- Improves elastic recoil of remaining lung
- Improves mechanics of diaphragm and intercostal muscles

IMAGING

General Features

- Best diagnostic clue
- Apical metallic staple line
- Location

o Lung apex

Radiographic Findings

- Pre-LVRS
 - Large lung volume, flattening of hemidiaphragms
 Increased AP diameter
 - Increased AP diameter
 - Increased retrocardiac and retrosternal clear spaces
- Post-LVRS
 - Reduced apical lung volume
 - Apical metallic staple line

CT Findings

- Pre-LVRS
 - CT used for patient selection and surgical planning
 - Evaluation of distribution of emphysema and fissural integrity
 - Confirmation of emphysema as principal cause of pulmonary hyperinflation
 - Heterogeneous severe emphysema with upper lobe predominance most likely to benefit from LVRS
 - Peripheral or subpleural distribution of severe emphysema, better target for LVRS
 - Quantitative computerized densitometric analysis more reproducible than qualitative pulmonary evaluation; not proven to provide better prediction of response to LVRS
 - Most commonly used qualitative technique is "density mask" analysis that identifies voxels with attenuation < -900 to -950 HU
 - Underlying bronchiectasis, interstitial lung disease, pleural disease, infection, cancer, or cardiovascular disease may preclude LVRS
 - Resection of small indeterminate pulmonary nodules can sometimes be performed at time of LVRS
 - Approximately 3-5% of LVRS candidates have undiagnosed non-small cell lung cancer
- Post-LVRS
 - o Direct visualization of surgical site and staple line
 - CT may show increase in functional lung volume

MR Findings

• Hyperpolarized Helium-3 and other agents, such as Xenon, under investigation for MR evaluation of extent and distribution of emphysema

Nuclear Medicine Findings

- V/Q scan
 - Regional blood flow patterns reflect distribution of emphysema; useful for surgical planning
 - Combination of CT and perfusion scintigraphy superior to either study alone in preoperative evaluation

Imaging Recommendations

- Best imaging tool
 - o CT useful for preoperative evaluation of severity and distribution of emphysema
 - Chest radiography helpful for evaluation of postoperative complications
 - Pneumothorax, pneumonia, hemorrhage

DIFFERENTIAL DIAGNOSIS

Bronchoscopic Lung Volume Reduction

- Instrumental obstruction of airways supplying hyperinflated lung segment or lobe
- Use of endobronchial 1-way valves; hyperdense on CT; lung collapse distal to endobronchial valve

Sublobar Resection

- Clinical history or preoperative CT most helpful
- More likely to be unilateral; LVRS more commonly bilateral

CLINICAL ISSUES

Demographics

- Patients with **disabling emphysema refractory to medical therapy**
- Patients with upper lobe predominant emphysema and low exercise capacity most likely to benefit from LVRS

Natural History & Prognosis

- LVRS
 - Restoration of respiratory mechanics
 - Reduction of oxygen and energy consumption of respiratory muscles
 - Improvement of exercise tolerance and quality of life
- Patients with lower lobe-predominant emphysema or α-1 antitrypsin deficiency less likely to benefit from LVRS
- Approximately 50% of patients have prolonged air leak (> 7 days)
- Overall survival advantage over best medical therapy in carefully selected patients

Treatment

- LVRS currently most commonly performed in both lungs through video-assisted thoracoscopic surgery (VATS)
- Median sternotomy or standard thoracotomy may also be used

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Lobectomy

KEY FACTS

TERMINOLOGY

- Lobectomy: Complete anatomic lobar resection
- Sleeve lobectomy: Resection of lobe and portion of common airway

IMAGING

- Radiography
 - Postsurgical changes and ipsilateral volume loss
 - Hyperexpansion of remaining lobes
 - Analysis of hila and neofissures to determine type of lobectomy
 - Compensatory ipsilateral hemidiaphragmatic elevation
- CT
 - Direct visualization of bronchial stump and absence of resected lobe/bronchial branches
 - Assessment of surgical staples and postoperative changes
 - o Ipsilateral volume loss
 - Hyperexpansion of remaining lobes

TOP DIFFERENTIAL DIAGNOSES

- Lobar atelectasis
- Sublobar resection
- Pneumonectomy

PATHOLOGY

- Lung cancer: Leading cause of cancer-related mortality in USA; 5-year survival: 19.4%
- Metastatic disease
- Bronchiectasis
- Lung abscess

DIAGNOSTIC CHECKLIST

- Consider prior lobectomy in patients with postsurgical change and ipsilateral volume loss
- Evaluate radiographic anatomy to determine type and extent of lobar resection
- CT provides direct visualization of bronchial stump and documents absence of resected lobe

(Left) PA chest radiograph of a patient with a history of prior right upper lobectomy demonstrates right lung volume loss, mild rightward mediastinal shift \square , and elevation of the right hemidiaphragm 🔁 (Right) Composite image with axial CECT of the same patient in lung (left) and soft tissue (right) window shows volume loss in the right hemithorax, a neofissure 🖾, and surgical staples 🔁 at the site of right upper lobe bronchus resection or bronchial stump.





(Left) PA chest radiograph of a patient with a history of prior right middle lobectomy shows volume loss in the right hemithorax and surgical staples \supseteq in the right infrahilar region. (Right) Composite image with axial CECT of the same patient in lung (left) and soft tissue (right) window demonstrates volume loss in the right hemithorax and surgical staples \supseteq along the neofissure. Neofissures are formed by the visceral pleural surfaces of the remaining lobes following lobectomy.





Definitions

- Lobectomy
 - Complete anatomic single lung lobe resection• Typically includes regional lymph node resection
- Sleeve lobectomy
 - Lobe resection, common airways, and re-anastomosis of airways

IMAGING

General Features

- Best diagnostic clue
 - CT identification of bronchial stump (absent corresponding lobe/bronchial branches, pulmonary artery, and veins)

Radiographic Findings

- Radiography
 - o General
 - Signs of lobar volume loss
 - Hyperexpansion of remaining lobes
 - Distorted remaining fissure, "neofissure"
 - Other findings
 - Surgical staples, thoracotomy changes, lymphadenectomy clips

• Right upper lobectomy

- Right lung volume loss
- Elevation of right hilum
 - Superior/lateral displacement of right mainstem bronchus and bronchus intermedius (BI)
 - Superior/lateral displacement of interlobar/proximal right lower lobe (RLL) pulmonary artery
- Juxtaphrenic peak of elevated right hemidiaphragm
- Decrease in tracheal bifurcation angle
- Neofissure
 - Superiorly extended right major fissure between visceral pleural surfaces of remaining right middle lobe (RML) and RLL
 - Displaced superiorly and anteriorly
 - □ Best visualized on lateral chest radiograph

• Right middle lobectomy

- Absent minor fissure, volume loss least apparent
- Neofissure
 - Inferiorly extended right major fissure with anterior displacement
 - Visceral pleural surfaces of right upper lobe (RUL) and RLL
 - Best visualized on lateral chest radiograph
- Slight lateral displacement of right mainstem
- bronchus and right interlobar pulmonary artery

• Right lower lobectomy

- Right lung volume loss
- Inferior displacement of right hilum
- Type 1 reorientation
 - Neofissure: Elongated minor fissure (pleura of RUL and RML)
 - RUL expands inferiorly, superior and anterior to neofissure, similar to left upper lobe (LUL)

- □ RML shifts and expands posteriorly and superiorly, posterior to neofissure, similar to RLL
- □ Right mainstem bronchus inferiorly displaced
- Frontal chest radiograph: Oblique orientation of neofissure with lateral aspect inferior to medial aspect
- □ Neofissure has appearance of left major fissure

Type 2 reorientation

- Neofissure: Reoriented minor fissure with flipped orientation of typical major fissure on lateral view
- RML remains anterior and expands superiorly
- RUL expands posteriorly and inferiorly
- Neofissure best visualized on frontal chest radiograph and lower than type 1
- Anterior portion of fissure is superior to posterior lower portion

• Left upper lobectomy

- Left lung volume loss
- No remaining interlobar fissure
- Elevation of left hilum
- Decrease in tracheal bifurcation angle
- Leftward shift of anterior mediastinum
- Juxtaphrenic peak of elevated left hemidiaphragm
- Hyperexpansion of left lower lobe (LLL)

• Left lower lobectomy

- Left lung volume loss
- No remaining interlobar fissure
- Inferior displacement of left hilum
- Leftward shift of anterior mediastinum
- Elevation of left hemidiaphragm
- Hyperexpansion of LUL

CT Findings

- CECT
 - o General
 - Direct visualization of bronchial stump and absence of resected lobe/bronchial branches
 - Follow bronchial tree from carina, identify bronchial stump, pulmonary artery/vein clips
 - Ipsilateral volume loss
 - Hyperexpansion of remaining lobes
 - Compensatory ipsilateral mediastinal shift
 - Compensatory ipsilateral hemidiaphragmatic elevation
 - Other findings: Surgical staples, thoracotomy changes

• Right upper lobectomy

- RML remains anterior and expands superiorly
 RML identified as anterior branch off BI
 - □ Posteriorly bound by expanded major fissure
- RLL remains posterior and expands superiorly and anteriorly
 - RLL identified as posterior branch off BI
 - Displaces fissure forward and upward
- Superior/lateral displacement of right mainstem bronchus and BI
- Superior/lateral displacement of proximal RLL pulmonary artery

• Right middle lobectomy

RUL remains anterior and expands inferiorly
 Thin line or band on CT

- □ Coronal orientation at all levels
- Less vertical orientation than left major fissure
- □ Inferior aspect located anterior to superior aspect
- □ Anterior to left major fissure at level of inferior pulmonary vein
- RLL remains posterior and expands anteriorly
- Lateral displacement of right interlobar artery
- Inferior displacement of RUL bronchus

• Right lower lobectomy

- Type 1 reorientation
 - Neofissure: Thin line or band on CT
 - $\hfill\square$ Absence of RLL bronchus and pulmonary artery
 - Inferior displacement of RUL bronchus

Type 2 reorientation

- □ Neofissure: Thin line or band on CT
- Neofissure anterior at subcarinal level and inferior aspect located posteriorly
- □ Absence of RLL bronchus and pulmonary artery
- □ Posterior/inferior displacement of RUL bronchus
- □ Hyperexpanded RUL
- □ RML smaller in volume than in type 1

$\circ \ {\rm Left} \ {\rm upper} \ {\rm lobectomy}$

- No neofissure
- Absence of LUL artery and bronchus
- Hyperexpansion of LLL
- Left lower lobectomy
 - No neofissure
 - Absence of LLL artery and bronchus
- Hyperexpansion of LUL

Imaging Recommendations

- Best imaging tool
 - CT: Identification of bronchial stump and documentation of absence of resected lobe/bronchial branches

DIFFERENTIAL DIAGNOSIS

Lobar Atelectasis

- No neofissure or postsurgical change
- Preserved tethering forces limit lung redistribution
- Less volume loss than lobectomy

Sublobar Resection

- Segmentectomy and wedge resection
- Small, peripheral, noninvasive neoplasms
- Less volume loss compared to lobectomy

Pneumonectomy

- Resection of entire lung; opaque hemithorax
- Large and locally invasive tumors
- More volume loss than lobectomy

PATHOLOGY

General Features

- Etiology
 - Lung cancer: Leading cause of cancer-related mortality in USA; 5-year survival: 19.4%
 - Survival varies markedly with stage at diagnosis
 - Other: Metastatic disease, bronchiectasis, lung abscess

Gross Pathologic & Surgical Features

• General

• Thoracotomy

- Posterolateral thoracotomy preferred
- Anterolateral and muscle-sparing lateral thoracotomy

Video-assisted thoracoscopic surgery

- Increasing utilization
- Lower complication rate
- Equivalent survival to open thoracotomy
- Shorter hospitalization

• Sleeve lobectomy

- Alternative to pneumonectomy
- o Lesions involving mainstem or lobar bronchi
 - Benign and low-grade malignant neoplasms
 - Airway stenosis
 - < 10% operable lung cancers

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Complications

- Early (postoperative day 1-30)

- Hemorrhage, pneumonia, edema, empyema, bronchopleural fistula, dehiscence, lung herniation, lobar torsion
- Late (postoperative > day 30)
 - □ Bronchopleural fistula, empyema, pneumonia, recurrent neoplasm, anastomotic stricture

Natural History & Prognosis

- Lobectomy
 - o Thoracotomy: Complication rate: 49%; mortality: 2.9%
 - Video-assisted thoracoscopic surgery
 - Complication rate: 31%; mortality: 0-2%
 - Variable recurrence rates
- Sleeve lobectomy
 - Postoperative day 1-30: Mortality 5%
 - o Locoregional recurrence: 4-22%

Treatment

- Bronchopleural fistula
 - Completion pneumonectomy
 - Vascularized flap covers bronchial stump
- Anastomotic stricture: Completion pneumonectomy

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Consider lobectomy in patients with surgical change and ipsilateral volume loss
- Evaluate radiographic anatomy for determination of type and extent of lobar resection
- CT: Direct visualization of bronchial stump and absence of resected lobe

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- Hoy H et al: Surgical treatment of lung cancer. Crit Care Nurs Clin North Am. 31(3):303-13, 2019

Lobectomy





(Left) PA chest radiograph of a patient with a history of prior right lower lobectomy demonstrates volume loss in the right hemithorax and inferior displacement of the right hilum 🔁. (Right) Composite image with axial CECT of the same patient in lung (left) and soft tissue (right) window shows volume loss in the right hemithorax and surgical staples \implies at the site of resection. The best imaging clues of lobectomy are identification of the bronchial stump and absence of the resected lobe.





(Left) PA chest radiograph of a patient with prior left upper lobectomy demonstrates volume loss in the left hemithorax, elevation of the left hilum \supseteq , and leftward shift \supseteq of the mediastinum. (Right) Composite image with axial CECT of the same patient in soft tissue (left) and lung (right) window shows volume loss in the left hemithorax, leftward deviation of the anterior junction line \square , and surgical staples at the site of left upper lobe bronchus resection 🔁. Left-sided lobectomies do not produce neofissures.





(Left) PA chest radiograph of a patient with prior left lower lobectomy demonstrates volume loss in the left hemithorax and leftward shift of the azygoesophageal recess ➡. The left upper lobe is hyperexpanded. (Right) Composite image with axial CECT of the same patient in soft tissue (left) and lung (right) window shows leftward deviation of the prevascular mediastinal fat 🔁 and surgical staples *at the site* of resection of the left lower lobe bronchus.

Lobar Torsion

KEY FACTS

TERMINOLOGY

• Bronchovascular pedicle rotation with resultant airway obstruction, venous compromise, ischemia, infarction, and gangrene

IMAGING

• Radiography

- o Reoriented major fissure may extend below hilum
- o Lobar loss of volume, subsequent volume increase
- Abnormally located "collapsed" lobe
- o Mediastinum may shift away from affected lung
- Diagnosis usually suggested based on chest radiographic abnormalities
- CT
 - Tapered obliteration of proximal pulmonary artery and bronchus
 - Delayed contrast filling of pulmonary artery
 - Bulging fissures with unusual orientation
 - Unexpected location of affected lobe

TOP DIFFERENTIAL DIAGNOSES

- Lobar atelectasis
- Pneumonia
- Infarction

PATHOLOGY

- Usually postoperative complication
- 70% after right upper lobe lobectomy, 15% after left upper lobe lobectomy

CLINICAL ISSUES

- Signs/symptoms
 - o Rapid development of shock in postoperative periodo Sudden cessation of postoperative air leak
- High mortality if unrecognized (10-20%)

DIAGNOSTIC CHECKLIST

• Consider lobar torsion in symptomatic patient with postsurgical findings resembling lobar atelectasis

(Left) AP chest radiograph of a patient with middle lobe torsion following right upper lobectomy shows right upper perihilar opacification 🖂 Middle lobe torsion is the most common lobar torsion and almost always occurs in the context of right upper lobectomy. (Right) Axial CECT of the same patient shows superior displacement of the *middle lobe. Note complete* opacification of the middle lobe 🔁 with intrinsic lucent foci, which suggest middle lobe infarction.





(Left) Coronal CECT of the same patient shows superior *displacement of the middle* lobe 🖂, which is related to middle lobe rotation as a result of torsion and is responsible for associated vascular compromise. Lucent foci within the consolidated lung are related to pulmonary infarction. (Right) Axial CECT of the same patient shows kinking of the middle lobe pulmonary artery 🔁, which contributes to vascular compromise of the middle lobe. There was also kinking of the pulmonary vein (not shown).





Synonyms

• Volvulus of lung lobe

Definitions

• Bronchovascular pedicle rotation: Airway obstruction, venous compromise, ischemia, infarction, gangrene

IMAGING

General Features

- Best diagnostic clue
- Rapid post surgical opacification of affected lobeLocation
 - Middle lobe torsion after right upper lobectomy
- Morphology
 Initial lobar volume loss followed by size increase

Radiographic Findings

- Fissure
 - Reoriented major fissure post right upper lobe lobectomy may extend below hilum
- Lobe
 - Lobar loss of volume, subsequent volume increase
 Rapid postoperative lobar opacification
 - o Abnormally located "collapsed" lobe
 - Lobar positional change on serial radiography
 - o Lobar air-trapping rare; may be seen in infants
- Hilum
 - o Paradoxical displacement in relation to "atelectatic" lobe
 - Abnormal pulmonary vascular course
 - Hilar vessels course laterally and superiorly
 - Bronchial cut-off or distortion
- Mediastinum: May shift away from affected lung
- Pleura
 - o New pleural effusion suggests infarction
 - May be obscured by ipsilateral pleural drain

CT Findings

- Hilum
 - Tapered obliteration of proximal pulmonary artery and bronchus
 - o Delayed contrast filling of pulmonary artery
 - Pulmonary artery acutely kinked
- Lobe
 - Volume may increase rather than decrease
 - Attenuation range from ground-glass to consolidation
 - Septal thickening from venous obstruction
 - o Bulging fissures with unusual orientation
 - Unexpected lobe location
 - Pulmonary infarction of affected lobe

Imaging Recommendations

- Best imaging tool
 - Portable chest radiography usually sufficient for suggesting diagnosis
 - Critical element: Awareness of radiographic signs of torsion
 - CECT may be useful in selected cases
 - Identification of hilar vessels

- Visualization of parenchymal involvement

DIFFERENTIAL DIAGNOSIS

Lobar Atelectasis

- Most common mimic of lobar torsion
 - Common postoperatively; retained secretions, splinting
- Torsed middle lobe may mimic atelectasis

Pneumonia

- Usually develops later in postoperative course
- Fever, ↑ white blood cell count; also occurs in torsion

Infarction

- Subacute
 - Later in postoperative course; not lobar

PATHOLOGY

General Features

- Etiology
 - o Usually **postoperative complication**
 - Right upper lobectomy \rightarrow middle lobe torsion
 - Left upper lobectomy \rightarrow left lower lobe torsion
 - Right upper lobectomy \rightarrow right lower lobe torsion

Gross Pathologic & Surgical Features

- Typically 180° clockwise (or counterclockwise) rotation (range: 90-360°)
- Venous obstruction may lead to infarction

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Rapid development of shock in postoperative period
 - Sudden cessation of postoperative air leak
- Other signs/symptoms
 - Hemorrhagic pleural effusion

Demographics

- Complicates 0.1% of pulmonary resections
- 70% after right upper lobe lobectomy, 15% after left upper lobe lobectomy

Natural History & Prognosis

- Diagnosis: Median 10 days after surgery
- High mortality if unrecognized (10-20%)

Treatment

- Prophylactic
 - Anchoring lobes to each other after lobectomy

DIAGNOSTIC CHECKLIST

Consider

• Lobar torsion in symptomatic patient with postsurgical findings resembling lobar atelectasis

SELECTED REFERENCES

- Eba S et al: [Assessment of computed tomography sagittal images for early diagnosis of pulmonary torsion after lung resection.] Kyobu Geka. 74(3):191-5, 2021
- Hammer MM et al: Clinical and imaging features in lung torsion and description of a novel imaging sign. Emerg Radiol. 25(2):121-7, 2018

Pneumonectomy

KEY FACTS

TERMINOLOGY

- Intrapleural pneumonectomy: Lung and visceral pleural resection
- Intrapericardial pneumonectomy: Intrapleural pneumonectomy with resection of pericardium or involved intrapericardial vasculature
- Extrapleural pneumonectomy: En bloc resection of lung, visceral and parietal pleura, hemidiaphragm, pericardium

IMAGING

- Radiography
 - Early: Air in pneumonectomy space gradually replaced by fluid, midline trachea and mediastinum
 - Late: Opaque hemithorax, ipsilateral mediastinal and tracheal shift
- **CT**: Direct assessment of pneumonectomy space, complications, recurrence
- **PET and PET/CT**: Restaging, detection of metachronous primary malignancy

TOP DIFFERENTIAL DIAGNOSES

- Empyema ± bronchopleural fistula
- Chylothorax
- Hemothorax

CLINICAL ISSUES

- Complications
 - Pulmonary edema: 80-100% mortality
 - o Bronchopleural fistula: 16-23% mortality
 - Acute respiratory distress syndrome: > 80% mortality
 - o Hemothorax/chylothorax/empyema
 - Postpneumonectomy syndrome

DIAGNOSTIC CHECKLIST

- Radiography used for postoperative follow-up
- CECT for evaluation of complications and surveillance of recurrent disease or new primary malignancy
- PET and PET/CT for staging and restaging

(Left) AP chest radiograph obtained on postoperative day 1 following a left pneumonectomy shows air and fluid within the left pneumonectomy space and left chest wall soft tissue gas. Note left thoracostomy tube in the pneumonectomy space. (Right) AP chest radiograph of the same patient obtained on postoperative day 5 shows increased fluid (~ 75%) and decreased gas in the left pneumonectomy space and decreased left chest wall soft tissue gas. These are expected postsurgical findings in the absence of complications.











Abbreviations

- Intrapleural pneumonectomy (IPP)
- Extrapleural pneumonectomy (EPP)
- Bronchopleural fistula (BPF)

Synonyms

• Intrapleural (classic) pneumonectomy

Definitions

- Intrapleural (classic) pneumonectomy: Lung and visceral pleural resection
 - Treatment of lung cancer, tuberculosis, bronchiectasis
- **EPP**: En bloc resection of lung, visceral and parietal pleura, hemidiaphragm, and pericardium
 - Used in young patients with curative intent for select malignancies: Malignant pleural mesothelioma, locally advanced lung cancer, high-risk (invasive) thymoma
- Intrapericardial pneumonectomy: IPP with resection of pericardial invasive disease or intrapericardial portions of pulmonary vasculature
- Sleeve pneumonectomy: Central tumor resection; contralateral mainstem bronchus anastomosed to trachea

IMAGING

General Features

- Best diagnostic clue
 - Opaque hemithorax
 - Ipsilateral surgical changes

Radiographic Findings

- Early
 - Air in pneumonectomy space
 - Midline trachea and mediastinum
 - o Progressive fluid filling of pneumonectomy space
 - Gradual cephalad migration of air-fluid level(s) on upright imaging
 - Gradual ipsilateral tracheal and mediastinal shift
 - Enlarged ipsilateral hilum: Seen when vascularized flap used to assist bronchial closure
- Late
 - Opaque hemithorax: Complete obliteration of air in pneumonectomy space; weeks to months
 - o Mediastinal and tracheal shift toward pneumonectomy
 - Heart rotates toward posterior aspect of pneumonectomy space
 - Contralateral lung hyperinflates and occupies anterior aspect of affected hemithorax
- Postsurgical complications

Pulmonary edema, pneumonia, acute respiratory distress syndrome (ARDS)

- Interstitial and airspace opacities in contralateral lung
- ± contralateral pleural effusion
- Hemothorax/chylothorax/empyema
 - Rapid fluid filling of pneumonectomy space
 - Contralateral mediastinal shift
 - Widening of ipsilateral intercostal spaces
- Bronchial dehiscence, bronchopleural or esophagopleural fistula
 - Failure of pneumonectomy space opacification

- ↓ fluid and ↑ air in pneumonectomy space
 □ ≥ 1.5-cm drop in air-fluid level
- Contralateral mediastinal shift
- − ↑ subcutaneous air (BPF)
- Cardiac herniation
 - Bulging or wide of cardiac contour
 - Pneumopericardium
- Postpneumonectomy syndrome
 - More common after right pneumonectomy
 - Ipsilateral displacement and rotation of heart and mediastinum, hyperinflated contralateral lung
- Late complications: Radiation pneumonitis/fibrosis, organizing pneumonia, tumor recurrence

CT Findings

- Direct evaluation of pneumonectomy space
 ~ 2/3 exhibit fluid in pneumonectomy space
 - $\sim 1/3$ exhibit minimal fluid and thick fibrous tissue
- Evaluation of postpneumonectomy complications
- Localization of bronchopleural/esophagopleural fistulae
 - Direct signs: Visible defect in bronchial stump, fistulous communication with esophagus
 - Indirect signs: Gas adjacent to bronchial stump
- o Empyema
 - Expansion of pneumonectomy space
 - Irregular thickening/enhancement of parietal pleura
- Hemothorax
 - High-attenuation fluid in pneumonectomy space
 - Hematocrit effect, fluid-hematocrit level
- Chylothorax: Expansion of pneumonectomy space with water attenuation fluid
- Postpneumonectomy syndrome: Compression of contralateral mainstem bronchus between pulmonary artery and aorta/spine
- Pulmonary artery stump thrombosis: Filling defect in distal pulmonary artery stump
- Recurrent malignancy
 - Distant or contralateral lung metastases
 - Locoregional intrathoracic recurrence
 - Mediastinal or contralateral hilar lymphadenopathy
 - Bronchial stump recurrence: Wall thickening,
 - endobronchial lesion
 - Pleural nodules
 - Rib or incision site lesions
 - New metachronous primary lung cancer: 1-2% risk per year

Nuclear Medicine Findings

- PET
 - PET or PET/CT useful for restaging after potentially curable locoregional recurrence or detection of metachronous primary malignancy

Imaging Recommendations

- Best imaging tool
 - Radiography for postoperative follow-up
 - CECT for evaluation of complications and surveillance of recurrent disease or new primary malignancy

DIFFERENTIAL DIAGNOSIS

Empyema ± Bronchopleural Fistula

- Infected fluid-filled pneumonectomy space
- Air-fluid levels indicate presence of BPF

Chylothorax

- Thoracic duct injury resulting in chylous effusion
- Water attenuation fluid in pneumonectomy space

Hemothorax

• CT helpful for identification of high-attenuation fluid &/or clot in pneumonectomy space

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Empyema
 - Chest pain
 - Fever and leukocytosis
- Other signs/symptoms
 - Postpneumonectomy syndrome
 - Dyspnea and stridor
 - Recurrent infection due to ↓ secretion clearance

Natural History & Prognosis

• Early complications of pneumonectomy

- Pulmonary edema (2.5-5% prevalence): > 80% mortality
 - More common after right pneumonectomy
 - Related to ↑ blood flow and hydrostatic pressure in remaining lung
 - Predisposing conditions
 - □ Fluid overload, low serum oncotic pressure
 - Fresh frozen plasma administration
 - 🗆 Arrhythmia
 - Diuresis
- Pneumonia (2-15% incidence): 25% mortality
 - Predisposing factors
 - Intubation/mechanical ventilation, aspiration
- ARDS: 5% incidence; > 80% mortality
 - Predisposing factors
 - □ Male; age > 60 years
- o Empyema (< 5% incidence): Can occur early or late
 - Predisposing factors
 - Right pneumonectomy, completion pneumonectomy
 - □ Pleural contamination and sepsis
 - Neoadjuvant radiation
- **Bronchial dehiscence/early BPF**: 5-8% incidence in EPP; 3-6% in IPP; 16-23% mortality
 - Typically occurs within 2 weeks of surgery
 - Vascularized muscular or omental flap often used to buttress bronchial stump and promote healing
 - 1 risk for empyema in pneumonectomy space and contralateral aspiration
 - Predisposing conditions
 - □ Inadequate/faulty stump closure
 - Perioperative infection
 - Positive pressure ventilation
 - □ Neoadjuvant radiation

- Cardiac herniation or torsion (rare)
 - Herniation through pericardial defect or dehisced pericardial patch
 - More common after right intrapericardial pneumonectomy or EPP
 - Requires emergent surgery: 40-50% mortality
 □ Rightward cardiac herniation typically results in ↓ venous return
 - □ Leftward cardiac herniation typically results in impaired ventricular output
- Pericardial patch restriction: Improper sizing resulting in "tight" pericardium and tamponade physiology
- Diaphragmatic patch dehiscence (EPP): Intrathoracic herniation of abdominal contents
- Esophagopleural fistula (rare)
- Late complications of pneumonectomy
 - BPF
 - Months to years following pneumonectomyMore common on right
 - Postulated etiology: Relative larger diameter of right mainstem bronchus, ischemia related to bronchial artery supply
 - Predisposing risk factors
 - □ Residual malignancy at resection margin
 □ Empvema: ↑ incidence of stump breakdown
 - □ Irradiation
 - Pulmonary artery stump thrombosis (12% of pneumonectomies)
 - More likely with longer pulmonary artery stumps (right stump typically longer than left)
 Likely related to altered flow dynamics
 - Risks of embolism considered small
 - Role of anticoagulation therapy unclear
 - Postpneumonectomy syndrome
 - Children and young adults typically < 2 years after surgery
 - Almost exclusively after right pneumonectomy
 - Marked rightward displacement of mediastinum → left mainstem bronchus compression → bronchomalacia
 - Inspiratory stridor, recurrent infection
 - Treatment: Central repositioning of mediastinum via insertion of saline implant in pneumonectomy space
- Overall morbidity 30-60%; mortality 3-11%
 - Risk factors
 - Cardiovascular disease
 - COPD with poor forced expiratory volume in 1 second (FEV₁)
 - Advanced age
 - Diabetes

Treatment

• Management tailored to specific postpneumonectomy complications

SELECTED REFERENCES

- 1. Duranti L et al: Extra-pleural pneumonectomy. J Thorac Dis. 11(3):1022-30, 2019
- Bommart S et al: Imaging of postoperative complications following surgery for lung cancer. Diagn Interv Imaging. 98(1):11-20, 2017

Pneumonectomy





(Left) AP chest radiograph obtained on postoperative day 1 following a right pneumonectomy for lung cancer shows gas and small volume fluid in the right pneumonectomy space. Note moderate reticular opacities and vascular indistinctness throughout the left lung, consistent with pulmonary edema. (Right) AP chest radiograph of the same patient obtained on postoperative day 4 shows increased fluid \supseteq in the pneumonectomy space and resolution of previous left lung pulmonary edema.





(Left) AP chest radiograph obtained on postoperative day 1 after a right pneumonectomy shows a small amount of fluid and gas in the pneumonectomy space and rightward mediastinal shift. (Right) AP chest radiograph of the same patient obtained on postoperative day 3 shows unexpected increased gas in the pneumonectomy space. The right upper thoracic curvilinear opacity 🔁 corresponds to an intercostal muscle flap. Dehiscence of the bronchial closure was confirmed at surgery.





(Left) PA chest radiograph obtained 1 month after a right pneumonectomy shows complete opacification of the pneumonectomy space and a midline position of the trachea, which was previously deviated to the right. New contralateral shift of the mediastinum should prompt further investigation. (Right) Axial CECT of the same patient shows hyperattenuating material in the pneumonectomy space, consistent with clot 🔁 from a hemothorax. CT is helpful in distinguishing hemothorax from empyema or chylothorax. (Left) Axial CECT of patient with respiratory distress years after a right pneumonectomy shows significant luminal narrowing of the left mainstem bronchus *→* as a result of rightward mediastinal shift, consistent with postpneumonectomy syndrome. Note the small in situ thrombus 🔁 in the ligated right pulmonary artery stump. (Right) Axial CECT of the same patient shows significant luminal narrowing of the left pulmonary veins $\overline{
ightarrow }$ as they drape over the adjacent descending thoracic aorta ₽.





(Left) Axial CECT of the same patient demonstrates a more central location of the mediastinum following the insertion of multiple saline implants ➡ in the right pneumonectomy space. (Right) Coronal CECT of the same patient shows the new position of the mediastinum following saline implant ➡ insertion in the right pneumonectomy space. Note persistent in situ thrombus ➡ in the ligated right pulmonary artery stump.





(Left) PA chest radiograph of a patient status post left intrapericardial pneumonectomy for lung cancer shows an opaque right hemithorax due to fluid in the pneumonectomy space. Note superior displacement of the left hemidiaphragm and underling bowel. (Right) Axial CECT of the same patient shows the pericardial reconstruction material \square , crowding of left-sided ribs, and small volume fluid 🔁 in pneumonectomy space. Note colon *≥* and abdominal fat in the left hemithorax due to left diaphragmatic elevation.





Pneumonectomy





(Left) Axial CECT of a patient with prior right pneumonectomy for lung cancer demonstrates a filling defect 🔁 in the right pulmonary artery stump, which had been stable over previous scans, consistent with in situ thrombus. (Right) Axial CECT obtained 2 years after a right pneumonectomy shows abnormal circumferential soft tissue \blacksquare that encases and narrows the right bronchial stump, consistent with local tumor recurrence.





(Left) Axial CECT obtained 15 months following a right pneumonectomy for squamous cell lung cancer shows lytic destruction of a right posterior rib and an adjacent enhancing soft tissue mass \supseteq . (Right) Axial fused FDG PET/CT of the same patient confirms the presence of an FDG-avid mass in the posterior right pneumonectomy space, consistent with tumor recurrence. PET/CT is not routinely performed for surveillance after pneumonectomy, but is useful for restaging suspected recurrent disease.





(Left) Axial CECT of the same patient shows abnormal irregular soft tissue thickening ➡ along the posterior aspect of the right pneumonectomy space and direct involvement of the adjacent right posterior chest wall 🖂. (Right) Axial fused FDG PET/CT of the same , patient shows FDG avidity corresponding to the soft tissue abnormality seen on CT, consistent with recurrent neoplasm. PET/CT is particularly useful for evaluating suspected tumor recurrence in the pneumonectomy space.

KEY FACTS

TERMINOLOGY

- Extrapleural pneumonolysis: Plombage, oleothorax
- Extrapleural apicolysis: Pleural tent, parietal pleurolysis
- Collapse therapy: Surgical upper lobe collapse used to treat cavitary tuberculosis

IMAGING

- Thoracoplasty
 - Segmental rib fractures (> 2 fractures/rib) and rib displacement into chest cavity
 - Resection of 6-7 ribs
- Extrapleural plombage
 - Extrapleural space created and enlarged with Lucite spheres or paraffin wax
- Lungs
 - o Loss of lung volume, cicatricial atelectasis
 - Thick pleura adjacent to thoracoplasty/plombage

TOP DIFFERENTIAL DIAGNOSES

- Thoracoplasty or extrapleural plombage
 - Tuberculous empyema
 - Post-traumatic/postsurgical chest wall deformity
 - o Malignant pleural mesothelioma
- Extrapleural apicolysis
 - Hydropneumothorax
 - Pancoast tumor

CLINICAL ISSUES

- Signs/symptoms
 - Thoracoplasty: Chronic pain, scoliosis, reduced chest wall mobility
 - Plombage: Pain uncommon, hemoptysis from vascular erosion

DIAGNOSTIC CHECKLIST

• History of prior tuberculosis is helpful in recognizing imaging findings of extrapleural plombage

(Left) PA chest radiograph of a patient with surgically treated tuberculosis shows a right waterfall thoracoplasty involving right ribs 1-9 ➡, right upper lobe volume loss, and right convex upper thoracic scoliosis 🛃 (Right) Axial CECT of a patient with remote pleuropulmonary tuberculosis shows findings of left thoracoplasty ₽, calcified tuberculous empyema \blacksquare , and calcified pulmonary granulomas 🔁. Thoracoplasty is still used in some countries to treat drug-resistant cavitary tuberculosis.





(Left) Coned-down PA chest radiograph of a patient with tuberculosis treated with Lucite sphere plombage shows multifocal, thin-walled, airfilled spheres \supseteq in the right upper hemithorax. (Right) Axial CECT of a patient with oleothorax collapse therapy for tuberculosis shows a large right extrapleural collection with predominant central low attenuation, intrinsic foci of calcification \blacksquare , and peripheral curvilinear calcification **⇒**. Chronic oleothorax usually does not exhibit fat attenuation on CT.





Synonyms

- Extrapleural pneumonolysis: Plombage, oleothorax
- Extrapleural apicolysis: Pleural tent, parietal pleurolysis

Definitions

- Collapse therapy
 - Surgical procedures designed to collapse upper lobe cavitary tuberculosis; used in mid 20th century before availability of effective antituberculous drug therapy
- **Thoracoplasty**: Surgical rib removal to approximate chest wall, collapse lung, or obliterate pleural space
- Extrapleural apicolysis (pleural tent): Performed to reduce apical pleural dead space after upper lobectomy
 - Apical parietal pleura pulled off chest wall, creation of extrapleural space, reduced intrapleural space

IMAGING

Radiographic Findings

- Thoracoplasty
 - Segmental rib fractures (> 2 fractures/rib) and rib displacement into chest cavity
 - Resection of 6-7 ribs
 - Apical chest wall deformity; ribs displaced medially toward spine
- Extrapleural plombage
 - Extrapleural space created and enlarged with Lucite spheres or paraffin wax
 - Spheres initially surrounded by air, later by fluid
- Lung
 - Loss of lung volume, calcified granulomas, cicatricial atelectasis
 - Pleural thickening adjacent to thoracoplasty or plombage
- Thoracoplasty complications (perioperative period)
 - Bronchopleural fistula
 - Prolonged air leak
 - o Hemorrhage
 - o Empyema
- Plombage complications (15%) (acute vs. long term)
 - Change in size, shape, appearance of previously stable plombage
 - Plombage migration
 - Erosion into major vessels or ribs
 - Dispersion of Lucite spheres; expanded extrapleural space
 - Acute or chronic local infection
 - Mediastinal compression by extrapleural mass
 - Secondary malignant neoplasms: Sarcoma, non-Hodgkin lymphoma, bronchogenic carcinoma
- Extrapleural apicolysis (pleural tent)
 - Initial: Air-containing space inseparable from air in pleural space
 - o Day 2: Apical air-fluid level as fluid fills extrapleural space
 - > 30 days: Air resorption, apical cap (fluid and soft tissue), gradually diminishes in size

CT Findings

• Direct visualization of chest wall, extrapleural space, plombage; assessment of complications

Imaging Recommendations

Best imaging tool
 Chest radiography usually sufficient for evaluation
 CT useful as problem-solving tool

DIFFERENTIAL DIAGNOSIS

Thoracoplasty or Extrapleural Plombage

- Tuberculous empyema
 - Focal pleural mass; variable thick peripheral calcification
 - Complications: Bronchopleural fistula, empyema necessitatis
- Post-traumatic/postsurgical chest wall deformity
- Malignant pleural mesothelioma
 - Circumferential nodular pleural thickening
 - o Chest wall deformity; ipsilateral volume loss
 - o Chest wall pain, weight loss, malaise

Extrapleural Apicolysis

- Hydropneumothorax
 - Loculated hydropneumothorax usually from inadequate chest tube drainage
- May lead to empyema
- Pancoast tumor
 - Apical pleural thickening
 - Skeletal erosion
 - o Pain, brachial plexus involvement, Horner syndrome

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Thoracoplasty: Chronic pain, scoliosis
- Other signs/symptoms
 - **Plombage**: Pain uncommon, hemoptysis from vascular erosion
 - Thoracoplasty
 - Reduced chest wall mobility, pneumonia
 - Rare right to left shunt through ipsilateral lung
 - Chronic hypoxia; pulmonary artery hypertension

Demographics

- Age
 - Older adults; thoracoplasty common in 1940s and 1950s
 Still performed worldwide in younger individuals

Natural History & Prognosis

- Collapse therapy **curative in 75%** of tuberculosis
- Plombage complications may occur decades later

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• History of prior tuberculosis is helpful in recognizing imaging findings of extrapleural plombage

SELECTED REFERENCES

 Krasnov D et al: Thoracoplasty for tuberculosis in the twenty-first century. Thorac Surg Clin. 27(2):99-111, 2017

Lung Herniation

KEY FACTS

TERMINOLOGY

• Extension of lung tissue outside thoracic cavity

IMAGING

- Radiography
 - Aerated lung outside thoracic cavity when imaged in profile
 - Sharply marginated focal thoracic radiolucency when imaged en face
- CT
 - Direct visualization of herniated lung tissue; subsegmental herniation
 - Direct visualization of chest wall defect; typically intercostal defect
 - Assessment of adjacent bone and soft tissue

• Best imaging tools

- o Orthogonal chest radiographs
- Unenhanced chest CT for indeterminate cases

TOP DIFFERENTIAL DIAGNOSES

- Chest wall infections
- Rib fractures and flail chest
- Thoracotomy
- Apical lung hernia

PATHOLOGY

- Thoracic surgery with failure of soft tissue closure
- Trauma
- Spontaneous
- Chronic corticosteroid use
- Congenital chest wall defect

CLINICAL ISSUES

- Most patients asymptomatic; require no treatment
- Symptomatic hernias may require treatment
 - Chest wall reconstruction, defect closure
- Strangulation rare

(Left) Coned-down PA chest radiograph of a patient status post left thoracotomy shows a rounded lucency with sharp lobular margins 🛃 projecting over the left upper hemithorax. (Right) Axial NECT of the same patient shows that the lucency represents focal lung herniation \boxtimes through an anterior chest wall defect ∋. The herniated lung contains normal bronchovascular structures and is contiguous with the intrathoracic left upper lobe. CT allows a definitive diagnosis when radiography is inconclusive.









(Left) Coronal NECT shows a left lateral chest wall defect through which there is herniation of normalappearing lung \supseteq status post remote left upper lobectomy. Note the gap 🛃 in the left lateral intercostal space. (Right) AP chest radiograph of the same patient obtained *immediately following left* thoracotomy shows the left lateral chest wall lung hernia with lung projecting outside the confines of the thoracic cage.

Synonyms

• Lung hernia

Definitions

• Extension of lung tissue outside thoracic cavity

IMAGING

General Features

- Best diagnostic clue
 Aerated lung parenchyma outside thoracic cavity
- Location
- Chest wall through intercostal space
- Size
 - Usually subsegmental
- Morphology
 - Sharp peripheral margins because of overlying pleura

Radiographic Findings

- Lucency (aerated lung) outside confines of thoracic cavity when imaged in profile
 - Continuity of herniated lung tissue with adjacent intrathoracic lung parenchyma
- Sharply marginated focal thoracic radiolucency when imaged en face

CT Findings

- Direct visualization of herniated lung tissue
 - Lung parenchyma extending into chest wall
 - Assessment of size/extent of herniation
 - Visualization of chest wall defect
 - Assessment of adjacent skeleton and soft tissues

Imaging Recommendations

- Best imaging tool
 - Orthogonal chest radiographs
 - Unenhanced chest CT for indeterminate cases

DIFFERENTIAL DIAGNOSIS

Chest Wall Infections

- Abscess: Loculated fluid and gas
- Empyema necessitatis: Extension of empyema into chest wall

Rib Fractures and Flail Chest

- Acute rib fractures
 Segmental or involving
- Segmental or involving large section of chest wall
- Lung remains confined within thoracic cavity
- Paradoxical motion with respiration

Thoracotomy

- Partial rib resection or osteotomy
- Lung remains confined within thoracic cavity
- Subcutaneous gas following surgery

Apical Lung Hernia

- Congenital defect
- Apical location

PATHOLOGY

General Features

Etiology

- Most related to **surgery**
 - Failure of soft tissue closure
 - Intercostal muscles
 - Endothoracic fascia
 - Procedures: Thoracotomy, chest tube placement, minimally invasive thoracic/cardiac surgery
- Chest trauma
- Spontaneous
 - Rare
 - Rigorous coughing or sneezing
- Chronic corticosteroid use
 - Muscle and connective tissue weakness
- Congenital chest wall defect

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - \circ Most patients asymptomatic
 - Physical examination
 - Chest wall deformity
 - Palpable crepitant mass
 - Varies in size with respiration, cough, Valsalva maneuver
- Other signs/symptoms
 - Focal pain with deep inspiration
 - o Dyspnea
 - Local tenderness
 - o Fever

Natural History & Prognosis

- Most require no treatment
- Symptomatic hernias may require treatment
- Strangulation rare

Treatment

- Chest wall reconstruction
 - o Primary closure
 - Mesh prosthesis

DIAGNOSTIC CHECKLIST

Consider

• Exclusion of normal postoperative subcutaneous gas or chest wall abscess in suspected lung herniation

Image Interpretation Pearls

• Herniated lung maintains continuity with intrathoracic lung and contains bronchovascular structures

Reporting Tips

• Description of hernia size and location, affected lobe(s), and defect size

SELECTED REFERENCES

 Subotic D et al: Surgical repair of the postoperative lung hernia by combining mesh interposition and chest wall stabilization by using synthes plates: a novel technique. Case Rep Surg. 2019:2107083, 2019

Sternotomy

KEY FACTS

TERMINOLOGY

- Median sternotomy (MS): Vertical incision through manubrium and sternum
 - o Access heart, pericardium, and anterior mediastinum
 - o Limited access to hila, lungs, pleura
 - Closure with cerclage or "figure 8" steel sutures/plates
- Clamshell sternotomy (CS): Broad transverse incision across sternum and 4th anterior intercostal spaces
- Access to both hemithoraces and mediastinumIndications for MS
 - CABG, valve and aortic surgery
 - Heart transplant, congenital heart disease
 - Placement of cardiac support devices
 - Anterior mediastinal mass
- Indications for CS
 - Double lung and heart-lung transplants
 - Resection of large mediastinal or cardiac mass
 - Resection of bilateral lung metastases

IMAGING

Radiography

- o Sternal wires/plates should be aligned and intact
- Osteotomy fragments should be fused
- CT
 - Assess for parasternal and mediastinal fluid collections/abscess and sternal dehiscence

CLINICAL ISSUES

- Most patients do well without need for intervention
- Signs/symptoms of sternal infection
 - Pain ± fever, incisional drainage, crepitus
 - Osteomyelitis: Bone destruction
 - o Pleural effusion, hemothorax, fibrothorax
- Treatment of sternal infection: Antibiotics, debridement

DIAGNOSTIC CHECKLIST

• Evaluation of sternotomy for integrity of sternal hardware and sternal fusion

(Left) Graphic shows the morphologic features of median sternotomy in which a vertical incision through the sternum is secured with steel wires 🔁 (or plates). Sternal wires may be displaced \supseteq due to infection, dehiscence, trauma, or devascularization. (Right) Intraoperative supine AP chest radiograph shows a sternotomy in progress with multiple cerclage wires 🔁 clamped before final closure. Note retained sponge 📨 along the right hemidiaphragm and transesophageal echocardiography probe 🖂.

(Left) AP portable chest radiograph of a patient status post sternotomy, now with an open sternum, shows multiple mediastinal drains \supseteq and packing material 🔁, skin staples 🔁 at the periphery of the sternotomy incision, and pneumomediastinum, all important clues to an open sternum. (Right) Axial CECT of the same patient shows the sternotomy defect \supseteq , the skin incision with staples \square , and multiple mediastinal drains 🔁. In delayed sternal closure, all retained material should be reported.









Abbreviations

- Median sternotomy (MS)
- Clamshell sternotomy (CS)

Synonyms

• CS: Transverse sternotomy, cross-bow incision

Definitions

- MS: Vertical incision through manubrium and sternum
 - Access to heart and anterior/prevascular mediastinum
 - Limited access to hila, lungs, pleura
 - o Indications
 - Cardiac and aortic surgery
 - □ Coronary artery bypass graft (CABG) most common
 - □ Ascending aortic aneurysm or dissection
 - Cardiac valve repair or replacement
 - Chest trauma exploration
 - Pulmonary embolectomy
 - Resection of anterior/prevascular mediastinal mass
 - Double lung transplant in some cases
 - o Closure with cerclage or "figure 8" steel sutures
 - 2-3 wires in manubrium, 4-5 in sternum body
 - Heals quickly with stable closure and minimal pain
 Stainless-steel wire sutures: Single wire, double wire,
 - figure-of-eight, Robicsek weave • Other
 - Sternal bands
 - Polymer cable ties
 - Sternal plates
 - Transverse rigid sternal plate fixation: May improve outcomes in patients at high risk for dehiscence, such as morbidly obese patients
- **CS**: **Broad transverse incision** across sternum and 4th anterior intercostal spaces
 - Excellent access to heart and both hemithoraces
 - Disrupts sternal pericardial attachments
 - Pleural spaces may communicate anteriorly
 - □ Chest tube may cross midline anteriorly
 - Indications
 - Double lung or heart-lung transplantation
 - Resection of large mediastinal or cardiac mass
 Resection of bilateral lung metastases (rare)
 - Closure with steel "figure 8" sternal sutures
 - Extensive disruption of chest wall musculature
 - Increased risk of sternal complications

IMAGING

General Features

- Best diagnostic clue
 - MS: Midline sternotomy wires, bands, plates
 - CS: "Figure 8" or lower sternal cerclage wires

Radiographic Findings

- Radiography
 - o MS: Midline sternotomy wires are vertically aligned
 - Determination of type of surgery; i.e., cardiac
 - Assessment of support devices and surgical complications

- Displaced sternal wires suggest dehiscence
- Absent or missing wires suggest debridementAssessment of other closure methods
- CS: "Figure 8" steel wires over inferior sternum
 - Determination of type of surgery, i.e., double lung transplant
 - Exclusion of sternal instability or pseudoarthrosis

CT Findings

- NECT
 - MS wires should be intact and vertically aligned
 - Sternal osteotomy fragments should be fused
 Exclusion of diastasis, "over-ride," pseudoarthrosis
 - □ Exclusion of parasternal or mediastinal abscess

Imaging Recommendations

- Best imaging tool
 - CT is optimal imaging modality for evaluating complications of thoracic surgery
- Protocol advice
 - Unenhanced chest CT for assessment of osteotomy and soft tissues
 - o CECT may improve detection of mediastinal abscess

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Sternal infection, dehiscence, nonunion
 - Pain ± fever, incisional drainage, crepitus
 - Osteomyelitis: Bone destruction
- Other signs/symptoms
 - Pleural and pericardial effusion, hemothorax, fibrothorax, mediastinitis

Natural History & Prognosis

• Most patients do well without need for intervention

Treatment

- Sternal infection
 - Conservative treatment: Antibiotics
 - Surgical debridement in some cases
 - Removal of sternal wires/hardware
 - Sternectomy in refractory cases

DIAGNOSTIC CHECKLIST

Consider

- Evaluation of sternotomy for integrity of sternal hardware and sternal fusion
- Identification of surgical indication; i.e., CABG, valve repair, tumor recurrence
- Evaluation of surgical complications and underlying disease

Image Interpretation Pearls

• Sternotomy wires should be aligned

SELECTED REFERENCES

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Sternotomy

(Left) Coned-down AP chest radiograph of a patient status post median sternotomy and coronary artery bypass graft (the most common indication for sternotomy) shows normal alignment of sternal wires 🔁 without fracture, and surgical clips 🖂 along the left upper mediastinum that indicate a left internal mammary artery graft. (Right) Coned-down AP chest radiograph of the same patient obtained days later shows interval displacement and rotation of multiple sternal wires ⊇, an important sign of post-operative sternal dehiscence.





(Left) Axial NECT of a patient status post median sternotomy complicated by dehiscence necessitating debridement shows a large defect \supseteq in the left aspect of the sternum with a chest wall drain 🔁 in place. (Right) Sagittal NECT of the same patient shows extensive inflammatory stranding 🔁 in the sternotomy bed and presternal soft tissues related to post-operative infection. Sternal infection is among the most common complications of median sternotomy, and CT may be used to evaluate for mediastinal fluid collections.





(Left) PA chest radiograph of a young adult with a history of surgically repaired tetralogy of Fallot shows characteristic small median sternotomy wires \supseteq , consistent with remote sternotomy in infancy or childhood. Note the enlarged pulmonary trunk 🔁. (Right) AP chest radiograph of the same patient after surgical pulmonic valve repair shows larger sternotomy wires 🔁 indicative of a re-do sternotomy. Staged repair of pulmonic stenosis is common in tetralogy of Fallot, and the morphology of the sternal wires can be a clue.





Sternotomy





(Left) AP portable chest radiograph of a patient status post median sternotomy and bioprosthetic aortic valve replacement shows a fractured sternal wire 🖂 Sternotomy wire fracture is an important indicator of complication in the immediate post-operative setting, but of doubtful clinical significance in the setting of remote surgery. (Right) AP chest radiograph of a patient status post re-do sternotomy and removal of sternal wires shows a temporizing sternal bar 🔁 in place and a retained sponge \triangleright





(Left) Graphic shows the clamshell sternotomy procedure, a transverse incision of the sternum that extends into both 4th intercostal spaces and allows the chest to be opened like a "clam" to access the heart and the bilateral hemithoraces. (Right) AP chest radiograph of a patient status post bilateral lung transplantation shows clamshell sternotomy wires ⇒ and a right pectoral port catheter ≥. Clamshell sternotomy is typically performed at the 4th intercostal space to facilitate access to both hila.





(Left) AP chest radiograph of a patient 1-year status post clamshell sternotomy for double lung transplantation shows "figure 8" cerclage wires D that secure the lower sternal incision. Bilateral hilar clips ➡ define the location of the bronchial anastomoses. (Right) Lateral chest radiograph of the same patient shows displaced sternal osteotomy fragments ➡ secondary to sternal nonunion and instability. Sternotomy complications may be difficult to detect on frontal radiography.

Heart Transplantation

KEY FACTS

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• Acute allograft rejection Cardiac allograft vasculopathy

DIAGNOSTIC CHECKLIST

cardiac transplantation

heterotopic heart transplants

> 5,000 heart transplants/year performed worldwide

• Acute rejection (12%) and infection (33%) are leading

• Familiarity with imaging features of orthotopic vs.

anastomosis of donor heart with native atria

• Orthotopic transplantation shows enlarged atria due to

Imaging assessment of complications associated with

causes of death in 1st year after surgery

• Neoplastic disease

CLINICAL ISSUES

TERMINOLOGY

• Treatment of end-stage heart failure

IMAGING

- Identification of orthotopic vs. heterotopic heart transplant • Orthotopic heart transplant most common
- Cardiac MR: Optimal imaging modality for identification of rejection, left and right ventricular failure
- Coronary CTA and IVUS: Optimal modalities for direct visualization of accelerated coronary atherosclerosis
- CTA: Identification of coronary artery wall thickening and intimal hyperplasia characteristic of cardiac allograft vasculopathy
- MR: Delayed hyperenhancement in myocardial necrosis (rejection) or subendocardial infarction (vasculopathy)
- Echocardiography: Monitoring of cardiac function

TOP DIFFERENTIAL DIAGNOSES

• Infection

(Left) Frontal chest radiograph of a patient with nonischemic dilated cardiomyopathy shows enlargement of the cardiac silhouette, a right pectoral defibrillator with lead \supseteq in the right ventricle and a left ventricular pacing lead \square in a cardiac vein. An abandoned defibrillator lead \supseteq is also present. (Right) AP chest radiograph of the same patient after orthotopic heart transplant shows decreased heart size. Sternotomy wires \square and abandoned lead fragments \square are clues to the nature of the surgical procedure.





(Left) Axial CECT of a patient status post orthotopic heart transplant shows surgical changes at the aorta \bowtie and pulmonary trunk 🖂. In a patient with a median sternotomy without evidence of coronary artery bypass or valve surgery, these surgical changes may be the only clue to the diagnosis. (Right) Axial CECT of the same patient shows elongation and abnormal contour 🔁 of the left atrium at the site of anastomosis. Note the right lower lobe consolidation 📨 due to pneumonia, a common late complication.





Definitions

- Most effective therapy for treatment of end-stage heart failure
- Most often performed for nonischemic cardiomyopathy, followed by ischemic cardiomyopathy
- Most common complications
 - o Infection
 - Acute allograft rejection
 - Cardiac allograft vasculopathy (CAV)
 - Post-transplantation lymphoproliferative disease

IMAGING

General Features

- Best diagnostic clue
 - Cardiac allograft may be placed in orthotopic or heterotopic position
 - Orthotopic heart transplant is most common procedure
 - Native heart removed through median sternotomy
 - Donor heart joined to native atria, aorta, and pulmonary trunk
 - Heterotopic heart transplant is rarely performed
 - Donor heart connected to native heart in parallel
 - Used for patients with severe pulmonary arterial hypertension
 - Used when donor heart is too small for recipient

Imaging Recommendations

- Best imaging tool
 - Cardiac MR: Optimal imaging modality to identify transplant rejection, left and right ventricular failure
 - Coronary CTA and IVUS: Optimal modalities for direct visualization of accelerated coronary atherosclerosis
 - Serial echocardiograms used to assess left and right ventricular function
 - ↑ cardiac uptake on Gallium-67 scintigraphy in moderate to severe transplant rejection
- Protocol advice
 - Monitoring of allograft systolic function is important in suspected or known rejection
 - Delayed enhancement and T2WI should be included in cardiac MR protocol
 - Renal regurgitation common: Iodinated contrast and gadolinium used judiciously and with precautions
 - Heart rate control may be challenging when performing coronary CTA

Radiographic Findings

- Immediate postoperative findings
 - Cardiac enlargement from pericardial effusion
 - o Pneumomediastinum, pneumopericardium
 - Mediastinal fluid collections
 - o Pleural effusion, pneumothorax
 - Subcutaneous gas
- **Double right atrium contour** (overlap of donor and native right atria in orthotopic heart transplant)
- Abandoned cardiac pacer wire fragments in thoracic veins
- Sternotomy wires

CT Findings

- Cardiac gated CTA
 - Evaluation of coronary arteries for thickening and intimal hyperplasia characteristic of CAV
 - 64-slice MDCT provides moderate to good test characteristics for detection of CAV when compared to IVUS as reference standard
- Evaluation of aortic and pulmonary artery anastomoses
- High and redundant pulmonary trunk
- Space between SVC and ascending aorta; ↑ space between aorta and pulmonary trunk
- Atrial waist due to anastomosis of right and left donor and native atria
- Vertical atrioventricular groove

MR Findings

- Hyperenhancement in delayed images
 - Myocardial necrosis indicates rejection in early postoperative period
 - Subendocardial enhancement indicates CAV in late postoperative period
- T2WI can demonstrate T2 prolongation in myocardium consistent with myocardial edema
- Abnormal T2 prolongation is strong predictor of biopsydefined rejection when clinically suspected
- **Spatial resolution** allows accurate measurement of ejection fractions
- Evaluation of quantitative changes in myocardial mass

Ultrasonographic Findings

- Echocardiography is primary noninvasive modality for monitoring cardiac function
- Pericardial effusion occurs frequently
- Myocardial edema may manifest as relative ↑ in wall thickness

Nuclear Medicine Findings

- Technetium-labeled agents for diagnosis of CAV
 Sensitivity of 86%, specificity of 80%
- Dobutamine stress test may be advantageous given inotropic response
- Normal dobutamine stress myocardial perfusion imaging study associated with 96-98% negative predictive value for major adverse cardiac events at 2 years

DIFFERENTIAL DIAGNOSIS

Infection

- 1st month of transplantation: *Pseudomonas aeruginosa, Staphylococcus aureus, Enterococci, Enterobacteriaceae*
- Later infections commonly caused by viruses (cytomegalovirus) and opportunistic fungi (*Pneumocystis*, *Candida, Aspergillus*)
- Aspergillus infection: Isolated pulmonary nodule, upper lobe predilection, cavitation
- Mediastinitis: Mediastinal fluid collections ± air, focal contrast enhancement

Acute Allograft Rejection

• T-cell mediated inflammatory response causing myocardial edema and cell damage

- Left ventricular dysfunction: Dyspnea, paroxysmal nocturnal dyspnea, orthopnea, palpitations, syncope
- Endomyocardial biopsy may be used for surveillance or diagnosis
- Rejection in 30% of transplant recipients in 1st year, usually 2 weeks to 3 months after transplantation
- Grading system based on biopsy findings

Cardiac Allograft Vasculopathy

- Concentric intimal hyperplasia (vs. eccentric disease in traditional coronary artery disease)
- Diffuse process; starts with small distal vessels, spreads to all coronary arteries
- Incidence: 8% at 1 year, 30% at 5 years, > 50% at 10 years
- High mortality rate: 10% of patients die within 12 months of diagnosis of CAV
- ↑ risk in recipients of male allografts; risk increases with donor age
- Exacerbation of vascular disease with hyperlipidemia, hypertension, diabetes, steroid use
- Difficult diagnosis; transplanted hearts are denervated
 Affected patients rarely present with chest pain
 - Blunted heart rate response to exercise decreases sensitivity of stress testing
- Due to lack of symptoms, surveillance coronary artery evaluation performed annually (typically cardiac catheterization with IVUS)

Neoplastic Disease

- Incidence of any malignancy: 35% by 10 years
- Most common neoplasms
 - Skin squamous cell carcinoma and basal cell carcinoma
 - Lung cancer
 - Lymphoproliferative malignancies
 - Prostate cancer
 - o Melanoma

PATHOLOGY

General Features

- Etiology
 - Disease processes that require transplantation
 - Nonischemic cardiomyopathy: 46%
 - Ischemic cardiomyopathy: 42%
 - Valvular disease: 3%
 - Adult congenital heart disease: 2%
 - Miscellaneous: 7%

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Early post-operative complications (< 30 days)
 - Mediastinitis, dehiscence, pulmonary edema
 - Opportunistic infection
 - Graft failure
 - □ Ventricular failure leading to hemodynamic compromise and cardiogenic shock; ↓ right and left ventricular systolic function, tricuspid regurgitation
 - Intermediate complications (1-12 months)
 - Subacute allograft rejection
 - Community-acquired pneumonia

- Valvular complications: Most commonly tricuspid regurgitation
- Constrictive pericarditis
- Drug toxicity
- Late complications (> 1 year)
 - CAV: Coronary artery disease (donor coronary arteries)
 - Malignancy: Leading cause of morbidity and mortality
 Lung cancer most common (after skin malignancies)
 - Lymphoma/post-transplant lymphoproliferative disease

Demographics

- Epidemiology
 - Over 5,000 cardiac transplants performed annually worldwide
 - 1st successful heart transplant performed in 1967
 - o Over 89,000 cardiac transplants reported worldwide

Natural History & Prognosis

- 1-year survival of heart transplant recipients > 80%
- 10-year survival rate approaches 50%
- Median survival (time at which 50% of recipients remain alive) for combined group of adult and pediatric heart recipients is currently 10 years
- Acute rejection (12%) and infection (33%) are leading causes of death in 1st year after surgery
- Improvement in early survival statistics
 - Establishment of recipient selection criteria
 - o Use of endomyocardial biopsy to diagnose rejection
 - o Improvements in immunosuppression techniques

Treatment

- Retransplantation required in 2% of cases
- Post-transplant immunosuppression often includes tacrolimus, mycophenolate mofetil, and prednisone

DIAGNOSTIC CHECKLIST

Consider

- Familiarity with imaging features of orthotopic vs. heterotopic transplantation
- Orthotopic transplantation shows enlarged atria due to anastomosis of donor heart with native atria
- Imaging assessment of complications
 - Impaired ventricular function: Echocardiography, cardiac MR, cardiac-gated CT
 - Atherosclerotic plaque and coronary stenosis: Coronary angiography, coronary CTA, IVUS
 - Rejection: Cardiac MR; hyperenhancement in delayed images and hyperintensity on T2WI suggest myocardial necrosis/edema
 - Chest radiography and CT: Assessment of lung and mediastinal infections and neoplasms

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Heart Transplantation





(Left) Four-chamber view cine cardiac MR of a patient status post orthotopic heart transplant shows tricuspid regurgitation \square and dilatation of the right heart. Tricuspid regurgitation is a known manifestation of primary graft failure. (Right) Four-chamber T2WI FS MR shows diffuse hyperintensity of the right ventricular free wall 🛃, suspicious for mural edema and transplant rejection. Cardiac MR is now the primary imaging modality used in the evaluation of allograft rejection.





(Left) Axial NECT of a heart transplant recipient with cytomegalovirus (CMV) pneumonia shows a middle lobe consolidation \blacksquare and patchy right lower lobe ground-glass
extstyle and nodularDopacities. CMV infection is the most important infectious cause of morbidity and mortality in heart transplant recipients. (Right) Axial NECT of a heart transplant recipient with pneumocystis pneumonia shows diffuse bilateral patchy ground-glass opacities. Pneumocystis pneumonia may superinfect patients with CMV pneumonia.





(Left) Axial CECT of a patient with lymphoma status post heart transplant shows mediastinal lymphadenopathy ➡. Suture material ➡ at the aortic anastomosis and sternotomy wires are clues to the history of prior heart transplant when clinical information is not provided. (Right) Coronal cardiac cine MR shows a heterotopic heart transplant. The native pulmonary artery ➡ and left ventricle ➡ are enlarged. Note the adjacent transplanted heart 🔁.

Lung Transplantation

KEY FACTS

TERMINOLOGY

- Synonym: Lung allograft
- Post-transplant lymphoproliferative disorder (PTLD)
- Chronic lung allograft dysfunction (CLAD)
- Surgical replacement of one/both lungs from cadaveric donor

IMAGING

- General
 - Thoracotomy (single) or clamshell sternotomy (double)
 - Surgical clips at hilum or bilateral hila
 - Residual disease in native lung
 - Asymmetric lungs
- Immediate post-transplant complications (< 1 month)
 - Bronchial dehiscence
 - Pneumothorax/pleural effusion
 - Hyperacute/acute rejection
 - Reimplantation response
 - o Infection

- Late post-transplant complications (> 1 month)
 - Infection
 - o Bronchial stenosis and bronchomalacia
 - Vascular anastomotic complication
 - Chronic rejection
 - o PTLD
 - o Malignancy

DIAGNOSTIC CHECKLIST

- New lung abnormalities should suggest rejection or infection
- Early allograft abnormalities: Consider reimplantation response
- Persistent pneumothorax or pneumomediastinum: Consider bronchial anastomotic complication
- PTLD usually occurs within first 2 years after transplant
- Expiratory CT useful for assessing air-trapping associated with chronic rejection
- Search for lung cancer in native lung of smokers

(Left) AP chest radiograph obtained immediately after a left lung transplant shows normal aeration of the graft. The native right lung is hyperlucent secondary to emphysema. (Right) AP chest radiograph of the same patient obtained 24 hours after transplantation shows fine linear opacities 🔿 representing interstitial edema from reimplantation response, left basilar atelectasis 🖾, and mild chest wall subcutaneous gas \square . The reimplantation response usually peaks at around 4 days and slowly resolves thereafter.





(Left) Axial HRCT shows patchy consolidations 🛃 and ground-glass opacities \boxtimes in the right lung allograft resulting from acute rejection. Note the normal appearance of the telescoped bronchial anastomosis 🖂. (Right) Axial HRCT shows a focal extraluminal mediastinal gas collection \supseteq that directly communicates with the right mainstem bronchus \square and represented focal bronchial dehiscence from ischemic necrosis. Patchy ground-glass opacities 🛃 were secondary to acute rejection.





Synonyms

• Lung allograft

Definitions

• Surgical replacement of one or both lungs from cadaveric donor

IMAGING

General Features

- Best diagnostic clue
 - Thoracotomy (single lung transplant) or clamshell sternotomy (double lung transplant)
 - Surgical clips at hilum or at bilateral hila
 - Residual disease in native lung; asymmetric lung parenchyma
- Location
 - o Unilateral or bilateral lungs

Radiographic Findings

- Radiography
 - Single lung transplant
 - Unilateral postsurgical changes
 - Surgical clips at ipsilateral hilum
 - Asymmetric lung parenchyma
 - Abnormal lung parenchyma in native lung

Double lung transplant

- Bilateral postsurgical changes
- Surgical clips at bilateral hila
- Symmetric-appearing lung parenchyma
- Bronchial dehiscence
 - Extensive pneumomediastinum
 - Pneumothorax despite adequate pleural drainage
- Radiography of post-transplantation complications

Immediate posttransplant (< 1 month)

- Pneumothorax
 - Usually small with adequate pleural drainage
 - Enlargement or persistence suggests air leak
- Pleural effusion
 - Common in first 2 weeks after transplantPersistent effusion should be evaluated
- Hyperacute rejection
 - Immediate acute opacification of allograft
- Acute rejection
 - Usually within first 3 months after transplant; typically within few days
 - Perihilar hazy opacity, septal lines
 - Radiograph may be normal
- Reimplantation response
 - Mimics interstitial edema
 - □ Usually develops within 24-48 hours after surgery; peaks at around 96 hours with slow resolution
- Infection
 - 🗆 Bacterial, viral, fungal
 - Nosocomial infections most common
 - Focal/multifocal consolidations/nodules

\circ Late posttransplant (> 1 month)

- Infection (bacterial, fungal, viral)
 - □ Focal/multifocal consolidations/nodules

- Bronchial stenosis
 - Segmental or lobar atelectasis
- Chronic lung allograft dysfunction (CLAD)
- Invariably develops in 40-50% of patients 5 years after transplant
- Bronchiolitis obliterans (BO), restrictive allograft syndrome (RAS), acute fibrinoid organizing pneumonia (AFOP)
- BO: Vascular attenuation reflects reflex vasoconstriction from regional hypoxia; hyperinflation in advanced disease
- RAS: Peripheral consolidations and ground-glass opacities, septal and subpleural thickening, bronchiectasis, architectural distortion, upper lobe predominant volume loss
- AFOP: Interlobular septal thickening and intralobular lines, extensive ground-glass opacities, peripheral consolidations
- Post-transplant lymphoproliferative disorder (PTLD)
 - Ranges from low-grade lymphoproliferative disorder to lymphoma
 - Much more common in donors seronegative for Epstein-Barr virus antibodies
 - Multiple lung nodules and lymphadenopathy; most common findings
- Malignancy
 - □ Growing lung nodule
 - Most commonly affects native lung

CT Findings

- NECT
 - Direct visualization of postsurgical changes
 - Evaluation of bronchial anastomoses
 - Direct visualization of pulmonary architecture
 - Evaluation of native lung and allograft
- CECT
 - Direct visualization of postsurgical changes
 Evaluation of vascular anastomoses
- CT/HRCT of post-transplantation complications
 - Immediate posttransplant (< 1 month)
 - Bronchial dehiscence
 - Small air collection adjacent to anastomosis common immediately after transplant
 - □ Enlargement or persistence of air collection indicates dehiscence
 - Vascular anastomotic complications
 - □ < 5% of patients
 - □ Arterial > venous anastomosis
 - $\hfill\square$ Stenosis or kink readily visualized on CECT
 - Hypoperfusion of affected lung
 - $\hfill\square$ Diffuse edema with venous stenosis
 - Infection
 - $\hfill\square$ Nodules, consolidations, ground-glass opacity
 - Isolated ground-glass opacity suggests pneumocystis pneumonia, less commonly cytomegalovirus (CMV) pneumonia

• Late posttransplant (> 1 month)

- Infection (bacterial, viral, fungal)
 - Consolidation, nodules, ground-glass opacity
 - Nodule predominant favors fungal infection
 - $\hfill\square$ Lobar consolidation favors bacterial infection

- Bronchial stenosis and bronchomalacia
 - □ Stenosis in up to 10% of patients
 - May cause obstructive atelectasis or pneumonia
 - □ Bronchomalacia optimally evaluated on expiratory CT; > 50-70% luminal collapse
- Acute rejection
 - Patchy ground-glass opacity and septal lines; nonspecific
- Chronic rejection
 - Mosaic attenuation
 - □ Low attenuation persists/accentuated on expiratory CT; air-trapping
 - Bronchial dilatation and wall thickening
 - Peripheral and upper lobe predominant
- consolidations and ground glass opacities – PTLD
 - Lung nodules and lymphadenopathy most common
 - □ Septal lines, consolidation, endobronchial lesion, thymic enlargement
 - Pericardial or pleural disease less common

Imaging Recommendations

- Best imaging tool
 - Chest radiography for surveillance
 - HRCT for problem solving or suspected lung disease
- Protocol advice
 - Expiratory HRCT for suspected or known constrictive bronchiolitis

DIFFERENTIAL DIAGNOSIS

Lung Metastases

• May mimic infection or PTLD

Lobar Atelectasis

- Secondary to bronchial stricture
- Centrally obstructing neoplasm
- PTLD

Eventration of Diaphragm

• May mimic phrenic nerve injury

PATHOLOGY

Microscopic Features

- Acute rejection
 - Perivascular and interstitial mononuclear infiltrates
- Chronic rejection
 - Lymphocytic infiltration of airway wall
 - Intraluminal polyps of granulation tissue
 - Advanced disease with obliteration of airway lumina by fibrosis
 - Pleuroparenchymal fibroelastosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Acute rejection: Fever, dyspnea, graft dysfunction
 BO syndrome
 - Progressive dyspnea, airflow obstruction

- Infection
 - Fever, cough, leukocytosis
- Drug toxicity
 - Fever, cough, leukocytosis
- o PTLD usually within first 2 years, median; 6 months
 - Viral-like illness
 - Weight loss, fatigue, night sweats
- Lung cancer in native lung; patients with smoking-related lung disease or fibrosis
 - Weight loss, fatigue, cough
 - Paraneoplastic syndromes

Natural History & Prognosis

- Mean 1-year posttransplant survival 85-90%
 Early death from acute graft failure or infection
- Mean 5-year post transplant survival approximately 50%
 Late mortality commonly related to chronic rejection

Treatment

- Acute rejection
 - o Corticosteroids/Immunosuppression management
- Chronic rejection
- Retransplantation for select patients
- Infection
- Broad-spectrum antimicrobials
- Bronchial anastomotic complications
 - o Dilatation, stenting, surgical repair
- PTLD
 - Reduction in immunosuppression
 - Antiviral agents
- Lung carcinoma
 - Resection, stereotactic radiation therapy, ablation

DIAGNOSTIC CHECKLIST

Consider

- Opportunistic infections and acute rejection with any new lung abnormality on imaging of lung transplants
 Nodules and consolidation favor infection
- Bronchial anastomotic complication with persistent pneumothorax or pneumomediastinum despite adequate pleural drainage

Image Interpretation Pearls

- Early allograft changes usually reimplantation response
 Failure to clear should suggest infection or rejection
- Typical appearance of telescoping bronchial anastomosis does not signify dehiscence
 - Small curvilinear perianastomotic air pocket
- Expiratory CT useful for assessing air-trapping associated with chronic rejection

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Lung Transplantation





(Left) Axial NECT shows a large area of ground-glass opacity with an intrinsic focal consolidation ➡ in the right lung allograft secondary to cytomegalovirus pneumonia. Note extensive pneumomediastinum ➡ from a ruptured bulla (not shown) in the active laft lung (Bipt)

in the native left lung. (Right) Axial NECT shows peripheral ground-glass opacities ➡ and consolidations ➡ with associated traction bronchiectasis ➡ in the setting of restrictive chronic lung allograft dysfunction.





(Left) Expiratory axial HRCT shows mosaic lung attenuation *⊡*, consistent with air-trapping secondary to bronchiolitis obliterans in the setting of chronic allograft rejection. Note the unaffected dense lung parenchyma ₽. (Right) Axial HRCT shows diffuse heterogeneous pulmonary attenuation due to chronic rejection. Areas of apparent ground-glass opacity ➡ represent relatively spared lung, while low-attenuation areas \implies reflect air-trapping. $Bronchiectasis \ge commonly$ develops with chronic rejection.





(Left) Axial HRCT shows a right lower lobe mass \boxtimes with air bronchograms in the fibrotic \supseteq native right lung. Biopsy showed posttransplant lymphoproliferative disorder, which can affect the mediastinum, the native lung, or the allograft. (Right) Axial HRCT shows a spiculated right lower lobe mass \implies in the emphysematous native lung. Patients with a history of tobacco abuse and emphysema are at increased risk of developing primary lung cancer in the native lung. Primary lung cancer is uncommon in the allograft.

Esophageal Resection

KEY FACTS

TERMINOLOGY

- Various surgical procedures for benign and malignant esophageal lesions
- Most common: Transthoracic esophagectomy through right thoracotomy (Ivor Lewis)

IMAGING

- Radiography
 - Initial postoperative assessment
 - Assessment of postoperative complications
 - Right mediastinal contour abnormality produced by gastric conduit
 - Contrast studies (Gastrografin): Exclusion of anastomotic leak
- CT
 - o Assessment of postoperative complicationso Assessment of tumor recurrence
- **PET/CT**: Staging and post-treatment restaging

TOP DIFFERENTIAL DIAGNOSES

- Achalasia
- Mediastinal mass

PATHOLOGY

- Stomach: Most convenient esophageal substitute
- Other: Gastric tube, colon, jejunum, free revascularized graft

CLINICAL ISSUES

- Frequent sources of morbidity: Pneumothorax, pleural effusion, pneumonia, respiratory failure
- Mediastinitis and sepsis: High morbidity/mortality

DIAGNOSTIC CHECKLIST

- Consider Gastrografin studies for evaluation of site and size of anastomotic leaks
- CT is optimal imaging modality for evaluation of surgical complications and tumor recurrence

(Left) Graphic illustrates the Ivor Lewis transthoracic esophagectomy. The native esophagus 🔁 is resected, and the stomach \blacksquare is "pulled through" into the thorax and anastomosed \triangleright to the proximal esophagus. (Right) Oblique upper GI series shows postsurgical changes of transthoracic esophagectomy and a normal esophagogastric anastomosis \square . This is the preferred surgical procedure for resectable tumors located in the middle 1/3 of the esophagus.





(Left) PA chest radiograph of a patient with prior Ivor Lewis esophagectomy and CABG shows mild dilatation of the air-filled gastric conduit \rightarrow , which protrudes to the right of *midline. Note post-surgical* changes \square in the right chest wall. (Right) Sagittal CECT post esophagectomy shows a mildly dilated gastric conduit \blacksquare , the gastric staple line \blacksquare , and vertebral compression fractures 🔁. CT is the optimal *imaging modality to evaluate* post-surgical complications and tumor recurrence.





Definitions

- Surgical procedures for benign and malignant esophageal lesions
 - Transthoracic esophagectomy through right thoracotomy (**Ivor Lewis** procedure)
 - Most common technique
 - Middle and lower 1/3 esophageal carcinomas
 - o Transhiatal esophagectomy without thoracotomy
 - Thoracic-cervicothoracic esophageal carcinoma
 - Achalasia, caustic injury
 - Transthoracic esophagectomy through left thoracotomy
 Benign and malignant distal esophageal lesions
 - Radical en-bloc esophagectomy
 - Potentially curable tumor (pre- and intraoperative staging)

IMAGING

Radiographic Findings

- Right mediastinal contour abnormality produced by gastric conduit
- Initial postoperative assessment
 - Wide mediastinum, pneumomediastinum, subcutaneous gas, pleural effusion
- Assessment of postoperative complications
- Wide mediastinum, pneumomediastinum
- o Pleural effusion
- Large air-fluid level in conduit
- Contrast studies (Gastrografin): Exclusion of anastomotic leak

CT Findings

- Assessment of anastomosis and staple lines
- Mediastinitis: Induration of mediastinal fat, fluid collections, extraluminal gas
- Anastomotic leak: Perianastomotic fluid/gas, mediastinal abscess; may not show leak site
- Delayed emptying: Dilated conduit, air-fluid level
- Tumor recurrence: Mass, lymphadenopathy
- Aspiration bronchiolitis: Common complication after esophagectomy; tree-in-bud opacities ± bronchiectasis

Ultrasonographic Findings

Endoscopic ultrasound
 Tumor invasion, lymphadenopathy

Nuclear Medicine Findings

- PET/CT
 - Assessment of distant metastases
 - Restaging after neoadjuvant therapy

DIFFERENTIAL DIAGNOSIS

Achalasia

- Longitudinal contour abnormality ± air-fluid
- Correlation with surgical history is critical

Mediastinal mass

- Lymphadenopathy
- Lymphoma

- Germ cell tumor
- Lymphangioma

PATHOLOGY

General Features

- **Stomach**: Most convenient esophageal substitute
- Other: Gastric tube, colon, jejunum, free revascularized graft
- Complications
- Surgical
 - Anastomotic Leak: Major complication
 - □ Early (2-3 days) or late (3-7 days)
 - □ Subclinical (50%)
 - □ Fistula to adjacent structures
 - Anastomotic stricture: Late postoperative period (exclusion of recurrence)
 - Mediastinitis: Life-threatening; associated with high morbidity and mortality
 - Delayed emptying: Large mediastinal air-fluid level
 Lack of pyloric drainage, hiatal obstruction
 - Redundant intrathoracic esophageal substitute
 - Pulmonary
 - Pneumonia, aspiration, acute respiratory distress syndrome, pulmonary edema, pleural effusion, pneumothorax, pulmonary embolism

• Postoperative tumor recurrence

- Local tumor recurrence
- Tumor of esophageal substitute; stomach, colon

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Frequent sources of morbidity
 - Pneumothorax, pleural effusion
 - Pneumonia (aspiration)
 - Respiratory failure

Natural History & Prognosis

• Mediastinitis and sepsis: High morbidity/mortality

Treatment

• Anastomotic leaks: Catheter or chest tube drainage, surgical treatment, temporal stenting

DIAGNOSTIC CHECKLIST

Consider

- Gastrografin studies for evaluation of site and size of anastomotic leaks
- CT is optimal imaging modality for evaluation of surgical complications and tumor recurrence

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KEY FACTS

TERMINOLOGY

- Radiation therapy (RT): Radiation to control cell growth by damaging DNA of cancerous tissue leading to cell death
- Treatment/palliation of thoracic neoplasms: Lung, breast, esophageal cancers; thymic epithelial neoplasms; lymphoma; malignant pleural mesothelioma

IMAGING

- Radiography
 - Opacities visualized with doses > 40 Gy
- CT
 - Opacities within radiation treatment field with sharp linear or curvilinear margins
 - Location and distribution depend on location of neoplasm, RT technique, treatment plan, and disease extent
 - Radiation pneumonitis (1-6 months after completion)
 - Ground-glass opacities &/or consolidation
 - Small ipsilateral pleural effusion

- Radiation fibrosis (6-12 months after completion)
 - → opacities; ↑ traction bronchiectasis, volume loss, architectural distortion
 - Smooth pleural thickening, pleural effusion

FDG PET/CT

- Radiation pneumonitis: Diffuse homogeneous ↑ FDG uptake that decreases over time
- Radiation fibrosis: Focal ↑ FDG uptake suggests recurrent disease

TOP DIFFERENTIAL DIAGNOSES

- Pneumonia
- Lymphangitic carcinomatosis
- Lung cancer (recurrent)

DIAGNOSTIC CHECKLIST

• Consider radiation-induced lung disease in patients treated with RT and new opacities; correlate with radiation treatment portals and treatment timeline

(Left) PA chest radiograph of a 76-year-old woman with primary squamous cell carcinoma shows a right upper lobe mass-like lesion 🖂 (Right) PA chest radiograph of the same patient obtained 12 weeks after completion of radiation therapy shows a decrease in the size of the right upper lobe lesion \supseteq . Note the absence of new pulmonary opacities. Decreased size of the primary tumor before development of pulmonary opacities may be an initial manifestation of radiation treatment.





(Left) PA chest radiograph of the same patient obtained 20 weeks after completion of radiation shows new patchy opacities \supseteq , consistent with postradiation pneumonitis. (Right) PA chest radiograph of the same patient obtained 3 years after radiation shows a dense right upper lobe opacity \square , consistent with radiation fibrosis. Note tracheal shift 🔁 to the right secondary to right upper lobe volume loss and a small loculated pleural effusion 🔁, a common finding after radiation, which should remain stable or decrease over time.





Abbreviations

• Radiation-induced lung disease (RILD)

Synonyms

- Radiation pneumonitis
- Radiation fibrosis

Definitions

- Radiation therapy (RT) uses ionizing radiation to control cell growth by damaging DNA of cancerous tissue leading to cellular death
 - Treatment/palliation of thoracic neoplasms: Lung, breast, esophageal cancers; thymic epithelial neoplasms; lymphoma; malignant pleural mesothelioma
- Conventional 2DRT uses 2 parallel beams with opposite directions (anteroposterior and posteroanterior)
 - Currently reserved for palliative treatment of painful bone metastases and hemoptysis
- New RT techniques developed to ↑ dose to target lesion and ↓ dose to surrounding structures
 - 3D image reconstructed from CT data used to determine target volume; multiple beams used to conform to target and deliver maximal radiation to neoplasm
 - 3D conformal RT (3DCRT): Each radiation beam shaped to fit profile of target volume (previously, radiation treatment matched height and width of target lesion)
 - □ 4D conformal RT uses respiratory gating
 - Intensity-modulated RT (IMRT): Next generation of 3DCRT; allows more precise conformation to 3D shape by modulating intensity of radiation beam in multiple small volumes
 - Stereotactic body RT (SBRT): Small number of fractions (hypofractionated) with higher dose per fraction to treat early non-small cell lung cancer (NSCLC)
 - Proton therapy: Use of protons as radiation source
 - Radiation delivered to certain depth with minimal dose beyond target lesion; useful for treatment of recurrent previously irradiated tumors, central tumors, and tumors close to critical structures

IMAGING

General Features

- Best diagnostic clue
- Pulmonary opacities within radiation treatment portals
 Location
 - Pulmonary abnormalities relate to location of treated neoplasm
 - NSCLC: Adjacent to primary lesion; paramediastinal if lymphadenopathy is included in treatment portals; treatment field that includes primary neoplasm has additional 2-cm margin around tumor edge and 1-cm margin around regional lymph nodes
 - Small cell lung cancer: Radiation portals include primary neoplasm and can be extended to cover supraclavicular, hilar, mediastinal, and upper abdominal lymph nodes; pulmonary opacities may develop in multiple sites

- Thymic epithelial neoplasms, esophageal cancer, lymphoma: Paramediastinal opacities; upper lobes in thymic neoplasms, lower lobes in distal esophageal cancers
- Mesothelioma: Lung, mediastinum, and chest wall adjacent to treated site
- Breast cancer: Upper lobes, middle lobe, and lingula; anterior subpleural distribution
- Size
 - Extent of pulmonary opacities depends on technique
 - More extensive with conventional 2DRT
 Less extensive with 3DCRT, IMRT, SBRT, and PT (limited to radiation portals)
- Morphology
 - Early stage: Pulmonary opacities in treated area

Radiographic Findings

- Radiography
 - Opacities visualized with doses > 40 Gy
 - Radiation pneumonitis (1-6 months after completion of radiation): Patchy airspace opacities &/or consolidations
 - Radiation fibrosis (6-12 months after completion of radiation, stabilizes after 12-24 months): ↓ airspace opacities/consolidations; ↑ traction bronchiectasis, volume loss, architectural distortion
 - Organizing pneumonia: Patchy or nodular consolidation; outside radiation portals, may affect contralateral lung
 - More frequent after RT for breast cancer (within 1 year of completing RT)
 - Could result from tangential irradiation in breast cancer; does not occur in other thoracic malignancies
 - ↓ tumor size may be seen before lung opacities

CT Findings

- HRCT
 - $\circ \downarrow$ in tumor size may be seen before lung opacities
 - Radiation pneumonitis
 - Conventional 2DRT: Ground-glass opacities, airspace opacities, &/or consolidation
 - Other techniques (3DCRT, IMRT, SBRT, PT)
 □ Patchy or diffuse ground-glass opacities &/or consolidation
 - Treated neoplasm within radiation pneumonitis
 - Opacities may resolve over 6 months or may evolve to fibrosis
 - CT findings may occur far from treated malignancy but are limited by radiation portals
 - Small ipsilateral pleural effusion
 - Radiation fibrosis
 - 2DRT: Dense consolidations, traction bronchiectasis, volume loss, architectural distortion
 - Other techniques (3DCRT, IMRT, SBRT, PT)
 - Modified conventional pattern (for new techniques): Dense consolidations, traction bronchiectasis, volume loss, architectural distortion (less extensive than with 2DRT)
 - Mass-like pattern
 - Scar-like pattern
 - Smooth pleural thickening/effusion (± loculated)
 Within 6 months of completion of radiation

- □ ↑ volume or development after 6 months should be investigated
- Organizing pneumonia
 - Ground-glass opacities &/or consolidations
 - Usually bilateral and peripheral; often migratory
 Reversed halo sign
- Bone CT
 - Rib sclerosis, fracture
 - o Usually seen 1 year after radiation

Nuclear Medicine Findings

- PET/CT
 - Used to detect distant metastases, recurrent neoplasm (after 3-6 months of completion of radiation)
 - Radiation pneumonitis: Diffuse and homogeneous ↑
 FDG uptake that decreases over time
 - Radiation fibrosis: Focal ↑ FDG uptake suggests recurrent disease

Imaging Recommendations

- Best imaging tool
 - CT: Assessment of evolution of postradiation pulmonary abnormalities
 - PET/CT: Identification of recurrence/metastases
 - PET/CT within 3-6 months after RT completion used to detect distant metastases or nonregional lymph nodes, not to evaluate primary tumor

DIFFERENTIAL DIAGNOSIS

Pneumonia

- Acute abnormalities outside radiation treatment field
- Airspace opacities, consolidations, centrilobular nodules, &/or branching linear opacities

Lymphangitic Carcinomatosis

- Known primary intrathoracic or extrathoracic malignancy
- Nodular interlobular septal thickening; peribronchovascular and fissural thickening, subpleural nodules

Lung Cancer (Recurrent)

- Usually occurs within first 2 years after treatment
- CT: ↑ attenuation of previously stable radiation fibrosis; new lobulated contours or nodules, obliteration of previously bronchiectatic airways
 - o Focal contrast-enhancement within radiation fibrosis
 - New lymphadenopathy, new pleural thickening/effusion

PATHOLOGY

General Features

• RT causes diffuse alveolar damage: Acute exudative phase, proliferative phase, chronic fibrosis

Microscopic Features

- Acute phase
 - Vascular congestion, ↑ capillary permeability, intraalveolar proteinaceous material, inflammatory cell infiltration
- Subacute or proliferative phase
 - Interstitial fibrosis, type 2 alveolar cell proliferation, disruption of capillary function (microvascular thrombus); may resolve or progress to chronic or fibrotic phase

- Fibrotic phase
 - Fibroblast proliferation, progressive alveolar septal thickening

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Radiation pneumonitis: Dyspnea, cough, low-grade fever
 - Radiation fibrosis: Asymptomatic or chronic dyspnea
- Other signs/symptoms
 - Esophagitis
 - Pericardial effusion
 - Cardiomyopathy
 - Coronary artery disease
 - Radiation-induced liver injury (distal esophageal carcinoma and malignant pleural mesothelioma)

Natural History & Prognosis

- Factors influencing radiation tissue damage
 - Radiation dose
 - Irradiated volume
 - Fractions (smaller number of fractions)
 - Concurrent chemotherapy
 - Previous RT
 - Preexisting lung disease (emphysema, pulmonary fibrosis)
 - o Age
 - Cigarette smoking
- No linear relation between radiation dose and lung damage
- Lung injury usually occurs after receiving > 40 Gy but occasionally with doses < 20 Gy
- Development of 2nd primary malignancy: 2.4/100 patientyear after chemoradiation for lung cancer

Treatment

• Corticosteroids for symptomatic patients

DIAGNOSTIC CHECKLIST

Consider

 RILD in patients treated with RT who develop new pulmonary opacities

Image Interpretation Pearls

• Correlate imaging abnormalities with radiation treatment portals and treatment timeline

Reporting Tips

• Opacities outside treatment portals or occurring early after or before completion of RT should suggest etiology other than malignancy

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(Left) Axial NECT of a 65-yearold woman with lung cancer treated with radiation 12 months previously shows a dense right upper lobe opacity \square with bronchiectasis and volume loss, consistent with radiation fibrosis. Note small right pleural effusion 🖾. (Right) Axial fused FDG PET/CT of the same patient shows low metabolic activity *in the right upper lobe opacity* similar to that of mediastinal background, consistent with radiation fibrosis. FDG PET/CT is useful for identification of recurrent tumor within radiation fibrosis.





(Left) Axial NECT of the same patient obtained 6 months later shows increased size of the right upper lobe lesion $\overline{\square}$, obliteration of previous intrinsic bronchiectasis, and marked progression of the right pleural effusion 🖂, findings concerning for recurrent malignancy. (Right) Axial fused FDG PET/CT of the same patient shows FDG avidity ⊇ in the right upper lobe lesion concerning for recurrence, which was confirmed on biopsy. Recurrent disease usually occurs in the first 2 years after completion of treatment.





(Left) Axial CECT of a 47-yearold woman with breast cancer treated with radiation 6 weeks previously shows patchy left lung consolidations 🖂 consistent with radiation pneumonitis, which may mimic infection. The subtle peripheral ground-glass attenuation 🔁 is characteristic of radiation to the breast. (Right) Axial NECT of the same patient shows a dense subpleural opacity in the left upper lobe], consistent with fibrosis. Fibrosis usually develops 6-12 months after completion of radiation therapy.

(Left) Axial NECT of a patient who received radiation therapy for malignancy shows subtle band-like ground-glass attenuation in the peripheral left lung, which crosses the fissure and exhibits a straight border 🔁 against the uninvolved normal lung. (Right) Axial CECT of a patient with biopsy-proven primary lung cancer shows a lobulated right upper lobe solid nodule ➡ on a background of centrilobular emphysema. The patient was not a surgical candidate and was referred to radiation oncology for definitive therapy.





(Left) Axial CECT of the same patient obtained 2 months after completion of radiation therapy to the lesion shows dense heterogeneous consolidation on a background of emphysema and obscuration of the right upper lobe nodule, consistent with radiation pneumonitis. PET/CT imaging of this abnormality would show FDG avidity. (Right) Axial NECT of the same patient obtained 10 months after completion of therapy shows decreased right upper lobe volume and an arcuate band-like opacity 🔁 that represents radiation fibrosis.





(Left) Axial NECT of a patient treated with radiation for breast cancer shows peripheral right lower lobe heterogeneous consolidations *⊡*. Biopsy demonstrated organizing pneumonia. (Right) Axial fused FDG PET/CT of a patient treated with palliative brain radiation for metastatic lung cancer who developed organizing pneumonia shows multifocal bilateral FDG-avid peripheral consolidations 🖂 Organizing pneumonia is a well-recognized manifestation of radiation-induced lung disease and occurs outside the radiation field.









(Left) Coronal fused FDG PET/CT of a 67-year-old woman with small cell lung cancer shows extensive FDGavid mediastinal \square and bilateral supraclavicular 🔁 lymphadenopathy as well as left lung postobstructive pneumonitis 🖾. Radiation therapy was administered for cytoreduction. (Right) Axial CT of the same patient obtained for planning intensitymodulated radiation therapy shows the beam configuration used to deliver a palliative radiation dose to the affected mediastinal and left hilar lymph nodes.





(Left) PA chest radiograph of the same patient obtained 8 weeks after therapy shows bilateral heterogeneous opacities in the left upper lobe *⊡* and the paramediastinal right upper lobe 🔁, consistent with radiation pneumonitis. (Right) PA chest radiograph of the same patient obtained 13 months after therapy shows traction bronchiectasis \supseteq in the right upper lobe opacity and residual linear and irregular opacities 🔁 in the left lung, consistent with radiation fibrosis. Radiation fibrosis usually stabilizes after 12-24 months.





(Left) PA chest radiograph of a woman with a remote history of left breast cancer treated with mastectomy and radiation who developed a radiation-induced primary lung cancer shows a left perihilar mass 🔁 (Right) Axial NECT of the same patient shows a mass-like consolidation \supseteq of the left upper lobe that was pathologically proven to represent primary lung adenocarcinoma that developed amid preexistent radiation fibrosis. Radiation is associated with an increased risk of malignancy in the radiation field.

KEY FACTS

TERMINOLOGY

• Drug-induced lung disease (DILD)

IMAGING

- **HRCT/CT**: Optimal characterization of disease patterns
 - Organizing pneumonia: Peribronchovascular, subpleural, perilobular opacities; reversed halo and atoll signs
 - Nonspecific interstitial pneumonia: Basilar ground-glass &/or reticular opacities, traction bronchiectasis
 - Usual interstitial pneumonia: Basilar subpleural honeycombing, traction bronchiectasis
 - Hypersensitivity pneumonitis: Ground-glass opacities &/or centrilobular nodules, air-trapping
 - o Eosinophilic pneumonia: Peripheral subpleural opacities
 - Diffuse alveolar damage: Dependent consolidation, ground-glass opacities
 - Diffuse alveolar hemorrhage: Ground-glass opacities
 - Sarcoid-like granulomatosis: Perilymphatic nodules, lymphadenopathy

TOP DIFFERENTIAL DIAGNOSES

- Pneumonia
- Pulmonary edema
- Interstitial lung disease and connective tissue inflammatory disorders
- Hypersensitivity pneumonitis

CLINICAL ISSUES

- Symptoms: Dyspnea, cough, fever, eosinophilia
- Drug toxicity influenced by ↑ age, smoking, preexisting lung disease, genetic predisposition, prior or concomitant radiation therapy, combination of anticancer agents
- Treatment: Drug withdrawal, corticosteroids

DIAGNOSTIC CHECKLIST

- Consider DILD in patient with history of drug therapy with new &/or progressive respiratory symptoms
- Diagnosis requires knowledge of drug history and specific patterns of injury

(Left) Axial CECT of a 61-yearold woman with bladder cancer undergoing treatment with durvalumab who presented with fever and cough shows subtle bilateral subpleural ground-glass 🔁 and linear \supseteq opacities. (Right) Axial CECT of the same patient shows subpleural opacities without honeycombing, compatible with a nonspecific interstitial pneumonia pattern. Symptoms resolved after discontinuation of durvalumab. Nonspecific interstitial pneumonia is a common injury or druginduced lung disease.





(Left) Axial CECT of a 68-yearold woman with ovarian cancer undergoing treatment with cisplatin and paclitaxel shows bilateral lung nodules *→* with intrinsic air bronchograms. (Right) Axial fused FDG PET/CT of the same patient shows increased FDG uptake within the nodules \rightarrow . Biopsy was performed to exclude infection but revealed organizing pneumonia, which typically manifests as peripheral and subpleural nodular opacities &/or consolidations.





Abbreviations

• Drug-induced lung disease (DILD)

Synonyms

• Drug-induced lung injury

Definitions

- DILD: Drug exposure that causes inflammation, which may resolve or evolve to fibrosis
 - Most commonly reported drugs: Antineoplastic, antiinflammatory, cardiovascular agents, antibiotics

IMAGING

General Features

- Best diagnostic clue
 - Diagnosis of exclusion
 - High index of suspicion after development of lung disease
 - Clinical &/or radiologic improvement may occur with cessation of therapy

Radiographic Findings

- Radiography
 - o Several patterns may coexist in same patient
- Specific disease patterns
 - Lung abnormalities

Organizing pneumonia (OP)

- Unilateral or bilateral patchy consolidations; may be migratory
- Peribronchial, perilobular, subpleural distribution
- Nonspecific interstitial pneumonia (NSIP)
 Basilar reticular &/or patchy peripheral opacities
- Hypersensitivity pneumonitis (HP)
 - Various stages: Nonfibrotic, fibrotic
 - □ Ground-glass opacity, consolidation, centrilobular ground-glass nodules, fibrosis
- Usual interstitial pneumonia (UIP)
 - Low lung volume
 - Basilar subpleural reticulation, honeycombing
- Eosinophilic pneumonia
 - Peripheral upper lobe opacities
 - May manifest with diffuse airspace disease
- Diffuse alveolar damage (DAD)
 - Identical to acute respiratory distress syndrome (ARDS) from other causes (all 4 lung quadrants)
- Pulmonary edema
 - Indistinguishable from noncardiogenic or cardiogenic edema
 - $\hfill\square$ Diffuse bilateral interstitial and alveolar opacities
- Diffuse alveolar hemorrhage (DAH)
 - Patchy or diffuse alveolar opacities (hemoptysis)
- Vasculitis
 - Patchy interstitial &/or airspace opacities
 - □ Subsegmental, peripheral distribution
 - Cavitation
- Sarcoid-like granulomatosis and lymphadenopathy
 Bilateral upper lobe opacities
 - Mediastinal and hilar lymphadenopathy

CT Findings

• HRCT

- Optimal characterization of pulmonary opacities: Ground-glass, alveolar, interstitial (reticular &/or nodular)
- Most commonly patterns: OP, NSIP, and HP
 Specific pulmonary patterns
 - **OP**
 - Peribronchovascular, peripheral, &/or subpleural opacities
 - Perilobular opacities, reversed halo or atoll signs
 NSIP
 - Basilar subpleural ground-glass opacities
 - Reticular opacities, traction bronchiectasis, &/or bronchielectasis suggest fibrotic NSIP
 - HP
 - □ Bilateral ground-glass opacities &/or small poorlydefined centrilobular nodules, air-trapping
 - UIP
 - □ Subpleural lower lobe predominant honeycombing, traction bronchiectasis, &/or bronchielectasis

Eosinophilic pneumonia

- Peripheral upper lobe homogeneous opacitiesDiffuse airspace disease
- - Consolidation predominantly in dependent lung
 - Patchy ground-glass opacities, may evolve to diffuse involvement

Pulmonary edema

- Interlobular septal thickening, ground-glass opacities
- □ Cardiomegaly, pleural effusion
- DAH
 - □ Bilateral patchy or diffuse ground-glass opacities
 - □ May exhibit crazy-paving pattern
- High-attenuation opacities
 - Characteristic of amiodarone DILD
 - Optimally demonstrated on NECT
- Sarcoid-like granulomatosis
 - Peribronchovascular nodules and irregular opacities, upper lobe distribution
 - Symmetric intrathoracic lymphadenopathy

Nuclear Medicine Findings

 FDG PET/CT: ↑ FDG uptake reported in early-stage disease even without symptoms

Imaging Recommendations

- Best imaging tool
 - HRCT: Detection and characterization of DILD
 - NECT: Evaluation of pleural/pericardial disease, lymphadenopathy
- Protocol advice
 - Thin-section (1- to 3-mm) CT
 - o Supine inspiratory and expiratory imaging

DIFFERENTIAL DIAGNOSIS

Pneumonia

- Viral &/or bacterial infection
 - BAL examination and culture

Pulmonary Edema

- Heart failure
 - o Interlobular septal thickening and pleural effusion

Interstitial Lung Disease and Connective Tissue Inflammatory Disorders

- OP
 - Polymyositis: Symmetrical painless muscle weakness
 - Inflammatory bowel disease: Bronchiectasis
 - o Environmental agents, infection (viral, bacterial, fungal)
- NSIP
 - Scleroderma: Dilated air-filled esophagus
 - Rheumatoid arthritis: Erosion of distal clavicle, synovitis of hands and feet
 - o Inflammatory bowel disease: Bronchiectasis
- UIP
 - Rheumatoid arthritis: Erosion of distal clavicle, synovitis of hands and feet

PATHOLOGY

General Features

- Etiology
 - Mechanism of DILD not fully understood; independent of drug administration route
 - Drug damage to alveolar and bronchial epithelia
 - Most drugs do not produce direct cell toxicity, but drug metabolites lead to cell injury
 - Possible etiologies
 - Higher drug concentration in lung than in other organs
 - Specific lung activation pathways
 - □ Induction of immune cascades
 - Most histologic abnormalities are nonspecific; few allow immediate identification of etiology (e.g., amiodarone)
 - OP: Amiodarone, nitrofurantoin, carbamazepine, bleomycin, methotrexate, cyclophosphamide
 - NSIP: Amiodarone, nitrofurantoin, bleomycin, methotrexate, docetaxel, irinotecan, gefitinib, erlotinib
 - UIP: Amiodarone, azathioprine, flecainide, ifosfamide, melphalan, nitrofurantoin, rituximab
 - HP: Mesalamine, fluoxetine, amitriptyline,cyclophosphamide, paclitaxel
 - DAD/interstitial fibrosis: Cyclophosphamide, methotrexate, gemcitabine, rituximab, interleukin, interferon
 - DAH: Anticoagulants, carbamazepine, bevacizumab, cytarabine
 - o Pulmonary edema from cardiotoxicity: Rosiglitazone, zidovudine, doxorubicin, daunomycin, sunitinib, imatinib, cyclophosphamide, cocaine, ethyl alcohol (ETOH)
 - o Pleural/pericardial effusion: Docetaxel
 - Hilar/mediastinal lymphadenopathy: Methotrexate, Ipilimumab
 - Thromboembolism: Gemcitabine, cisplatin, bevacizumab, sunitinib, sorafenib
 - Sarcoid-like granulomatosis and lymphadenopathy: Ipilimumab, pembrolizumab
 - Pneumothorax: Pazopanib, bevacizumab, sorafenib, sunitinib

Gross Pathologic & Surgical Features

• Most lung biopsies not pathognomonic; exclusion of other diseases and documentation of injury pattern

Microscopic Features

- OP
 - Immature fibroblasts plug respiratory bronchioles and alveolar ducts
- NSIP
 - Hyperplastic type II pneumocytes, interstitial infiltration by mononuclear cells, mild interstitial fibrosis
- UIP
 Dense interstitial fibrosis; honeycombing
- HP
 - Nonfibrotic: Interstitial lymphocytes infiltrates, edema, noncaseating granulomas, and bronchiolitis obliterans
 Fibrotic: Fibrosis
- Eosinophilic pneumonia
 - Eosinophil, lymphocyte, and plasma cell infiltration of alveolar septa
- DAD
 - Acute exudative phase: Hyaline membranes
 - Reparative phase: Proliferation of type II pneumocytes and fibrosis
- Sarcoid-like granulomatosis and lymphadenopathy • Granulomatous inflammation resembling sarcoidosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Variable: Dyspnea, cough, fever, variable onset from immediate to years after drug initiation
 - Drug toxicity is frequently overlooked as etiology

Natural History & Prognosis

- Drug toxicity influenced by ↑ age, smoking, preexisting lung disease, genetic predisposition, prior or concomitant radiation therapy, combination of anticancer agents
- Symptom improvement after drug discontinuation

Treatment

- Drug withdrawal 1st and most important step
- Corticosteroids in very symptomatic patients or in those with DILD progression in spite of drug discontinuation

DIAGNOSTIC CHECKLIST

Consider

 DILD in patient with history of drug therapy with new &/or progressive respiratory symptoms

Image Interpretation Pearls

• Diagnosis requires investigation of drug history and individual pattern of pulmonary injury

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(Left) Axial CECT of a 68-yearold woman treated with cisplatin demonstrates bilateral subpleural heterogeneous opacities 🔁 characterized by central ground-glass attenuation and peripheral consolidation (reversed halo sign), compatible with organizing pneumonia. (Right) Axial CECT of the same patient obtained 8 weeks after cessation of therapy shows residual ground-glass opacity \supseteq in the right lung base. Affected patients have a variable prognosis that depends on the severity of lung injury.





(Left) Axial CECT of a 64-yearold woman with Crohn disease undergoing treatment with infliximab shows air-space consolidation in the peripheral right upper lobe. (Right) Coronal CECT of the same patient shows bilateral airspace consolidations \supseteq and ground-glass opacities 🖾. The imaging findings are suggestive of eosinophilic pneumonia, which was confirmed at biopsy. Peripheral eosinophilia and parenchymal opacities associated with administration of a known drug strongly suggest the diagnosis.





(Left) PA chest radiograph of 32-year-old woman with lymphoma undergoing treatment with cyclophosphamide shows diffuse bilateral subtle lung opacities. (Right) Axial NECT of the same patient shows subtle bilateral ground-glass opacities. Bronchoalveolar . lavage showed greater than 20% hemosiderin-laden macrophages, consistent with the diagnosis of diffuse alveolar hemorrhage. Patients with pulmonary hemorrhage usually present with dyspnea, and hemoptysis that may be absent in 35-40% of cases.

Ablation Procedures

KEY FACTS

TERMINOLOGY

- **Thermal ablation**: Treatment of primary or metastatic lung malignancies in medically inoperable patients
 - Radiofrequency ablation (RFA): Use of electrical current
 Microwave ablation (MWA): Use of high-frequency electromagnetic waves
- **Cryoablation (CA)**: Use of compressed argon gas to induce intracellular ice formation and cellular necrosis

IMAGING

- Ground-glass opacity halo ≥ 5 mm is desirable immediately after nodule ablation
- Cavitation in ablation zone and adjacent pleural thickening common after 1 month post ablation
- Focal nodular enhancement or FDG avidity 3 months after ablation suggests local tumor progression

TOP DIFFERENTIAL DIAGNOSES

• Recurrent malignancy

• Pulmonary infection

CLINICAL ISSUES

- Most common complication following ablation is pneumothorax
- Chest pain and dyspnea may be due to delayed onset pneumothorax
- Postablation syndrome
 Fever and fatigue

DIAGNOSTIC CHECKLIST

- Radiologists must differentiate expected normal postablation imaging findings from tumor progression
- Percutaneous biopsy should be considered when tumor progression suspected

(Left) Axial NECT of a 57-yearold woman with metastatic hepatocellular carcinoma shows a radiofrequency probe advanced into a left lower lobe pulmonary metastasis 🔁 and a previously treated left upper lobe lesion 🖾. (Right) Axial NECT immediately after ablation shows a ground-glass $opacity rim \square around the$ tumor indicative of successful treatment. Thermal ablation near large vessels is negatively affected by cooling effects of flowing blood, which may lower the ablation temperature. This is known as "heat sink" effect.





(Left) Axial CECT of the same patient obtained 2 months after ablation shows a triangular subpleural nodule \square with intrinsic cavitation, an expected normal evolution of the ablation zone. (Right) Axial CECT of the same patient obtained 6 months after treatment demonstrates a residual dense nodule 🔁 and resolution of previously noted cavitation. Although there is no universal consensus, patients with lesions \leq 3 cm and with < 5 lesions are considered better candidates for percutaneous ablation.





Abbreviations

- Thermal ablation (TA)
 Radiofrequency ablation (RFA)
 Microwave ablation (MWA)
- Cryoablation (CA)

Synonyms

• Percutaneous lung ablation

Definitions

- TA: Tissue injury produced by increased tissue temperature: Used to treat limited-stage lung malignancy in medically inoperable patients, oligometastases (< 3-5) and recurrent malignancy after radiation or surgery; CT and CT fluoroscopy used for percutaneous probe placement
 - Heat sink: Cooling effect of flowing blood and air in wellperfused lung may lower ablation temperature and impair tumor destruction
 - RFA
 - Uses electrical current system
 - Current frequency: 400-500 kHz
 - Single treatment typically lasts 10-12 minutes
 - − Tissue heating \ge 60°C → protein denaturation → cell death
 - Treatment time 12-15 minutes

• MWA

- Uses electromagnetic radiation
- Frequency: 915 MHz to 2.45 GHz; generates higher temperatures
- Single treatment typically lasts 10 minutes
- Treatment time 2-5 minutes
- CA: Uses compressed argon gas to induce intracellular ice formation and extracellular ice crystals
 - Temperatures as low as -140°C within extracellular space
 → cell dehydration → cell membrane rupture → cell death
 - Ice ball may be imaged with CT during procedure; allows assessment of treatment zone
 - Longer procedure time: Freeze-thaw cycles

IMAGING

General Features

- Location
 - Pulmonary or chest wall masses may be treated with TA
 Peripheral tumors are preferable
 - MWA creates larger ablation zone and is less affected by heat skin effects
 - Tumors close to large vessels: MWA is preferred over RFA
 - CA preserves collagenous matrix tissue and lung architecture in treated area; may be used near large airways, vessels, pericardium, &/or bone
 - o Both TA and CA used to treat lung metastases
- Size
 - o Nodules ≤ 3 cm; primary lung malignancy or metastases
 - Larger tumors require several treatments; may be performed simultaneously with multiple applicators

CT Findings

- Early phase: < 24 hours to 1 month
 - Ablation zone should be at least 1 cm larger than original tumor to include treatment of microscopic disease
 - Immediately after ablation: Central consolidation + concentric ground-glass rings **(Cockade phenomenon)**
 - Central area represents tumor and necrotic lung, mid layers represents fluid-filled alveoli, outer layers represent hyperemia and hemorrhage
 - Ground-glass halo ≥ 5 mm desirable immediately after ablation; indicates successful treatment
 - Ice ball formation during CA manifests as low attenuation surrounded by high-attenuation hemorrhage
- Intermediate phase: 1-3 months
 - Resolution of ground-glass rings
 - Postablation area manifests as dense consolidation representing granulation tissue and fibrosis
 - Development of central cavitation
 - Focal pleural thickening, small pleural effusion
 - Reactive locoregional lymph nodes may demonstrate enlargement
- Late phase: > 3 months
 - Residual rounded or linear opacity
- Focal nodular enhancement any time after ablation is suspicious for local tumor progression
- Surveillance imaging using both CT and PET/CT following TA
 - CECT or NECT at 1 and 3 months, PET/CT at 6 months, then alternating CT and PET/CT every 3 months for first 2 years after ablation
 - Beyond 2 years, imaging with CT or PET/CT every 6 months is reasonable

MR Findings

- MR uncommonly used to follow pulmonary ablation but has been used to evaluate chest wall ablation
 - Focal enhancement is suspicious for local tumor recurrence

Ultrasonographic Findings

• Ultrasound may be used to guide TA of chest wall masses

Imaging Recommendations

- Best imaging tool
 - Close imaging follow-up with both CECT and PET/CT critical for detection of tumor progression
- Protocol advice
 - Follow-up NECT and CECT suggested; enhancement > 15 HU suspicious for local tumor progression

Nuclear Medicine Findings

- PET/CT
 - Early phase: FDG-uptake secondary to inflammation
 - o Intermediate phase: Similar to blood pool by 2nd month
 - Late phase: Similar to blood pool
 - FDG-avid foci within ablation zone 6 months after ablation are highly suspicious for malignancy; tissue sampling should be performed

Image-Guided Biopsy

• Commonly performed prior to ablation; in selected patients, both procedures can be performed in 1 session with on-site cytology

DIFFERENTIAL DIAGNOSIS

Recurrent Malignancy

- Up to 43% of ablated lesions
- Typically after ablation of lesions > 3 cm
- New or growing nodules within ablated tissue
- FDG avidity &/or contrast enhancement

Pulmonary Infection

- Focal pneumonia
- Fever, leukocytosis

PATHOLOGY

General Features

• Ablation commonly used to treat primary lung cancers and pulmonary metastases

Staging, Grading, & Classification

- Modified RECIST (Response Evaluation Criteria in Solid Tumors) may be used to identify disease progression
 - Any 2 of following suggest disease progression
 - 20% increase in sum length of tumor
 - Solid mass with invasion of adjacent structures
 - Increased FDG uptake

Gross Pathologic & Surgical Features

- Ground-glass opacity immediately following ablation corresponds to 3 histologic layers
 - **Peripheral layer**: Nonnecrotic and hemorrhagic debris containing viable cells
 - Intermediate layer: Fluid in alveolar spaces
 - **Central layer**: Nuclei with condensed chromatin suggesting cell death

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain and dyspnea may be due to delayed pneumothorax; rare complication
 - Most pneumothoraces occur within 2 hours of ablation
 - Rib fractures may be seen in proximity of ablation zone in 22% of cases at 2 years
- Other signs/symptoms
 - Fever and fatigue common; referred to as **postablation syndrome**

Natural History & Prognosis

- RFA
 - Complications
 - Pneumothorax is reported in up to 46%
 - More common with emphysema, centrally located tumors, ablation of multiple tumors
 - Pleural effusions in up to 50%
 - Postablation syndrome (fever and flu-like symptoms)
 Common following ablation

- Treated symptomatically
- Hemoptysis in 4-9%
- May require angiography/embolization or surgery
- Bronchopleural fistula: Rare complication
 May require treatment with blood patch,
 - endobronchial valves, or surgery
 - Associated with tumor abutting visceral pleura
- Death < 1%
- Local tumor progression in 30-43% of treated tumors; more frequent in those > 3 cm
 - Recurrent disease may be treated again; no limit to number of ablations
- o Stage IA non-small cell lung cancer overall survival
 - 91.7% at 1 year and 58.3 % at 3 years
 - Shorter hospital stay for patients treated with ablation
- MWA
 - Less clinical data than RFA
 - Complications
 - Pneumothorax: 39%
 - Hemoptysis: 6%
 - Stage IA non-small cell lung cancer overall survival
 - 100% at 1 year, 92.6% at 2 years, and 50% at 3 years
- CA
 - Less clinical data than both RFA and MWA
 - Complications
 - Hemoptysis: Up to 62%
 - Pneumothorax: 12%
 - Limited long-term local tumor progression and outcome data
 - Stage IA non-small cell lung cancer overall survival 67.8% at 5 years

Treatment

- Ablation is typically an outpatient procedure that requires local anesthesia and conscious sedation (rarely requires general anesthesia)
- Choice of ablation modality depends on available technology, operator experience, and local resources
- Combined multimodality treatment using ablation and external beam radiation advocated in small series; may provide survival benefit at increased cost
- CA generates antitumor immune response
 - CA + immune checkpoint inhibitors currently under clinical investigation
- Irreversible electroporation: New non-TA modality that uses electric pulses to induce cell death
 - Few studies evaluating electroporation of lung tissue in humans

DIAGNOSTIC CHECKLIST

Consider

- Immediately following ablation, 5- to 10-mm ground-glass halo is desirable
- Percutaneous biopsy should be considered if disease progression is suspected

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Ablation Procedures





(Left) Axial NECT of a 73-yearold woman with an abdominal wall leiomyosarcoma shows a right lower lobe lobe metastasis 🔁. (Right) Axial CECT of the same patient immediately after microwave ablation shows a new larger $opacity \supseteq surrounding the$ treated nodule. Note the right pneumothorax 🖘, the most common complication of percutaneous lung ablation. In general, percutaneous ablation has a low mortality rate and is an acceptable option for patients who are not surgical candidates.





(Left) Axial NECT of the same patient obtained 3 months later shows central groundglass opacity surrounded by a dense soft tissue ring \boxtimes in the ablation zone. The ablation zone is usually larger than the original lesion at 3 months but progressively decreases in size by 6 months. (Right) Axial NECT of the same patient obtained 8 months later shows decreased size of the previously demonstrated lesion 🔁. An ablation zone that enlarges after 3 months or exhibits FDG avidity on PET/CT suggests tumor гесиггепсе.





(Left) Axial CECT of a 71-yearold woman previously treated with radiation for left upper lobe large cell neuroendocrine carcinoma ≧ shows a new 1.2-cm right upper lobe nodule ➡, which was a biopsy-proven adenocarcinoma. (Right) Axial NECT obtained during cryoablation shows a lowattenuation ice ball \supseteq and a high-attenuation rim of hemorrhage around the margin of the ice ball 🖂 Cryoablation preserves collagenous tissue architecture and, hence, may be used close to the trachea, airways, aorta, &/or bone.



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Introduction

The pleura is a continuous thin membrane that lines the thoracic cavity. It consists of visceral and parietal components that line the parenchymal and nonparenchymal thoracic surfaces, respectively. The apposition of the visceral and parietal pleurae forms a potential pleural space, which contains a small amount of serous fluid that facilitates lung movement during respiration.

The normal pleura manifests as a thin, smooth, linear soft tissue structure often visualized as an interlobar fissure on radiography or as a 1- to 2-mm soft tissue attenuation thin line along interlobar fissures or intercostal regions on computed tomography (CT).

Pleural Abnormalities

A variety of abnormalities and diseases may affect the pleura and consist of pleural air (pneumothorax), fluid (pleural effusion), thickening &/or calcification, and neoplasms.

Pneumothorax

Pneumothorax is defined as gas in the pleural space and is frequently iatrogenic secondary to invasive medical procedures or barotrauma or secondary to blunt or penetrating chest trauma. Pneumothorax may be spontaneous and is classified as primary (no underlying lung disease) or secondary (underlying cystic, cavitary, neoplastic, or diffuse infiltrative lung disease).

Pneumothorax manifests on imaging as a thin pleural line outlined by alveolar air in the subjacent lung and air in the pleural space. As pneumothorax is often an unexpected finding in a patient with acute chest pain, its diagnosis should elicit prompt communication to the clinical team so that it can be monitored &/or evacuated. Tension pneumothorax is a medical emergency in which pneumothorax produces mediastinal displacement that may lead to fatal vascular compromise.

Pleural Effusion

Pleural effusion is the abnormal accumulation of fluid in the pleural space. Most pleural effusions are transudates related to heart failure and often resolve with medical treatment. Exudative pleural effusions have more serious implications and are typically related to infection or malignancy. Infected pleural effusions may become loculated empyemas that may be complicated by bronchopleural fistula or empyema necessitatis as the infected fluid drains to the tracheobronchial tree or the adjacent chest wall, respectively. Malignant pleural effusion is frequently secondary to lung or breast cancer and denotes advanced stage IV disease.

Pleural effusion often manifests radiographically as blunting of the posterior &/or lateral costophrenic angles and produces a water density meniscus-like morphology in these areas. Small free pleural effusions may be diagnosed with decubitus radiography. Larger pleural effusions may completely obscure the hemidiaphragm(s) or completely opacify a hemithorax. Pleural effusions in supine patients and those in subpulmonic locations may produce atypical radiographic findings. CT allows assessment of the entire pleura and has high sensitivity for detection of pleural fluid, which manifests as water attenuation material that separates or "splits" the normally apposed visceral and parietal pleurae. CT also allows identification of associated abnormalities including lung consolidations, masses, &/or nodules and intrathoracic lymphadenopathy. Associated nodular pleural thickening is virtually pathognomonic for malignancy. High-attenuation pleural fluid may produce the so-called hematocrit effect characteristic of hemothorax. Magnetic resonance (MR) imaging has high sensitivity for pleural fluid but is not routinely used. FDG PET/CT allows identification of metabolic activity in pleural abnormalities consistent with infection, inflammation, or malignancy. Finally, ultrasound has high sensitivity for identification of small pleural effusions and is frequently used to guide thoracentesis &/or pleural biopsy.

Pleural Thickening

Pleural thickening may be focal, multifocal, or diffuse and may exhibit punctate, nodular, discontinuous, or diffuse calcification. Pleural plaques from asbestos-related pleural disease typically manifest as bilateral discontinuous pleural thickening and often exhibit calcification. Unilateral continuous pleural calcification is often the result of prior hemothorax or tuberculous empyema and may produce fusion of the pleural surfaces, obliteration of the pleural space, and resultant fibrothorax. Continuous diffuse smooth pleural thickening may occur as a result of pleural fibrosis, but requires close monitoring or tissue sampling to exclude malignancy.

Pleural Neoplasms

The most common pleural neoplasm is metastatic disease, and primary lung and breast cancers are the most common etiologies. Pleural metastases frequently manifest as malignant pleural effusions that may reach large sizes &/or nodular pleural thickening, nodules, or masses. Malignant pleural mesothelioma is the most common primary pleural neoplasm and is intimately associated with asbestos exposure. It manifests as circumferential nodular pleural thickening that encases the lung, involves the interlobar fissures, and commonly invades adjacent structures. Localized fibrous tumor of the pleura is the second most common primary pleural neoplasm and typically manifests as a focal noninvasive pleural nodule or mass.

Focal pleural masses may exhibit the incomplete border sign on radiography, which confirms their extrapulmonary anatomic location. Imaging features of pleural malignancy include unilateral pleural effusions, which may be large or massive and pleural thickening, nodules, or masses. Imaging features of malignant pleural thickening include: Nodular pleural thickening, circumferential pleural involvement, involvement of the mediastinal pleura, and pleural thickening > 1 cm.

Summary

Radiologists are uniquely equipped to play an important role in the assessment of pleural diseases and should be familiar with the imaging manifestations of common pleural abnormalities and those of mimics of pleural malignancy such as thoracic splenosis and prior talc pleurodesis. An important role of the radiologist is to correctly identify features of benign and malignant pleural abnormalities in order to inform appropriate follow-up imaging and management and positively impact patient care.

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Approach to Pleural Diseases

Pneumothorax





(Left) Composite image with PA chest radiographs of the right and left lungs shows a right pneumothorax that manifests with a thin visceral pleural line 🔁. The normal apposed left visceral and parietal pleural surfaces are not visible on radiography. (Right) Composite image with PA chest radiographs of small (left) and moderate (right) pleural effusions shows a meniscus-shaped opacity \square in the costophrenic sulcus and a moderate pleural effusion that extends into the minor \blacksquare and major 🔁 fissures.

Pleural Thickening





Focal Pleural Mass

(Left) Composite image with axial CECT of normal pleura (left) and pleural thickening (right) shows the inconspicuous appearance of normal pleura that manifests as a 1- to 2-mm soft tissue line , and pleural thickening, which manifests as a thicker soft tissue line/band ➡ that merges with extensive pleural calcification 🔁. (Right) Composite image with PA (left) and lateral (center) chest radiographs and axial NECT (right) shows a pleural mass that exhibits the incomplete border sign and obtuse angles \supseteq with the adjacent pleura.

Pleural Masses



Malignant Pleural Disease



(Left) Graphic shows the variable shapes of pleural masses. Those along fissures may be fusiform 🛃, while those along the peripheral pleura may be symmetrically or asymmetrically lenticular with obtuse or acute angles at their interface with the adjacent pleura. (Right) Composite image with PA chest radiograph (left) and coronal fused FDG PET/CT (right) shows malignant mesothelioma that manifests as FDG-avid \rightarrow circumferential nodular pleural thickening 🔁 that encases the lung.

KEY FACTS

TERMINOLOGY

• Transudate: Plasma ultrafiltrate with low cell and protein content

IMAGING

• Radiography

- Blunt costophrenic sulci
- Subpulmonic pleural effusion
- Supine radiography: ↓ sensitivity for pleural fluid
- Fissural fluid: Pseudotumor
- CT
 - High sensitivity for pleural fluid
 - HU measurements do not discriminate between exudates and transudates
 - Smooth thin pleural surfaces (no enhancement), extrapleural fat attenuation
- Ultrasound
 - Anechoic effusion may be transudate or exudate
 - High sensitivity for detection of pleural fluid

TOP DIFFERENTIAL DIAGNOSES

- Exudative pleural effusion
- Diaphragmatic paralysis
- Diaphragmatic eventration
- Chronic pleural fibrosis
- Pleural mass

PATHOLOGY

- Intact pleura
- Imbalance of Starling forces
- Associated conditions: Heart failure, hypoalbuminemia: < 1.5 g/dL

CLINICAL ISSUES

- Signs and symptoms
 - Dyspnea, mild nonproductive cough, chest pain
- Treatment
 - Management of underlying condition
 - Thoracentesis, chest tube, pleurodesis

(Left) Graphic shows features of transudative pleural effusions, which are typically free and occur without associated pleural thickening or nodularity. (Right) AP chest radiograph of a patient with chronic heart failure shows blunt costophrenic angles and the meniscus sign \supseteq , consistent with bilateral pleural effusions. Note associated cardiomegaly, peribronchial cuffing, and fissural thickening, consistent with interstitial edema. Bilateral pleural effusions are common in the context of heart failure.





(Left) Axial CECT of a patient with chronic heart failure shows small to moderate bilateral pleural effusions 🖂 and associated right greater than left relaxation atelectasis Note coexistent cardiomegaly, a common finding in patients with chronic heart failure. (Right) Long-axis ultrasound of the same patient shows a large anechoic right pleural effusion ► Ultrasound helps identify septations that may indicate loculation and guides pleural interventions (e.g., thoracentesis and placement of thoracostomy chest tubes).





Definitions

- Transudate: Plasma ultrafiltrate with low cell and protein content
- Rate of pleural fluid production exceeds reabsorption
- Diagnostic criteria
 - o < 1,000 cells/mm³; lymphocytes, mesothelial cells
 - Light criteria
 - Ratio of pleural fluid:serum protein < 0.5
 - Ratio of pleural fluid:serum lactate dehydrogenase (LDH) < 0.6
 - Pleural fluid LDH < 2/3 of upper limit of normal serum value

IMAGING

General Features

- Best diagnostic clue
- Blunt costophrenic angle (CPA)Location
- Pleural space (usually bilateral)
- Size
 - Variable: Small to massive
- Morphology
 Variable

Radiographic Findings

- Sequence of fluid accumulation on upright radiography
 Subpulmonic → posterior CPA → lateral CPA
- Blunt costophrenic sulci
 - Blunt posterior costophrenic sulcus (lateral radiograph);
 50 mL of pleural fluid
 - Blunt lateral costophrenic sulcus (frontal radiograph); 200 mL of pleural fluid
- Subpulmonic pleural effusion
 - Interface between basilar lung and fluid: Pseudohemidiaphragm
 - o Flattening and elevation of pseudohemidiaphragm
 - Lateral shift of pseudohemidiaphragm apex
 - Separation of gastric bubble from pseudohemidiaphragm (normal < 1.5 cm)
 - Rock of Gibraltar sign on lateral radiography: Morphologic appearance of affected basilar pleural space resembles geographic landmark
- Hemidiaphragmatic inversion
 - Large pleural effusion: > 2,000 mL
 - o Medial displacement of gastric air bubble
- Fissural fluid
 - Preferential accumulation fluid or air in chronic obstructive pulmonary disease
 - Pseudotumor (mass-like fissural fluid)
 - Concave curvilinear edge toward hilum
 - May exhibit incomplete border sign
- Mediastinal shift away from effusion: > 1,000 mL
- Supine radiography: Reduced sensitivity for fluid detection
 - Diffuse increase in hemithorax density with visible vascular structures, meniscus not seen
 - Sensitivity 70%, up to 500 mL for reliable detection
 - Apical cap: Apical pleural space most dependent in supine position

• Common associated conditions

• Heart failure

- Bilateral pleural effusions, relatively equal size
- Cardiomegaly, perihilar haze, peribronchial cuffing, airspace disease from alveolar edema
- $\circ \,\, \text{Hepatic cirrhosis} \,\,$
 - Right effusion (70%); left (15%); bilateral (15%)
- Small to massive (hepatic hydrothorax)

CT Findings

- High sensitivity for detection of pleural fluid
 Identification of volumes as small as 10 mL
- HU measurements do not discriminate between exudates and transudates
- Homogeneous pleural fluid attenuation (water)
- Smooth thin pleural surfaces (no enhancement), extrapleural fat attenuation
- Pleural effusion vs. ascites
 - Pleural fluid peripheral; ascites central
 - Pleural fluid displaces diaphragmatic crus anteriorly, posterior to bare area of liver
 - Pleural fluid interface with liver or spleen indistinct, sharp with ascites
 - Pleural fluid appears progressively smaller from cephalad to caudad
 - o Pitfall: Findings reversed if inverted hemidiaphragm

Ultrasonographic Findings

- High sensitivity for detection of pleural fluid
- Anechoic effusions may be transudates or exudates (50%)

Imaging Recommendations

- Best imaging tool
 Lateral decubitus radiography: Detection of as little as 5 mL of pleural fluid
 - Documentation of free pleural fluid
- CECT: Identification of pleural fluid, assessment of fluid quantity, pleural surfaces, and underlying lung parenchyma
- Ultrasound useful for thoracentesis guidance
 - May be performed at bedside; may be used for chest tube placement

DIFFERENTIAL DIAGNOSIS

Exudative Pleural Effusion

- No reliable differentiation on imaging
- Loculation more common in exudate
- Pomegranate sign: Hydropneumothorax with tiny round air-bubbles along air-fluid level
- Heterogeneous or higher than fluid attenuation
- Nodular thickened pleural surfaces

Diaphragmatic Paralysis

- Sharp CPAs, apex not shifted laterally
- No diaphragmatic movement with respiration on ultrasound
- Fluoroscopic sniff test: Absent or paradoxical movement of affected hemidiaphragm

Diaphragmatic Eventration

- Commonly affects older females; often asymptomatic
- Sharp CPAs

- Most commonly involves anterior and medial right hemidiaphragm; may be diffuse
- Sniff test for differentiation from paralysis

Chronic Pleural Fibrosis

- Common cause of blunt CPA
- No free fluid on decubitus imaging
- No fluid on ultrasound

Pleural Mass

- May simulate loculated effusion
 CECT often required for differentiation
- Attenuation/enhancement consistent with soft tissue
- Solid lesion on ultrasound

PATHOLOGY

General Features

- Etiology
 - Heart failure (most frequent cause, usually bilateral)
 - Cirrhosis: Transdiaphragmatic movement of ascites (hepatic hydrothorax)
 - Atelectasis: Increased negative intrapleural pressure
 - Peritoneal dialysis: Transdiaphragmatic movement of peritoneal dialysate
 - Hypoalbuminemia: < 1.5 g/dL (fluid collections rarely isolated to pleura)
 - Nephrotic syndrome: Hypoalbuminemia, hypervolemia, increased hydrostatic pressure (typically subpulmonic)
 - Urinothorax: Retroperitoneal urine leakage with transdiaphragmatic migration via lymphatics (iatrogenic or traumatic)
 - Central line placement in pleural space: Infusothorax

Physiologic Features

- Pleural fluid forms as ultrafiltrate from parietal pleura capillaries
 - Removed by lymphatics draining lower costal, mediastinal, and diaphragmatic pleura
 - Removed by capillaries across visceral pleural mesothelium
- Starling forces: Balance between
 - Hydrostatic and oncotic forces in visceral and parietal pleural vessels
 - Lymphatic drainage
- Pleural effusions result from imbalance of Starling forces

Gross Pathologic & Surgical Features

- Normal pleural fluid volume: Approximately 5 mL total (2.5 mL/hemithorax)
- Normal pleural surface area: 2,000 cm², no communication between bilateral pleural spaces

Microscopic Features

• Intact visceral and parietal pleural surfaces

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Dyspnea
 - Mild nonproductive cough
 - o Chest pain

- Large pleural effusions may invert hemidiaphragm and impair ventilation
- Asymptomatic pleural effusions common in heart failure, postsurgery, and postpartum
- Other signs/symptoms
 - Physical findings do not usually manifest unless pleural effusions > 300 mL
 - Heart failure treated with diuretics; associated pleural effusions may be incorrectly diagnosed as exudative

Demographics

- Age
- Neonatal to older adults
- Sex
 - o M:F = 1:1
- Epidemiology
 - Common: 300 cases of pleural effusion per 100,000 population each year
 - Heart failure is most common cause
 - Bilateral (88%)
 - Unilateral right (8%)
 - Unilateral left (4%)

Natural History & Prognosis

- Treated heart failure: Fluid resorbs in days to weeks
- Ex vacuo effusions: Resolve as lung expands

Treatment

- Heart failure: Diuretics, digitalis, afterload reduction
- Thoracentesis
 - May partially relieve symptoms
 - Fluid analysis to differentiate transudate from exudate
- Relative contraindications for thoracentesis
 - Effusions < 1-cm thickness on lateral decubitus radiography, bleeding diathesis, systemic anticoagulation
 - Mechanical ventilation; cutaneous disease over puncture site
- Complications of thoracentesis
 - Pneumothorax, hemothorax, empyema, chest wall hematoma, reexpansion pulmonary edema
- Chest tube drainage for symptomatic effusions
- Pleurodesis with doxycycline or talc for refractory large pleural effusions
 - Heart failure: May result in increased contralateral pleural effusion

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

• Pleural pseudotumor typically occurs in pleural effusions related to heart failure

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Transudative Pleural Effusion





(Left) PA chest radiograph of a patient with chronic heart failure and a right loculated pleural effusion 🔁 shows a moderate likely loculated right pleural effusion along the lateral pleural space and a large mass-like component 🔁 within the right major fissure. (Right) Lateral chest radiograph of the same patient shows a lenticular mass \bowtie along the upper right major fissure. This abnormality is often referred as pseudotumor, vanishing tumor, or phantom tumor, as it may disappear as heart failure is treated.





(Left) Axial NECT of a 75-yearold man with dyspnea and lower extremity edema shows bilateral right greater than left water-attenuation pleural $effusions \implies$ with associated relaxation atelectasis \implies that predominantly affects the right lower lobe. (Right) Axial NECT of the same patient shows smooth interlobular septal thickening \supseteq consistent with interstitial edema. This finding is typical of pulmonary edema, which is simply defined as extravascular lung water.





(Left) Axial CECT of a 45-yearold man with myxedema shows a right transudative pleural effusion \blacksquare that resolved after 3 months of thyroid hormone replacement. Note right basilar relaxation atelectasis 🛃. (Right) Axial CECT of a 16-year-old girl with acute nephrotic syndrome shows a transudative left pleural effusion \blacksquare and left lower lobe relaxation atelectasis 🛃. Transudative pleural effusions commonly affect patients with decreased plasma oncotic pressure due to entities such as cirrhosis and nephrotic syndrome.

KEY FACTS

TERMINOLOGY

- Pleural fluid with high protein content
- Increased pleural permeability due to pleural inflammation &/or lymphatic obstruction

IMAGING

- Radiography
 - Free pleural fluid conforms to dependent pleural space
 - Loculated fluid does not displace with change in position
 - o Air-fluid levels: Empyema with bronchopleural fistula
- CT
 - Empyema: Biconvex or multiloculated pleural effusion ± air-fluid levels
 - Pleural metastases: Nodular pleural thickening
- **Ultrasound**: Echogenic loculated fluid, with septations, ± pleural thickening suggests exudate
- MR: Identification of pleural enhancement and nodularity
- **PET/CT**: High sensitivity (95%) and moderate specificity (82%) for malignancy

TOP DIFFERENTIAL DIAGNOSES

- Transudative pleural effusion
- Pleural mass

PATHOLOGY

- Infection
- Malignancy
- Reactive, embolic disease
- Abdominal/esophageal disease
- Collagen vascular disease, drug-induced
- Hemothorax, chylothorax

CLINICAL ISSUES

• Fever, chest pain, dyspnea

DIAGNOSTIC CHECKLIST

- Diagnosis: Thoracentesis, biopsy
- Treatment: Management of underlying disease, thoracentesis, thoracostomy tube, decortication

(Left) Graphic shows morphologic features of exudative pleural effusions that may include smooth \supseteq and nodular \bowtie thickening of the visceral and parietal pleural surfaces. (Right) AP chest radiograph of a 70-yearold man with dyspnea shows a large loculated right pleural effusion. As opposed to transudative pleural effusions, exudative pleural effusions tend to exhibit a loculated morphology that does not conform to the dependent pleural space.





(Left) Axial CECT of a 65-yearold-old woman with metastatic stage IV breast cancer shows a large malignant exudative left pleural effusion that inverted the left hemidiaphragm with multiple enhancing pleural nodules and pleural thickening \blacksquare . Pleural nodules may be subtle on CT. Intravenous contrast and thicker slices increase the conspicuity of these abnormalities. (Right) Axial FDG PET/CT of the same patient shows extensive FDGavid nodular left basilar pleural thickening, consistent with solid pleural metastases.





Definitions

- Accumulation of pleural fluid with high protein content
- Increased pleural permeability due to pleural inflammation &/or lymphatic obstruction
- Pleural fluid analysis (Light criteria)
 Pleural fluid protein:serum protein > 0.5
 - Pleural fluid LDH:serum LDH > 0.6
 - Pleural fluid LDH > 2/3 of upper limit of serum LDH
- Parapneumonic pleural effusion refers to pleural effusion associated with adjacent pulmonary infection
 - **Empyema**: pH < 7.0; glucose < 40 mg/dL

IMAGING

General Features

- Morphology
 - Loculated pleural fluid; peripheral, lenticular, mass-like pleural fluid collection
 - Absence of meniscus configuration on erect radiography

Radiographic Findings

- Free or loculated pleural effusion
 - Free pleural fluid conforms to dependent pleural space whether on upright, supine, or lateral decubitus radiography
- Air-fluid levels
 - Almost always correspond to bronchopleural fistula in context of empyema
 - o Gas-forming bacteria in pleural fluid exceedingly rare
- Loculated pleural fluid does not displace with changes in position

CT Findings

- NECT
 - o Empyema
 - Unilateral, associated with consolidation (or chest wall infection)
 - Peripheral, biconvex, or multiloculated pleural fluid collection; displaces lung
 - Air-fluid level indicates bronchopleural fistula
 - o Chylothorax
 - Low-attenuation pleural fluid, usually unilateral (may be bilateral)
 - Malignant pleural disease
 - Nodular pleural thickening (> 1 cm), circumferential, involvement of mediastinal pleura
 - o Pleural metastases
 - Nodular pleural thickening, may invade chest wall
 - Consider: Lung, breast, gastric, or colon cancers and melanoma.
- CECT
 - Thick enhancing parietal and visceral pleura (split pleura sign), intrinsic septa, and adjacent consolidation suggest empyema

MR Findings

- T1WIFS
 - o Hemothorax: Hyperintense on T1WI (blood products)

- o Chronic hemothorax: Heterogeneous, hypointense on T1WI and T2WI (hemosiderin deposits)
- T2WIFS
- Lower signal intensity on T2WI (compared to transudate); heterogeneous, pleural enhancement, intrinsic septa
- T1WI C+ FS
 - Pre- and postcontrast sequences may demonstrate pleural enhancement and nodularity

Ultrasonographic Findings

- Not reliable for differentiating exudate from transudate; fluid sampling required
- Exudates may manifest as echogenic loculated pleural fluid with septations ± pleural thickening

Nuclear Medicine Findings

- PET
 - FDG PET: High sensitivity (95%) and moderate specificity (82%) for pleural malignancy
 - Moderate sensitivity (81%) and specificity (74%) for differentiating benign from malignant pleural effusions

Imaging Recommendations

- Best imaging tool
 - CECT: Assessment of pleural surfaces, lung, lymph nodes, chest wall
 - Thicker slices facilitate identification of small pleural nodules
 - US for diagnostic or therapeutic procedures

DIFFERENTIAL DIAGNOSIS

Transudative Pleural Effusion

- Free pleural fluid, smooth pleural surface
- Differentiation relies on fluid sampling

Pleural Mass

- May mimic loculated pleural effusion on radiography
- Localized fibrous tumor of pleura, pleural lymphoma, etc.
- Image-guided tissue sampling for diagnosis

PATHOLOGY

General Features

- Etiology
 - o Infectious: Bacterial, viral, fungal, parasitic
- Neoplastic
 - Metastatic disease: Lung, breast, ovarian, gastric, or pancreatic cancer, lymphoma, malignant melanoma
 - Malignant pleural mesothelioma
 - Localized fibrous tumor of pleura
- Reactive: Reactive pleuritis from underlying pneumonia (i.e., parapneumonic)
- o Embolic disease: Pulmonary thromboembolism
- Abdominal/esophageal disease: Pancreatitis, cholecystitis, hepatic or splenic abscess, esophageal perforation after esophageal sclerotherapy
- o Collagen vascular disease: Rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrome, granulomatosis with polyangiitis
- Drug/induced: Nitrofurantoin, dantrolene, methysergide, dasatinib, amiodarone, interleukin-2, procarbazine, methotrexate, phenytoin, β-blockers, ergot drugs
- o Hemothorax
- Chylothorax: Most commonly post trauma or in patients with lymphoma
- Gynecologic: Ovarian hyperstimulation, Meigs syndrome, endometriosis, postpartum complications
- o Other causes
 - Benign asbestos-related pleural effusion
 - Post cardiac surgery or myocardial infarction (Dressler)
 - Uremic pleuritis
 - Yellow nail syndrome:
 - Rhinosinusitis, pleural effusion, bronchiectasis, lymphedema, yellow nails

Gross Pathologic & Surgical Features

- Pleural fluid
 - Hemorrhagic: Trauma, anticoagulation, iatrogenic, metastases, uremia
 - Blood-tinged: Metastases, mesothelioma, benign asbestos-related pleural effusion, pulmonary embolism, tuberculosis, pancreatitis
 - o Milky: Chylous
 - Brown: Amebic abscess
 - Black: Aspergillus
 - Yellow-green: Rheumatoid
 - Golden, iridescent: Chronic chylothorax, tuberculosis, rheumatoid
 - o Opaque: Mesothelioma, chronic empyema
 - Putrid odor: Anaerobic infection

Microscopic Features

- Parapneumonic pleural effusion, neutrophils, and bacteria; mycotic pleurisy, granulomas
- Chylothorax
 - High lipid content (neutral fat, fatty acids); low cholesterol
 - Sudanophilic fat droplets
 - Triglycerides > 110 mg/dL
- Cholesterol pleural effusion: Cholesterol crystals, up to 1 g/dL; low neutral fat and fatty acids
- Immunohistochemistry and electron microscopy to differentiate mesothelioma from adenocarcinoma

Laboratory Findings

- High amylase, red blood cell count, high LDH level, lymphocytes, neutrophils, eosinophils, plasma cells
- High antinuclear antibody, rheumatoid factor titer, cholesterol crystals
- Low glucose, pH, complement
- Exudative pleural fluid characteristics
- Elevated procalcitonin in bacterial empyema

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Fever
 - Dyspnea on exertion
 - Chest pain

- Other signs/symptoms
 - Post cardiac injury syndrome (Dressler syndrome)
 - Post myocardial infarction, cardiac surgery, chest trauma, pacemaker implantation, angioplasty
 - Fever, pleuropericarditis, unilateral/bilateral small to moderate pleural effusions, lung opacities

Demographics

- Age
- o Adults
- Sex
 - Males; rheumatoid arthritis, pancreatitis

Natural History & Prognosis

- Benign asbestos-related pleural effusion; 5 to > 30 years post exposure
- Malignant pleural effusion; life expectancy 3-6 months

Diagnosis

Thoracentesis

- Chemical, bacteriologic, cytologic fluid analysis
- US-guided fluid sampling recommended
- Biopsy

o CT/ultrasound-guided pleural biopsy

- Video-assisted thoracoscopic surgery (VATS)
- Open biopsy

Treatment

- Treatment of underlying abnormality
- Antibiotics, steroids, chemotherapy, surgery

• Thoracentesis

- Relief of dyspnea
- Removal of < 1,000 mL of fluid at a time

• Thoracostomy tube

- Empyema, hemothorax, large malignant pleural effusion
- Pleurodesis or fibrinolysis
 - Drainage of pleural fluid prior to instillation of sclerosing agents
- Decortication in cases of fibrothorax

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Visualization of split pleura sign does not denote empyema; may be seen with chronic pleural effusion
- Important distinction of empyema from lung abscess
 Empyema treated with early chest tube
 - drainage/surgery; lung abscess treated with antibiotics
- Drainage not indicated for tuberculous pleural effusion; drainage indicated for tuberculous empyema

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Exudative Pleural Effusion





(Left) Axial NECT of a patient with empyema shows a multiloculated right pleural effusion. This appearance should raise suspicion for exudative pleural effusion and should prompt pleural fluid analysis for exclusion of pleural infection. (Right) Axial CECT of a patient with metastatic gastric adenocarcinoma shows an enhancing right pleural nodule and a large right effusion. Malignant cells were identified on thoracocentesis. Malignant exudative pleural effusions may exhibit nodular pleural thickening.





(Left) Axial CECT of a patient with empyema shows a loculated right pleural effusion that exhibits enhancement of the pleural surfaces 🔼, the so-called split pleura sign. While the latter is common in empyema, it is also often present in other chronic pleural effusions. (Right) Axial CECT of a 60-year-old man with a right hilar lung cancer shows a large exudative right pleural effusion, with an airfluid level 🔼, consistent with the presence of a bronchopleural fistula.





(Left) Coronal NECT of a patient with acute pancreatis shows a large loculated exudative left pleural effusion ➡. Note associated retroperitoneal 🔁 and left chest wall ➡ soft tissue stranding. (Right) Axial NECT of a patient status post esophagectomy and gastric pull-up shows contrast leakage \bowtie and gas bubbles \blacksquare within a right exudative pleural effusion/empyema secondary to an anastomotic leak. Exudative pleural effusions may result from traumatic or inflammatory gastrointestinal disorders.

Hemothorax

KEY FACTS

TERMINOLOGY

• Pleural effusion + variable amounts of blood products IMAGING

• Radiography

- Pleural effusion; frequent loculation
- Rib fractures (in trauma)
- Sequela: Pleural calcification, fibrothorax, trapped lung
- CT
 - o Pleural effusion with loculation &/or pleural thickening
 - Rib fractures increase likelihood of hemothorax
 - NECT: High-attenuation pleural effusion
 - CECT: Arterial blush indicates active bleeding and need for intervention
 - Identification of pleural calcification, assessment of fibrothorax, trapped lung
- Ultrasound: Rapid assessment in trauma
 - High likelihood of pleural fluid detection
 - Echogenic pleural effusion, loculation

TOP DIFFERENTIAL DIAGNOSES

- Transudative pleural effusion
 Heart failure: pleural fluid trains
- Heart failure; pleural fluid typically 10-20 HUExudative pleural effusion
- Empyema; variable attenuation, typically loculated fluid
- Malignant pleural effusion
 High-attenuation pleural podules manual
 - High-attenuation pleural nodules may mimic hemothorax
 - Hemorrhagic pleural effusion
- Chylothorax

CLINICAL ISSUES

- Dyspnea, chest pain, hypotension, acute anemia
- Etiology: Trauma, anticoagulation, surgery, ruptured acute aortic syndrome, iatrogenic, malignancy, pulmonary thromboembolism
- Treatment
 - Thoracostomy tube: Removal of pleural blood and gas
 - o Surgery: Pleural fluid evacuation, control of bleeding site

(Left) Axial CECT of a patient with a large post-traumatic hemothorax shows a left posterior rib fracture 🔁 and a large left hemothorax 🔁 with active bleeding \supseteq , as depicted by contrast extravasation to the pleural space. (Right) Sagittal NECT of a patient who developed a hemothorax *i* ⇒ secondary to anticoagulation shows a large right hemothorax that exhibits the so-called hematocrit 🔁 effect from sedimented blood. Anticoagulation is among the most common causes of hemothorax.





(Left) Sagittal CECT of a patient with a ruptured aortic intramural hematoma shows a large left pleural effusion that exhibits a hematocrit effect ➡. Note the segmental area of intramural hematoma 🔁 along the descending aorta. (Right) Axial NECT of a patient who developed a hemothorax after placement of a pulmonary artery catheter shows a moderate right pleural effusion 🔁 with a hematocrit level 🔁. Hemothorax and pneumothorax are common complications of pacemaker and central line placement.





- Abbreviations
- Hemothorax (HTX)

Definitions

- Pleural effusion + variable amounts of blood products
- Pleural fluid hematocrit > 50% of peripheral blood hematocrit
- Massive HTX: Volume > 1,000 mL in clinical setting of shock &/or hypoperfusion

IMAGING

General Features

- Best diagnostic clue
 - o High-attenuation pleural effusion
- Size
 - Low-pressure bleeding from lung; tamponade effect of pleural fluid
 - High-pressure bleeding from systemic artery or large mediastinal vessel typically unremitting
 - Patient may exsanguinate into pleural space

Radiographic Findings

- Radiography
 - Pleural effusion
 - Meniscus sign, blunt costophrenic angle
 - Lateral lung border displaced from chest wall
 - Variable size: > 200 mL obscured hemidiaphragm
 - Rib fractures (in trauma)
 - Frequent loculation
 - Sequela (chronic non-treated HTX): Pleural calcification, fibrothorax, trapped lung

CT Findings

- NECT
 - High-attenuation pleural effusion
 - > 35 Hounsfield units (HU): Fresh blood
 - > 70 HU: Clotted blood
 - Hematocrit effect with layering of serum and sedimented red blood cells
 - Low-attenuation fluid in patients with anemia or longstanding HTX
 - Rib fractures increase likelihood of HTX
 - Loculation &/or pleural thickening
 - Identification of pleural calcification, assessment of fibrothorax, trapped lung
- CECT
 - Arterial blush indicates active bleeding and need for intervention
 - Ruptured acute aortic syndrome (i.e., aortic dissection, intramural hematoma, penetrating aortic ulcer) or aneurysm should be excluded

Ultrasonographic Findings

- Trauma protocol: High likelihood of fluid detection
- Echogenic pleural effusion, loculation

Imaging Recommendations

Best imaging tool
 CT: High-attenuation pleural fluid

- Protocol advice
 - NECT typically diagnostic
 - CECT for identification of active bleeding

DIFFERENTIAL DIAGNOSIS

Transudative Pleural Effusion

• Heart failure; pleural fluid typically 10-20 HU

Exudative Pleural Effusion

• Empyema; variable attenuation; typically loculated fluid

Malignant Pleural Effusion

- Pleural effusion with nodular pleural thickening
- High-attenuation pleural nodules may mimic HTX
- Hemorrhagic pleural effusion

Chylothorax

Water-attenuation pleural fluid; fat attenuation is rare

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Dyspnea, chest pain, hypotension, acute anemia
- Etiology
 - Trauma (e.g., rib fracture, acute traumatic aortic injury, diaphragmatic rupture, etc.)
 - Anticoagulation
 - o Post-surgical
 - Ruptured acute aortic syndrome or aneurysm
 - o Malignancy (e.g., lung cancer, metastasis)
 - Iatrogenic: Central catheter, pacemaker, etc.
 - o Pulmonary thromboembolism (pulmonary infarct)
 - Thoracic endometriosis

Natural History & Prognosis

- Untreated HTX: Progression to fibrothorax/trapped lung
- Superimposed infection may occur

Treatment

- Thoracostomy tube to remove pleural blood and gas
- Surgery; HTX evacuation, control of bleeding site
- Blood transfusion
- Embolization in selected cases (e.g., active bleeding)
- Intracavitary fibrinolytic therapy

DIAGNOSTIC CHECKLIST

Consider

• HTX in patients with high-attenuation pleural effusion; identification of bleeding source

Reporting Tips

• Localize blood within pleural or extrapleural space

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Chylothorax

KEY FACTS

TERMINOLOGY

• Definition: Extravasation of chyle into pleural space

IMAGING

- Radiography
 - Large pleural effusion, usually unilateral
 - Typically post cardiothoracic surgery or trauma
- CT
 - Large unilateral water attenuation pleural effusion
- MR: High signal intensity due to fat content
 - Heavily T2WI 3D TSE + FS: Extent of chylothorax
 - T1WI SPGR FS dynamic study: Identification of thoracic duct leak

TOP DIFFERENTIAL DIAGNOSES

- Exudative pleural effusion
- Transudative pleural effusion
- Empyema
- Hemothorax

PATHOLOGY

- Etiology
 - Traumatic/iatrogenic thoracic duct disruption
 - Thoracic duct obstruction from lymphadenopathy
 - Lymphatic disorders
- Milky opaque pleural fluid with high lipid content: Triglyceride concentration > 110 mg/dL

CLINICAL ISSUES

- Signs/symptoms
 - o Pleural effusion that decreases with fat fasting
- Therapy: Management of underlying condition
 Low chyle output: Conservative treatment
 - High chyle output: Surgical treatment

DIAGNOSTIC CHECKLIST

- Most chylothoraces are iatrogenic or secondary to trauma
- Rapid onset of large unilateral pleural effusion after trauma or cardiothoracic surgery should suggest chylothorax

(Left) Graphic shows a right chylothorax and the anatomic course of the thoracic duct \supseteq , which arises from the cisterna chyli at the L2 vertebra, courses along the right paravertebral region, crosses to the left at the carina (T5 vertebra), and drains into the left brachiocephalic vein. Thoracic duct injury may result in chylothorax. (Right) Axial CECT obtained after a left pneumonectomy shows a left tension chylothorax that manifests as a large water attenuation left pleural effusion with contralateral mediastinal shift 🔁.





(Left) Axial CECT of a 24-yearold patient who developed bilateral chylothoraces after surgical resection of a retroperitoneal mass shows moderate bilateral, freeflowing, water attenuation pleural effusions 🖂. (Right) Axial NECT of a 40-year-old woman with lymphangioleiomyomatosis shows a moderate right chylous pleural effusion 🖂 and profuse bilateral small thin-walled pulmonary cysts. Lymphangioleiomyomatosis is an unusual etiology of

chylothorax.





Synonyms

• Chylous pleural effusion

Definitions

• Extravasation of chyle into pleural space

IMAGING

General Features

- Best diagnostic clue
 - Large pleural effusion, usually unilateral
- Location
 - o Unilateral in 84% cases, 50-60% right-sided
 - Injury of lower 1/3 of thoracic duct: Right chylothorax
 - Injury of upper 2/3 of thoracic duct: Left chylothorax
 - Injury of thoracic duct as it crosses **midline: Bilateral** chylothoraces
- Size
 - Typically large: Production > than 2 L of chyle/day may lead to tension chylothorax

Radiographic Findings

• Pleural effusion: Typically large and unilateral

CT Findings

- Large unilateral water attenuation pleural effusion
- No pleural thickening, nodularity, or lung entrapment

MR Findings

- T1WI
 - High signal intensity due to fat content
- T2WIFS
 - Heavily T2WI 3D TSE + FS: Assessment of chylothorax extent
- Dynamic contrast-enhanced MR lymphangiography
 - T1WI SPGR FS dynamic study allows identification of thoracic duct leak

Angiographic Findings

Lymphangiography with iodinated contrast or radionuclide
 Localization of thoracic duct leak or obstruction

Imaging Recommendations

- Best imaging tool
 - Anatomic assessment of thoracic duct with lymphoscintigraphy or MR lymphangiography

DIFFERENTIAL DIAGNOSIS

Exudative Pleural Effusion

- Common in cancer, pneumonia, pulmonary embolism, autoimmunity, etc.
- No specific differentiating imaging features

Transudative Pleural Effusion

- Common in chronic heart failure
- No specific differentiating imaging features; typically free

Empyema

- Complication of pneumonia; often infectious symptoms
- Effusion often loculated with enhancing pleural thickening
- Air-fluid level should suggest bronchopleural fistula

Hemothorax

- Trauma, iatrogenic (central line placement)
- Occurs in acute setting
- CT may show high-attenuation fluid; hematocrit effect

PATHOLOGY

General Features

- Etiology
 - Traumatic/latrogenic thoracic duct disruption
 Rapid onset of large pleural effusion
 - Thoracic duct obstruction by lymphadenopathy
 Lymphoma, lung cancer, tuberculosis, sarcoidosis
 - Lymphatic disorders
 - Lymphangioleiomyomatosis
 - Lymphangioma
 - Diffuse pulmonary lymphangiomatosis
 - Gorham disease
 - Chylous ascites

Gross Pathologic & Surgical Features

- Milky opaque pleural fluid with high lipid content • Triglyceride concentration > 110 mg/dL
 - Pleural fluid chylomicrons confirm diagnosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Large pleural effusion; decreases with fat fasting

Natural History & Prognosis

- 50% resolve spontaneously
- Thoracic duct **ligation successful in 90%** of refractory chylothoraces

Treatment

- Management of underlying condition
- Low chyle output (< 1,100mL/day, < 1,000/day x 5 days) → conservative treatment
 - Thoracentesis
 - Dietary modifications
 - Fluid and electrolyte replacement
 - Somatostatin analogues
- High chyle output (≥ 1,100mL/day, ≥ 1,000/day x 5 days)
 → surgical treatment
 - Ligation of thoracic duct and tributaries
 - Thoracic duct embolization
 - o Talc pleurodesis in refractory cases

DIAGNOSTIC CHECKLIST

Consider

• Most chylothoraces are iatrogenic or secondary to trauma

Image Interpretation Pearls

• Rapid onset of large unilateral pleural effusion after trauma or cardiothoracic surgery should suggest chylothorax

SELECTED REFERENCES

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Empyema

KEY FACTS

TERMINOLOGY

• Empyema: Pleural space infection; abscess • Typically infected parapneumonic effusion

IMAGING

- Best diagnostic clue: Loculated pleural effusion in febrile patient
- Radiography
 - Loculated pleural effusion
 - o Lentiform shape on lateral or frontal radiography
 - Incomplete border sign
 - May contain air, air-fluid levels; indicative of bronchopleural fistula
- CT: Most findings are not specific for empyema
 - Loculated pleural fluid
 - May contain air; indicative of bronchopleural fistula
 - Split pleura sign, pleural thickening
 - Hypertrophy of extrapleural fat

TOP DIFFERENTIAL DIAGNOSES

- Malignant pleural effusion
- Malignant pleural mesothelioma
- Iatrogenic pleural loculation
- Abdominal causes: Catamenial hemothorax, pancreatic pseudocyst

PATHOLOGY

• Typically pleural involvement by adjacent pneumonia

CLINICAL ISSUES

- Symptoms: Chest pain, fever, rigors
- M > F; median age: 50 years
- Early diagnosis depends on high index of suspicion
- Antibiotics and drainage are first lines of therapy

DIAGNOSTIC CHECKLIST

• Consider empyema in any febrile patient with a loculated pleural effusion or unexplained pleural air

(Left) Axial CECT of a patient with empyema shows a right pleural effusion with lobulated borders, a lung $abscess \blacksquare, and enhancement$ of the pleural surfaces 🛃. The circumferential nature of the pleural fluid collection is indicative of loculation, which would be inconsistent with a simple transudative pleural effusion. (Right) Coronal CECT of a patient with empyema shows a large loculated right pleural effusion 🛃, pleural enhancement 🛃, and a large basilar fibrin ball \rightarrow .





(Left) Axial CECT of a patient with fever shows a loculated left pleural effusion with intrinsic air collections 🔁 and enhancement of thickened left pleural surfaces \blacksquare . In this clinical setting and in the absence of prior intervention, the findings are diagnostic of empyema with bronchopleural fistula. (Right) Graphic shows the morphologic features of empyema, which may include loculation, mass effect on the adjacent lung parenchyma, and gas \square in the pleural space from associated bronchopleural fistula.





Definitions

• Pleural space infection; abscess

- o Typically infected parapneumonic pleural effusion
- May result from hematogenous seeding of bacteria
- Rare but dangerous complication of chest surgery, trauma, mediastinitis, esophageal perforation
- Complication of other disease process, e.g., subdiaphragmatic abscess
- Empyema necessitatis
 - Empyema that drains spontaneously to chest wall; pleurocutaneous fistula
 - o Typically: Tuberculosis, fungal infection, actinomycosis
- Tension empyema
 - Large or rapidly expanding pleural infection with lung compression and mediastinal shift
 - Rarely complicated by cardiac arrest

IMAGING

General Features

- Best diagnostic clue
 - o Loculated pleural effusion in febrile patient
 - Pleural effusion may contain air pockets
 - Suggests development of bronchopleural fistula
 - Empyema may result in fistula, or fistula may precede empyema
- Location
 - Typically posterior or basal
 - May affect nondependent portions of pleural space
- Size
- o Variable
- Morphology
 - Loculation: Lentiform fluid collection, including fissural fluid (pseudotumor)

Radiographic Findings

- Blunt costophrenic angle
- Loculated pleural effusion
 - Morphology different than meniscus sign suggests loculation
 - Lack of change on decubitus radiography
- May contain air-fluid-levels indicating **bronchopleural fistula**
- Lentiform shape on lateral or frontal radiography
- Incomplete border sign
 - Sharp borders when imaged tangentially
 - Discrepant border visualization, shape, size on orthogonal views
 - o Indicates loculated fluid, not specific for empyema
- Loculated fissural pleural fluid; **pseudotumor**
 - May mimic lung mass
 - Incomplete border sign
 - Conforms to anatomic location of fissures

CT Findings

- CECT
 - Loculated pleural effusion
 - Indistinguishable from other loculated effusions
 Malignant pleural effusion

- □ Sterile reactive pleural effusion
- $\hfill\square$ Pleural effusion from abdominal source

• Air-fluid level in pleural space

- Indicative of bronchopleural fistula in absence of prior pleural intervention
- **Split pleura sign**; not specific for empyema, indicates chronic pleural inflammation
 - Thickening and enhancement of visceral and parietal pleura, "split" by intervening pleural fluid
- Pleural thickening
 - May be associated with noninfected pleural effusions
 - Typically thicker in cases of empyema
 - Tuberculous pleuritis may produce thick pleural calcification, rib thickening, adjacent trapped lung
- Hypertrophy of extrapleural fat
 - May be seen with noninfected pleural fluid
 - Typical of tuberculous or fungal pleural effusions
 - Indicative of chronic benign cause of pleural thickening; less common in malignancy
- CT essential for treatment planning
 - Differentiation of empyema from lung abscess
 - Location and extent of pleural fluid collection
 - Evaluation of loculations, multiple collections

MR Findings

- MR offers no diagnostic advantage over CT
 - o Most CT features of empyema have MR correlates
- Provides exquisite demonstration of empyema septations

Ultrasonographic Findings

- Variable ultrasound features according to disease stage
 Early stage may manifest as simple, anechoic or hypoechoic nonseptated pleural fluid
 - Complex pleural fluid collections: Hyperechoic with internal echoes and septations
 - Echogenic material and septa may be seen in noninfected pleural fluid
 - Identification of septa important for treatment planning
 - Increased likelihood that surgical intervention will be needed
 - Shadowing from gas pockets

Imaging Recommendations

- Best imaging tool
 - Chest radiography is best initial study; CT often needed to plan intervention
 - Ultrasound is preferred for needle or catheter selection/placement during thoracentesis
- Protocol advice
 - Intravenous contrast useful for demonstrating pleural enhancement but not essential

DIFFERENTIAL DIAGNOSIS

Malignant Pleural Effusion

- Most common tumors
 - o Adenocarcinoma
 - Breast, ovary, lung
 - o Invasive thymoma
- Pleural thickening or nodularity may be absent

Empyema

Malignant Pleural Mesothelioma

- Unilateral circumferential nodular pleural thickening
- Variable amount of pleural fluid
- Asbestos-related pleural plaques in 25%
- Iatrogenic Loculated Pleural Effusion
- Pleurodesis; often for malignant pleural effusions

Abdominal Etiologies

- Catamenial hemothorax
- Pancreatitis

PATHOLOGY

General Features

- Etiology
 - Typically due to spread from adjacent pneumonia
 - Parapneumonic pleural effusions may be bland or infected
 - Similar imaging appearances
 - Overall, pleural effusions related to pneumonia are more common in patients with diabetes mellitus
 - Tuberculosis
 - Noninfected pleural effusion from delayed hypersensitivity reaction to tuberculous antigens
 - Reactive pleural effusions much more common than empyema
 - May be **iatrogenic**
 - Overall incidence ~ 1% after lung resection for cancer
 - May occur early or late
 - Late cases may be due to hematogenous seeding of bland pleural fluid collections
 - ~75% with associated bronchopleural fistula
 - May be secondary to bronchial stump breakdown
 - Organisms: *Staphylococcus* most common,
 - Streptococcus, anaerobes, Gram-negative rods
 - May result from fistulous connections to gastrointestinal tract or skin
 - Chest wall infections, fasciitis
 - Tumor erosion from skin or esophagus
- Associated abnormalities
 - Bronchopleural fistula
 - May be associated with necrotizing lung infection or airway invasion by tumor

Staging, Grading, & Classification

- Empyema evolves through 3 stages, none of which is distinct on imaging
 - Exudative stage
 - Sterile fluid with normal glucose and normal pH
 - Fibrinopurulent stage
 - Accumulation of neutrophils, bacteria, fibrin
 - Decreased glucose and pH
 - Chronic organizing stage
 - Pleural peel develops and encases lung
 - Exudate is thick and frankly purulent
- Evolution may take weeks or days

Gross Pathologic & Surgical Features

- Thick pleural rind
- Often tightly adherent to underlying lung
- Purulent pleural fluid

• If underlying lung noncompliant, may not reexpand ("trapped lung") after pleural fluid drainage

Microscopic Features

• Fibrinous exudate, microbial organisms, associated hemorrhage

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain, fever, rigors
- Other signs/symptoms
 - o Tuberculous empyemas may produce fewer symptoms

Demographics

- Age
 - Median age in most series: ~ **50 years**
 - o May affect children, mostly related to pneumonia
 - Older adults, outcome often based on concomitant illness
- Sex
- M>F
- o Most published series include more men than women
- High mortality; up to 22%

Natural History & Prognosis

- Early diagnosis depends on high index of suspicion
 - Early thoracentesis essential for diagnosis
 - Nonspecific imaging features and symptoms
- Median hospital stay is ~ 20 days
- Overall mortality of ~ 22%
 - Worse outcome with fungal infection or afebrile patient (indicating inadequate host response)

Treatment

- Antibiotics and drainage are first lines of therapy
- Tube thoracostomy
 - Imaging guidance to access separate areas of involvement
 - Infusion of fibrinolytic agents into pleural space
- Video-assisted thoracoscopy
- Open drainage
 - Required for complex or unresponsive cases, assessment of underlying lung
 - Long-term open drainage post pneumonectomy
 - Clagett thoracotomy
 - Eloesser flap procedure

DIAGNOSTIC CHECKLIST

Consider

• Empyema in any febrile patient with loculated pleural effusion or unexplained pleural air

- 1. Garvia V et al: Empyema 2020
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Empyema





(Left) Axial CECT of a patient with a chronic right basilar empyema shows pleural thickening and a small right pleural effusion 🔁 with involvement of the adjacent chest wall by a fluid collection ➡, indicative of empyema necessitatis. (Right) Axial CECT of the same patient shows a small right hemithorax and a loculated right pleural effusion with surrounding pleural thickening \bowtie . Adjacent atelectasis or consolidation is present and is commonly seen in association with pleural fluid collections.





(Left) Right lateral decubitus chest radiograph shows a large air-fluid level \blacksquare in the right hemithorax. The elongated shape of the gasfluid collection is consistent with a complicated loculated pleural effusion rather than a lung abscess. (Right) Sagittal CECT of the same patient shows a large empyema with pleural enhancement 🔁 and mass effect on the adjacent lung 🛃. Heterogeneous $hypoattenuation \blacksquare of the$ atelectatic lung suggests underlying pneumonia. The air-fluid level is indicative of bronchopleural fistula.





(Left) Coronal NECT of a patient with chronic . aspergillus pneumonia, empyema, and bronchopleural fistula shows right lung consolidation, a coarsely calcified right pleural $collection \blacksquare$ with internal debris and gas, and adjacent pleural thickening and calcification 🛃. (Right) Coronal NECT of the same patient obtained at a later date shows a right pneumonectomy and Eloesser flap 🖅 procedure for endstage lung infection and chronic empyema and bronchopleural fistula.

KEY FACTS

TERMINOLOGY

• Pneumothorax due to medical procedure/treatment

IMAGING

- Radiography
 - Upright: Visualization of curvilinear visceral pleural line
 - Supine: Basilar pneumothorax with increased sharpness of mediastinal/diaphragmatic margins
 - Deep sulcus sign, double diaphragm sign
- CT
 - Visualization of air in pleural space
 - Air in nondependent pleural space

TOP DIFFERENTIAL DIAGNOSES

- Primary spontaneous pneumothorax
- Pneumothorax ex vacuo
- Skin fold
- Bullae or cysts

PATHOLOGY

- Needle biopsy, thoracentesis, subclavian/internal jugular venipuncture
- Positive pressure ventilation
- Thoracotomy, bronchoscopy, bronchial valves
- Placement of catheters, chest/endotracheal/enteric tubes, pacemaker electrodes

CLINICAL ISSUES

- Signs/symptoms
- Chest pain, dyspnea
- May be asymptomatic
- Prognosis: Generally good
- Treatment: Chest tube, supplemental oxygen

DIAGNOSTIC CHECKLIST

• Consider tension pneumothorax in patient with contralateral mediastinal shift and depression of ipsilateral hemidiaphragm

(Left) Axial NECT of a patient with lung cancer status post CT-guided biopsy shows a right upper lobe lobulated subpleural mass \blacksquare and a small anterior pneumothorax *⊡*. (Right) Supine AP chest radiograph of a critically ill intubated patient shows a right basilar lucency, a sharp right hemidiaphragmatic margin, and the so-called deep sulcus sign \boxtimes secondary to a right pneumothorax. Note middle lobe atelectasis ➡. latrogenic pneumothorax may result from thoracic interventions or barotrauma.





(Left) AP chest radiograph of patient status post right thoracentesis shows a right apical pleural line secondary to a small pneumothorax 🔁 and a moderate right pleural effusion 🛃. (Right) PA chest radiograph of a patient with malignant pleural mesothelioma status post right thoracentesis shows a right pneumothorax ex vacuo due to failure of the right lung to reexpand because of a thickened visceral pleural surface 🛃. Note multifocal right pleural masses \blacksquare and nodules, characteristic of mesothelioma.





Definitions

- Accumulation air within pleural space secondary to medical procedures or treatments
- Common cause of pneumothorax

IMAGING

Radiographic Findings

- Upright radiography
 - Apical lucency conforming to shape of pleural space
 - Pleural line
 - Visualization of curvilinear visceral pleura that separates vessel-containing lung from avascular airfilled pleural space
- Supine radiography
 - Increased sharpness of mediastinal/diaphragmatic margins
 - **Deep sulcus sign**: Basilar pleural air produces larger/deeper lateral costophrenic sulcus compared to contralateral sulcus
 - **Double diaphragm sign**: Simultaneous visualization of anterior costophrenic sulcus and diaphragmatic dome
 - Medial retraction of middle lobe with visualization of its borders
 - Upper and lower lobes maintain contact with lateral chest wall
- Identification and assessment of support devices consistent with thoracic intervention or barotrauma

CT Findings

- Visualization of air in pleural space
 Air accumulation in nondependent pleural space
- More sensitive and specific than radiography for diagnosis of pneumothorax

Ultrasonographic Findings

- Comet-ail artifact with reverberations extending from echogenic pleural line to edge of image
- Absence of normal lung beneath echogenic pleural line

Imaging Recommendations

- Best imaging tool
 - O Upright chest radiography usually diagnosticO CT highly sensitive for small or atypical pneumothorax

DIFFERENTIAL DIAGNOSIS

Primary Spontaneous Pneumothorax

• Occurs spontaneously without preceding procedure or medical treatment

Pneumothorax Ex Vacuo

- Follows drainage of pleural fluid with failure of lung reexpansion
 - Lung entrapment
 - Thick visceral pleura or obstructing central lesion
- Usually asymptomatic; chest tube placement not indicated

Skin Fold

- May extend beyond chest wall inner margin
- Thicker linear/curvilinear opacity with sharp outer edge

Bullae or Cysts

- Convex inner margin; does not conform to expected lung shape
- Vanishing lung syndrome (large lucency with absent lung markings from extensive emphysema); may be difficult to differentiate from pneumothorax

PATHOLOGY

General Features

- Etiology
 - Transthoracic needle aspiration/biopsy, thoracentesis, subclavian/internal jugular venipuncture
 - Positive pressure ventilation
 - o Thoracotomy, bronchoscopy, bronchial valves
 - Placement of catheters, chest tubes, endotracheal tubes, enteric tubes, pacemaker electrodes

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain, dyspnea
 - May be asymptomatic
- Other signs/symptoms
 - Tachypnea, tachycardia, hypotension with tension pneumothorax

Demographics

- Epidemiology
 Transthoracic needle aspiration/biopsy; emphysema,
 - long needle path, increased number of pleural punctures

Natural History & Prognosis

- Generally good prognosis
- Unrecognized tension pneumothorax associated with mechanical ventilation may be fatal

Treatment

- Chest tube for symptomatic, enlarging, or moderate to large iatrogenic pneumothorax
 - Reported duration of chest tube treatment of iatrogenic pneumothorax; average of 4.7 days
- Supplemental oxygen enhances rate of pleural air absorption
- Needle aspiration may be sufficient for treatment of small pneumothorax secondary to needle biopsy

DIAGNOSTIC CHECKLIST

Consider

• Tension pneumothorax with contralateral mediastinal shift and depression of ipsilateral diaphragm

Image Interpretation Pearls

• Careful assessment of the entire pleura after invasive thoracic procedures in patients with suspected pneumothorax

- 1. Brzezinski RY et al: The yield of immediate post lung biopsy CT in predicting iatrogenic pneumothorax. BMC Pulm Med. 20(1):91, 2020
- 2. Ojeda Rodriguez JA et al: latrogenic Pneumothorax 2020

KEY FACTS

TERMINOLOGY

- Definition: Pneumothorax that occurs **without precipitating event** in **otherwise healthy subject** without evidence of underlying lung disease
- Most cases associated with apical bullae

IMAGING

- Radiography
 - o Visualization of visceral pleural line
 - Visible subpleural bullae in up to 15% of cases
 - Deep sulcus sign on supine radiography
 - Mimics: Skin fold, subpleural gas
- CT
 - o Increased sensitivity for pneumothorax
- Assessment of lung parenchyma

TOP DIFFERENTIAL DIAGNOSES

- Secondary spontaneous pneumothorax
- Vanishing lung syndrome

PATHOLOGY

- Ruptured bulla(e)
- Subpleural fibrosis with fibroblastic foci in adjacent lung parenchyma

CLINICAL ISSUES

- Signs and Symptoms
 Chest pain, dyspnea, rarely asymptomatic
- Risk factors: Tall, thin individuals, males, smokers
- Age: 20-40 years
- Often occurs in winter months
- Treatment: 100% oxygen, chest tube placement, resection of bullae, talc pleurodesis

DIAGNOSTIC CHECKLIST

- Visualization of visceral pleural line without peripheral lung markings is diagnostic of pneumothorax
- Consider primary spontaneous pneumothorax in young, thin, tall individuals with acute unilateral chest pain

(Left) PA chest radiograph of a patient who presented with acute left chest pain shows a visceral pleural line 🖂 along the left upper and lateral hemithorax, consistent with a left pneumothorax. (Right) Coronal NECT of the same patient shows a left apical bulla *⊡* and a small associated left pneumothorax *⊡*. There is no evidence of emphysema, and with the exception of the bulla, the visualized lung appears normal. These findings are characteristic of primary spontaneous pneumothorax.





(Left) PA chest radiograph of a 20-year-old man with a history of prior pneumothorax and new acute left chest pain shows a large left pneumothorax and complete left lung atelectasis. (Right) Coronal NECT of the same patient after left chest tube placement shows a small residual left apical pneumothorax 🔁, biapical bullae &/or blebs 🛃, but no centrilobular emphysema. Patients with recurrent primary spontaneous pneumothorax often exhibit apical bullae and blebs on chest CT.





Abbreviations

- Pneumothorax (PTX)
- Primary spontaneous pneumothorax (PSP)

Definitions

- PTX that occurs **without precipitating event** in **otherwise healthy patient** without obvious evidence of underlying lung disease
 - Most cases associated with apical bullae

IMAGING

General Features

- Best diagnostic clue
 - Visualization of **visceral pleural line**; absence of peripheral lung markings
- Location
 - Upright radiography: Apical pleural space
 - Supine radiography: Basilar pleural space, at costophrenic angle or medially along mediastinal border
 - Slightly more common on right
 - Rarely bilateral
- Size
 - o Small: < 20% of hemithorax volume
 - Large: > 20% of hemithorax volume
- Morphology
 - May be loculated
 - May be associated with ipsilateral pleural fluid (hydropneumothorax)

Radiographic Findings

- Visualization of visceral pleural line
 - Typically apical on upright chest radiography
 - Lateral or basilar PTX may occur with apical pleural adhesions
- Visible **apical subpleural bullae** in up to **15%** of cases
 - o Apical subpleural bullae rarely visible in absence of PTX
 - o Typically normal-appearing lung
- Pleural effusion in 15%
- Expiratory radiography does not increase sensitivity for PTX
- Tension PTX: Mediastinal shift, tracheal deviation, ipsilateral diaphragmatic flattening, rib splaying
- Deep sulcus sign; supine radiography
 - Hyperlucent deep costophrenic angle and ipsilateral upper abdomen
 - o Sharply marginated adjacent hemidiaphragmo Underestimates PTX size (i.e., usually larger)
- Decubitus radiography may help differentiate PTX from apical bullous disease
- Measurement of pleural separation for follow-up assessment
- Volume estimation
 - Measurement of transverse diameters of hemithorax and aerated lung
 - [Hemithorax diameter³ aerated lung diameter³] / hemithorax diameter³
 - Example: 2-cm PTX with hemithorax diameter of 10 cm: $[10^3-8^3]/10^3 = 48.8\%$
 - Not often used in clinical practice

CT Findings

- Increased sensitivity for PTX
- Evaluation of underlying lung
- Frequent paraseptal &/or centrilobular emphysema
- Pleural blebs indistinguishable from subpleural bullae
- Contralateral disease commonly identified
 Important for operative planning

Imaging Recommendations

- Best imaging tool
 - Upright radiography usually diagnostic
 - CT more sensitive to assess lung parenchyma for secondary causes of PTX and identification of contralateral disease
 - CT can be used for problem solving; particularly in severe emphysema
- Protocol advice
 - Decubitus radiography useful in differentiating PTX from apical bullae
 - Expiratory radiographs do not improve diagnostic sensitivity of PTX
 - Contrast not helpful when performing CT for evaluation of PTX

DIFFERENTIAL DIAGNOSIS

Secondary Spontaneous Pneumothorax

- PTX associated with predisposing lung disease
 - Emphysema and bullae
 - Most common cause
 - Smoking-related lung destruction
 - o Infection
 - Necrotizing pneumonia; e.g., Staphylococcus aureus
 - Pneumatocele; e.g., Pneumocystis jirovecii
 - Cavitary disease; e.g., tuberculosis
 - Septic emboli
 - o Vasculitis
 - Granulomatosis with polyangiitis
 - $\hfill\square$ Multiple cavitary nodules, masses, or consolidations
 - May be associated with hemoptysis and diffuse pulmonary opacities
 - Cystic lung disease
 - Lymphangioleiomyomatosis
 - Pulmonary Langerhans cell histiocytosis
 - Birt-Hogg-Dubé syndrome
 - o Malignancy
 - Lung cancer
 - Mesothelioma
 - Metastases: Classically osteosarcoma
 - o Collagen vascular disease
 - Marfan syndrome
 - Ehlers-Danlos syndrome
 - Autoimmunity
 - Rheumatoid arthritis
 - Bronchopleural fistula from subpleural necrobiotic nodules
 - Interstitial lung disease (i.e., diffuse fibrosing interstitial lung disease)
 - Catamenial PTX; ectopic endometrial tissue
 - o Other: Asthma, bronchiolitis, cystic fibrosis

Vanishing Lung Syndrome

- Severe bullous disease involving 1 lung or significant portion of lung; may simulate large PTX
- CT may be required to differentiate from PTX
- Chest tube placement into bulla may produce bronchopleural fistula

Mimics

- Skin fold: May extend beyond thoracic cavity; not present on decubitus radiography
- External support or monitoring devices: Should be removed and radiograph repeated if equivocal diagnosis of PTX
- Pneumomediastinum: May be indistinguishable from loculated medial PTX, extrapleural air may simulate PTX

PATHOLOGY

General Features

- Etiology
 - Ruptured bulla
 - Typically apical and subpleural
 - Development of blebs, bullae, and pleural porosity linked to various factors
 - Distal airway inflammation
 - Hereditary predisposition
 - Anatomic abnormalities of bronchial tree
 - Ectomorphic physiognomy with more negative intrapleural pressures
 - Apical ischemia
 - □ Low body mass index
 - Caloric restriction
 - Abnormal connective tissue

Gross Pathologic & Surgical Features

- Subpleural bullae and visceral pleural blebs
- Frequent eosinophilic infiltrates adjacent to pleural blebs
- Subpleural fibrosis with fibroblastic foci in adjacent lung
- Buffalo chest
 - Communication between right and left pleural spaces
 May be congenital or iatrogenic
 - Affected patients with bilateral PTX may be treated with unilateral chest tube placement

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Chest pain 90%
 - o Dyspnea 80%
 - Rarely asymptomatic
- Other signs/symptoms
 - Tension PTX (clinical diagnosis)
 - Tachycardia
 - Hypotension
 - Cyanosis
- Clinical profile
 - Risk factors
 - Tall, thin individuals
 - Males
 - Smokers
 - May be precipitated by coughing or sneezing

• PSP often occurs in **winter months**

Demographics

- Age
 - \circ 20-40 years
- Sex
 - Men 5x more commonly affected than women
 - When controlling for height, no significant sex discrepancy
- Body habitus
 - More common in tall, thin individuals

Natural History & Prognosis

- Pleural gas absorbed 1.5% per day on room air
 - Complete absorption and complete lung reexpansion; average of 3 weeks
 - Daily radiography of little utility in stable patients
- Recurrent spontaneous PTX in up to 50% of patients
 - Most occur within 2 years
 - Risk of additional recurrence up to 85%
 - Recurrent PTX may be contralateral to prior PTX

Treatment

- 100% oxygen
- o Small PTX
- Pleural gas resorbed up to 4x faster than on room air
- Chest tube
 - Urgent chest tube placement for tension or symptomatic PTX
 - Small chest tubes as effective as large chest tubes in treating uncomplicated PTX
 - Chest tubes managed with suction, water seal, or 1-way valve based on presence of air leak
- Open thoracotomy or video-assisted thoracoscopic surgery
 - $\circ~\mbox{Resection}$ of bullae
 - Talc pleurodesis
 - o Both
- Incomplete lung reexpansion may be due to malpositioned chest tube, bronchopleural fistula, or trapped lung from pleural thickening
- Patients with PSP should avoid air travel for 6 weeks and scuba diving for life

DIAGNOSTIC CHECKLIST

Consider

- PSP in young, thin, tall individuals who present with acute onset of unilateral chest pain
- Decubitus radiography or chest CT for equivocal diagnosis of PTX; particularly in patients with emphysema

Image Interpretation Pearls

• Visualization of visceral pleural line without peripheral lung markings is diagnostic of PTX

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(Left) PA chest radiograph of a patient with primary spontaneous pneumothorax shows a large right $pneumothorax \longrightarrow$ with apical, lateral, and basilar components. Note right upper lobe subpleural bullae &/or blebs 🔁 (Right) Axial NECT of the same patient shows a right pneumothorax and *multiple small subpleural* bullae ⊇. While patients with primary spontaneous pneumothorax are commonly smokers, there is usually no evidence of centrilobular emphysema.





(Left) PA chest radiograph of a patient with vanishing lung syndrome shows paucity of bronchovascular markings in the mid and upper right lung simulating a right pneumothorax. The latter is excluded based on absence of a visible pleural line. (Right) Axial CECT of the same patient shows extensive emphysema and bullae with preferential severe involvement of the right upper lobe. Such cases may be misinterpreted as pneumothorax and may undergo unnecessary thoracostomy tube placement.





(Left) PA chest radiograph of a patient with a pneumomediastinum shows an apparent left apical visceral pleural line \square formed by extrapleural gas. This finding may mimic a pneumothorax. (Right) Coronal NECT of the same patient shows the extrapleural left apical subpleural gas collection. Pneumomediastinum may dissect along the subpleural space and may mimic a pneumothorax. Dissection of pneumomediastinum along bronchovascular structures is known as the Macklin effect.

KEY FACTS

TERMINOLOGY

• Pneumothorax associated with underlying lung disease in absence of trauma or intervention

IMAGING

- Radiography
 - Thin visceral pleural line parallel to chest wall
 - Absence of peripheral lung markings
 - Focal, diffuse, or cystic/cavitary lung disease
- CT
 - Air within pleural space
 - Increased sensitivity and specificity for diagnosis
 - o Optimal evaluation of underlying pulmonary disease

TOP DIFFERENTIAL DIAGNOSES

- Primary spontaneous pneumothorax
- Mimics of pneumothorax
 - Skin fold, external monitoring device, pneumomediastinum, extrapleural air

PATHOLOGY

- Etiologies: Focal or diffuse infiltrative, cystic, or cavitary disease
 - o Emphysema, bullae
 - o Infection
 - o Vasculitis
 - Cystic lung disease
 - o Neoplasm
 - o Interstitial lung disease

CLINICAL ISSUES

- Clinical presentation
 - Chest pain, sudden dyspnea
 - o Cyanosis, sweats, tachycardia
- Treatment
 - Observation of small, minimally symptomatic secondary spontaneous pneumothorax (SSP)
 - Chest tube drainage for large, symptomatic SSP
 - o Treatment of underlying lung disease

(Left) PA chest radiograph of a patient with a secondary spontaneous pneumothorax due to underlying emphysema and bullous disease shows a moderate to large right pneumothorax 🔁 with apical, lateral, and basilar components and underlying bullae 🔁. (Right) Axial NECT of the same patient after chest tube placement shows lung reexpansion, a right thoracostomy tube *⊡*, a small right pneumothorax 🔁, and large pulmonary bullae 🖂 Emphysema is the most common cause of secondary spontaneous pneumothorax.





(Left) Axial NECT of a patient with septic embolism and bilateral spontaneous pneumothoraces 🖂 shows bilateral cavitary lung nodules, some with intrinsic air-fluid levels \square , which may result in pneumothorax due to bronchopleural fistula. (Right) Axial CECT shows a cavitary left lower lobe pneumonia with an air-fluid level \supseteq , a bronchopleural fistula \square , and a left pneumothorax \boxtimes . Primary and secondary lung neoplasms as well as cavitary lung lesions may produce secondary spontaneous pneumothorax.





Abbreviations

• Secondary spontaneous pneumothorax (SSP)

Definitions

• Pneumothorax associated with underlying lung disease in absence of trauma or intervention

IMAGING

General Features

- Best diagnostic clue
 - Radiography: Thin visceral pleural line, absence of peripheral lung markings underlying lung disease
 - CT: Air within pleural space; optimal evaluation of underlying lung disease
- Location
 - Nondependent pleural space
 - Upright imaging: Apical pleural space
 - Supine imaging: Anterior basilar pleural space
 - Decubitus imaging: Lateral nondependent pleural space
- Size

o Variable: Small, moderate, large

Radiographic Findings

- Thin visceral pleural line parallel to chest wall
- Absence of peripheral lung markings
- Focal, diffuse, or cystic/cavitary lung disease
- Sensitivity depends on patient position
- Supine radiography
 - o Least sensitive, inaccurate size assessment

• Deep sulcus sign

- Air in anterior inferior pleural space
- Hyperlucent deep costophrenic angle and ipsilateral upper abdomen
- Sharply marginated ipsilateral hemidiaphragm
- Underestimates pneumothorax size (i.e., usually larger)
- Lateral decubitus radiography; equal or superior to upright imaging

CT Findings

- Air within pleural space
- Increased sensitivity and specificity for diagnosis
- Optimal evaluation of underlying pulmonary disease

Imaging Recommendations

- Best imaging tool
 - Upright radiography
 - o Expiratory imaging does not increase sensitivity
 - CT most sensitive and specific for diagnosis of SSP and assessment of pulmonary disease

DIFFERENTIAL DIAGNOSIS

Primary Spontaneous Pneumothorax

- Spontaneous pneumothorax without apparent cause
- Associated apical blebs or bullae
- Risk factors: Thin tall individuals, smoking

Mimics of Pneumothorax

- Skin fold: May extend beyond chest cavity, absent on decubitus radiography
- External monitoring devices: Remove and repeat radiograph if pneumothorax diagnosis in doubt
- Pneumomediastinum may mimic loculated medial pneumothorax
- Extrapleural air extending from pneumomediastinum

PATHOLOGY

General Features

- Etiology
 - Chronic obstructive pulmonary disease: Emphysema and bullae (most common)
 - o Infection (e.g., pneumonia, septic emboli, *P. jirovecii*, tuberculosis)
 - o Vasculitis (e.g., granulomatosis with polyangiitis)
 - Cystic lung disease (e.g., lymphangioleiomyomatosis, pulmonary Langerhans histiocytosis, lymphoid interstitial pneumonia, Birt-Hogg-Dubé syndrome)
 - Neoplasm [e.g., lung cancer, metastases (e.g., metastatic osteosarcoma/angiosarcoma)]
 - Interstitial lung disease (i.e., diffuse fibrosing interstitial lung disease)
 - o Collagen vascular disease
 - Marfan syndrome: Abnormal fibrillin; pneumothorax in 4-15%, associated bullous disease
 - Ehlers-Danlos syndrome: Typically type IV, associated skeletal abnormalities
 - Autoimmunity
 - Rheumatoid arthritis: Bronchopleural fistula from subpleural necrobiotic nodules
 - Catamenial pneumothorax
 - SSP near time of menses; usually parous women
 - Majority (90%) right-sided, small, recurrent
 - Diaphragmatic defect allows passage of peritoneal air vs. pleural endometrial implants
 - Pulmonary infarction
 - Bronchopleural fistula in subpleural lung
 - Typically from pulmonary embolism

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
- Chest pain, sudden dyspnea
- Other signs/symptoms
 Cyanosis, sweats, tachycardia

Treatment

- Observation of small, minimally symptomatic SSP
- Chest tube drainage for large, symptomatic SSP
- Treatment/management of underlying lung disease

SELECTED REFERENCES

 Ruppert AM et al: Detection of secondary causes of spontaneous pneumothorax: comparison between computed tomography and chest Xray. Diagn Interv Imaging. 101(4):217-24, 2020 (Left) Axial CECT of a patient with pulmonary Langerhans cell histiocytosis complicated by secondary spontaneous pneumothorax shows profuse pulmonary micronodules, small lung cysts ➡, and a small right pneumothorax ➡. (Right) Coronal CECT of a patient with

lymphangioleiomyomatosis complicated by secondary spontaneous pneumothorax shows profuse bilateral welldefined thin-walled pulmonary cysts 2 and a small right pneumothorax 2.





(Left) Axial NECT of a patient with secondary spontaneous pneumothorax due to lymphoid interstitial pneumonia shows multiple thin-walled cysts 🛃, small solid nodules \square , and a left pneumothorax 🖂 (Right) Coronal NECT of a patient with granulomatosis with polyangiitis and a secondary left spontaneous $pneumothorax \supseteq shows$, scattered areas of lung scarring \bowtie with associated volume loss (more conspicuous in the upper lobes) that represent sequela of recurrent episodes of vasculitis.





(Left) PA chest radiograph of a patient with sarcoidosis shows a moderate to large secondary right spontaneous hydropneumothorax 🔁 and bilateral peribronchovascular opacities with intrinsic lucency , concerning for cavitation. (Right) Coronal NECT of the same patient obtained after right thoracostomy tube 🖂 placement shows bilateral peribronchovascular mass-like lesions \supseteq , some with cavitation 🔁 Although uncommon in sarcoidosis, cavitation may result in secondary spontaneous pneumothorax.









(Left) PA chest radiograph of a patient with secondary spontaneous pneumothorax secondary to metastatic undifferentiated carcinoma shows a large right basilar pneumothorax $\overline{\mathbb{D}}$ and a right mid lung zone metastasis 🔁 (Right) Sagittal CECT of the same patient shows a right upper lobe lobulated solid metastasis 🔁 and a small residual pneumothorax 🔁 after insertion of a right thoracostomy tube. Diffuse right lower lobe opacities are secondary to reexpansion pulmonary edema.





(Left) PA chest radiograph of a patient with recurrent catamenial pneumothoraces shows a right hydropneumothorax and an air-fluid level earrow in the right basilar pleural space. (Right) Axial CECT of the same patient shows a small right anterior pneumothorax 🖅 and right pleural soft tissue nodules \blacksquare , suggestive of endometrial pleural implants. Catamenial pneumothorax is a rare form of secondary spontaneous pneumothorax.





(Left) Axial CECT of a patient with rheumatoid arthritis and necrobiotic lung nodules shows a right upper lobe cavitary lesion \supseteq with an intrinsic eccentric soft tissue nodule. (Right) Axial CECT of the same patient shows more cavitary subpleural necrobiotic nodules 🛃 and a small right pneumothorax D drained by a right thoracostomy tube 🔁. CT allows evaluation of the pleural surfaces and underlying parenchymal disease in patients with secondary spontaneous pneumothorax.

Apical Cap

KEY FACTS

TERMINOLOGY

- Synonyms
- (Pulmonary) apical cap, apical pleural cap, apical scar Definition
 - Apical pleuroparenchymal thickening

IMAGING

- Crescentic apical soft tissue opacity < 5 mm thick
- Sharp, smooth, or undulating margin
- Often symmetric or thickness usually within 5 mm of contralateral side
- Subpleural apical soft tissue on CT
- Extrapleural fat often thickened

TOP DIFFERENTIAL DIAGNOSES

- Pancoast tumor (superior sulcus tumor)
- Tuberculosis or other inflammatory disease
- Mediastinal hemorrhage
- Radiation fibrosis

• Extrapleural fat

PATHOLOGY

- Postulated chronic apical lung ischemia
- Pleuroparenchymal fibrosis
- Cicatricial emphysema adjacent to scar
- Peripheral pneumocyte hyperplasia may mimic carcinoma associated with scar

CLINICAL ISSUES

- Asymptomatic radiographic abnormality
- Incidence increases with age
 - o 5% at age 40; 50% at age 70

DIAGNOSTIC CHECKLIST

- Consider apical cap in asymptomatic older patients with stable or symmetric apical thickening
- Benign bilateral apical caps are within 5 mm in thickness
- Exclude malignancy in cases of asymmetric indistinct apical caps with associated skeletal destruction

(Left) Graphic shows biapical subpleural fibrosis 🔁 and extrapleural fat thickening \bowtie , which often account for apical caps seen on radiography. (Right) PA chest radiograph (top) shows an irregular right apical opacity \blacksquare and destruction of adjacent ribs and vertebrae. Coronal T2WI MR (bottom) confirms an invasive apical lung cancer 🔁 (Pancoast tumor) with chest wall invasion. More than 5 mm of asymmetry of apical opacities should raise suspicion, particularly if evidence of long-term stability is not available.





(Left) PA chest radiograph of a patient with left shoulder pain shows a unilateral opacity at the apex of the left lung \supseteq , consistent with an apical cap. In an acute, symptomatic presentation, an apical cap is suspicious for hemorrhage extending along the superior sulcus of the lung. (Right) Digital subtraction angiography of the same patient shows a left subclavian artery pseudoaneurysm 🔁 secondary to vasculopathy. Apical caps in the setting of trauma or line placement should be further evaluated.





Synonyms

• (Pulmonary) apical cap, apical pleuroparenchymal thickening, apical pleural cap, apical scar

Definitions

• Apical pleuroparenchymal thickening on radiography

IMAGING

Radiographic Findings

- Crescentic apical opacity; usually < 5 mm thick
- Sharp, smooth, or undulating margin
- Bilateral more common than unilateral
 - Bilateral; often symmetric; apical cap **within 5 mm in thickness** compared to contralateral side
 - Unilateral, more common on right

CT Findings

- Subpleural soft tissue adjacent to lung apex
- Extrapleural fat often thickened
- Adjacent paracicatricial emphysema

MR Findings

• Multiplanar imaging may help exclude apical mass

DIFFERENTIAL DIAGNOSIS

Pancoast Tumor (Superior Sulcus Tumor)

- Apical lung cancer
- Associated rib or vertebral body destruction
- Inferior margin may be indistinct
- Asymmetry > 5 mm suspicious for malignancy

Tuberculosis or Other Inflammatory Disease

- Apical cicatricial scar, often contains small calcified nodules, associated hilar retraction from upper lobe volume loss
- Thickened extrapleural fat common on CT
- Usually irregular apical cap > 5 mm thick

Mediastinal Hemorrhage

- Extrapleural blood from great vessel injury dissecting along subclavian artery
- Unusual as isolated radiographic abnormality
- More common on left

Radiation Fibrosis

• Lung apex in radiation field for head and neck cancer, lymphoma, breast cancer (supraclavicular therapy)

Peripheral Upper Lobe Collapse

• Apical &/or posterior upper lobe segment atelectasis

Pleural Effusion (Supine)

• Lung apex most dependent portion of pleural space in supine position

Excess Extrapleural Fat

- Usually bilateral
 - May be seen in normal subjects
 - Obesity, corticosteroids, Cushing syndrome
- Fat attenuation on CT

Malignant Pleural Mesothelioma

• Typically diffuse irregular pleural thickening

Extrapleural Neoplasm

- Invasive thymoma with extrapleural involvement
- Perivascular spread of lymphoma in superior sulcus
- Paravertebral mass; neurogenic neoplasm

Vascular Abnormalities

- Dilatation/ectasia of subclavian vessels
- Post-traumatic aneurysm or arteriovenous fistula

PATHOLOGY

General Features

- Etiology
 - Postulated chronic apical lung ischemia
 - Histologic vascular abnormality similar to lung infarct
 - Apical lung ischemia leads to pleuroparenchymal fibrosis

Gross Pathologic & Surgical Features

- Depressed apical plaque with triangular cross-sectional morphology
- Overlying pleural thickening with sharp lateral margins

Microscopic Features

- Hyaline fibrosis of visceral pleura identical to pleural plaque in 50% of cases
- Collapsed but intact elastic framework and increased fibers
- Cicatricial emphysema adjacent to scar
- Peripheral pneumocyte hyperplasia may mimic carcinoma associated with scar

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic, incidental radiographic finding

Demographics

- Epidemiology
 Incidence increases with age
 - 5% by age 40; 50% by age 70

Natural History & Prognosis

• Normal process of aging

DIAGNOSTIC CHECKLIST

Consider

- Benign apical cap in asymptomatic older patients with stable or symmetric apical thickening
- Exclusion of malignancy in cases of asymmetric indistinct apical cap with associated skeletal destruction
- In cases of trauma or line placement and asymmetric apical cap, consider hemorrhage along superior sulcus

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<u>Pleural</u> Plaques

KEY FACTS

TERMINOLOGY

• Definition: Parietal pleural fibrohyaline acellular lesion

IMAGING

• Radiography

- Bilateral, multifocal nodular discontinuous pleural thickening ± calcification
- Along diaphragm and adjacent to 6th-9th ribs
- May exhibit incomplete border sign
- Calcified plaques; holly leaf appearance
- CT
 - More sensitive than radiography
 - Bilateral multifocal nodular discontinuous pleural thickening
 - Calcification in 10-15% of plaques; increases over time after exposure
 - Assessment of associated lung parenchymal abnormalities
 - o Typically spares apices and costophrenic angles

TOP DIFFERENTIAL DIAGNOSES

- Chest wall trauma
- Pleural fibrosis and fibrothorax
- Pleural metastases
- Primary pleural neoplasms
 - Malignant pleural mesothelioma
 - Localized fibrous tumor of pleura
- Talc pleurodesis
- Extrapleural fat

CLINICAL ISSUES

- Etiology: Occupational asbestos exposure
- Symptoms: Asymptomatic patients
- Treatment: Supportive

DIAGNOSTIC CHECKLIST

• Bilateral calcified pleural plaques are virtually diagnostic of asbestos-related pleural disease

(Left) PA chest radiograph of an asymptomatic patient with a history of asbestos exposure shows bilateral calcified pleural plaques $rac{2}{a}$ along the paravertebral pleura and sharply marginated calcified plaques \blacksquare that spare the apices and costophrenic angles and exhibit the socalled holly leaf morphology. (Right) Lateral chest radiograph of the same patient shows calcified pleural plaques along the undersurfaces of anterior and posterior ribs \blacksquare and over the central tendinous portions of the hemidiaphragms \square .





(Left) Axial CECT of a patient with prior asbestos exposure shows bilateral calcified and noncalcified pleural plaques involving the undersurfaces of anterior and posterior ribs as well as along the paravertebral pleura 🔁. (Right) Coronal CECT of a patient with prior asbestos exposure shows the predilection of calcified pleural plaques to involve the undersurfaces of ribs \blacksquare and the pleura over the central tendinous portions of the hemidiaphragms 🔁.





Definitions

- Fibrohyaline acellular lesion predominantly involving parietal pleura
 - Often along diaphragm and rib undersurfaces

IMAGING

General Features

- Best diagnostic clue
- Bilateral, multifocal pleural lesions ± calcification
- Location
 - Usually limited to parietal pleura; occasionally visceral pleura and interlobar fissures
 - Most common along diaphragmatic and posterolateral pleura; rarely involves mediastinal pleura
 - Typically spares apices and costophrenic angles
- Size
 - Range: 2 mm to 10 cm
- Morphology
 - Flat or nodular soft tissue lesions; may exhibit intrinsic calcification

Radiographic Findings

- General
 - o Radiography is 40% sensitive in detecting pleural plaques
 - Pleural plaques: Most frequent radiographic manifestation of asbestos exposure
- Bilateral, multifocal discontinuous nodular pleural thickening ± calcifications
 - Plaques over diaphragmatic pleura best visualized on lateral radiography
 - Plaques over posterolateral pleura best visualized on oblique radiography
 - Calcified plaques over anterior or posterior pleura may exhibit foliate **holly leaf** morphology on frontal radiography
- Noncalcified plaques may exhibit smooth margins and form obtuse angles adjacent pleura: **Incomplete border sign**
 - Unable to differentiate from other pleural lesions
- May mimic parenchymal nodules
- Rarely extend over > 4 rib interspaces
- Associated findings
 - Unilateral or bilateral small pleural effusions
 - Earliest manifestation of asbestos-related pleural disease; precedes plaque formation
 - Most common manifestation during first 20 years after exposure
 - Rounded atelectasis
 - Rounded or ovoid peripheral subpleural mass
 - May mimic malignancy

CT Findings

- Much more sensitive than radiography for detecting pleural plaques
 - Easily detected when calcified and paravertebral or subjacent to ribs
 - Noncalcified pleural plaques may be overlooked when small &/or adjacent to intercostal muscle

- Bilateral, multifocal discontinuous nodular pleural thickening
 - Calcification in 10-15% of cases: Propensity to calcify increases with time from exposure
 - Size range: 2-5 mm to 10 cm
 - Thin layer of extrapleural fat
 - Typically affect pleura along central hemidiaphragms and adjacent to 6th-9th ribs
 - Coronal reformatted images extremely helpful in characterizing diaphragmatic pleural plaques
- Associated findings
 - o Small unilateral or bilateral pleural effusions
 - Rounded atelectasis in 10% of patients with asbestosrelated pleural disease
 - Round peripheral lung mass adjacent to pleural thickening/plaque with volume loss and swirling bronchovascular structures (comet-tail sign)
 - Atypical findings should prompt tissue sampling
 - Parenchymal bands, subpleural reticulation, bronchiectasis, honeycomb lung with apical-basilar gradient often indicate asbestosis
 - Diffuse pleural thickening
 - ~ 20% of asbestos-exposed workers
 - Can occur in conjunction with plaques or independently
 - Visceral pleura and costophrenic angles
 - Pleural thickening affecting > 25% of pleural surface
 □ > 3-mm thickness, > 5 cm in lateral dimension, spanning > 8 cm in craniocaudal dimension

MR Findings

- Plaques have variable signal intensity on T1WI and T2WI
 Calcification can result in susceptibility artifact
- May be incidentally detected on MR performed for other reasons, such as thoracic spine MR

Ultrasonographic Findings

- Grayscale ultrasound
 - Differentiation of pleural fluid from pleural plaque
 - Image-guided biopsy of suspicious pleural nodules/masses or atypical pleural plaques
- Soft tissue pleural nodules; may exhibit intrinsic calcification

Imaging Recommendations

- Best imaging tool
 - CT significantly more sensitive than radiography in detecting and characterizing pleural plaques
 - Coronal and sagittal reformatted images help characterize diaphragmatic plaques
- Protocol advice
 - Intravenous contrast helps characterize pleural lesions, particularly if associated with pleural fluid

DIFFERENTIAL DIAGNOSIS

Chest Wall Trauma

- Pleural thickening ± calcification adjacent to rib fractures
- Often lateral or posterior chest wall, unilateral
- Diaphragmatic pleura usually spared unless associated with hemothorax

Pleural Fibrosis and Fibrothorax

- Chronic pleural thickening following trauma or infectious parapneumonic effusion/empyema
- Usually unilateral diffuse pleural thickening ± calcification
- Often associated with adjacent parenchymal scarring or bronchiectasis

Pleural Metastases

- Pleural invasion by primary lung or chest wall neoplasms
- Hematogenous metastases from breast, renal, gastrointestinal, ovarian, thyroid, and prostate cancers
- High-risk thymomas may produce drop pleural metastases

Primary Pleural Neoplasms

- Malignant pleural mesothelioma
 - Circumferential nodular pleural thickening; fissural and mediastinal pleural involvement
 - Associated pleural effusion and ipsilateral volume loss
 - Calcification can occur; typically focal rather than diffuse
 - Patients usually symptomatic
- Localized fibrous tumor of pleura
 - Well-circumscribed focal soft tissue pleural mass; may be pedunculated and mobile
 - Large lesions typically symptomatic
 - Small lesions often incidental

Talc Pleurodesis

- Therapeutic obliteration of pleural space for recurrent pleural effusion or pneumothorax
- High-attenuation pleural nodules/thickening interposed between thick visceral and parietal pleurae
- Posteriorly, along basilar pleural surfaces or within interlobar fissures

Extrapleural Fat

- Symmetric bilateral mid thoracic pleural thickening
 Lateral pleural thickening on frontal radiography
 - CT demonstration of fat attenuation is diagnostic

PATHOLOGY

General Features

- Etiology
 - Occupational asbestos exposure: 20-30 years after exposure
 - Postulated mechanism: Asbestos fiber deposition in alveoli, subsequent interstitial and transpleural migration, resultant pleural inflammation and plaque formation
 - Asbestos fiber dimension and composition influence fibrogenicity and carcinogenicity
 - □ Chrysotile fibers: More easily cleared
 - Amphibole (amosite, crocidolite, tremolite) fibers:
 More durable, penetrate deeper into lung
 - Concurrent exposure to other noxious substances (cigarette smoking) play additive role in fibrogenicity and carcinogenicity
- Associated abnormalities
 - Pleural effusion
 - Earliest manifestation of asbestos-related pleural disease; > 10 years before pleural plaques

Gross Pathologic & Surgical Features

- Opalescent well-defined foci of firm fibrous tissue involving parietal pleura
- Not premalignant

Microscopic Features

- Dense acellular collagen in characteristic basket weave pattern
- Dystrophic calcification
- No evidence of malignant degeneration

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Asymptomatic patients; incidental finding

Demographics

- Epidemiology
 - Highest incidence in patients with occupational exposure to asbestos (50-60%)
 - Incidence increases with intensity and duration of exposure

Natural History & Prognosis

- Plaques do not confer increased risk of lung cancer nor are they premalignant
 - Asbestos exposure is risk factor for lung cancer, mesothelioma, and asbestosis
- Plaques commonly enlarge or coalesce over time
- Dystrophic calcification develops over time
 - Calcification seldom present in workers with exposure interval < 30 years prior
- Diffuse pleural thickening may result in restrictive lung disease

Treatment

• Supportive

DIAGNOSTIC CHECKLIST

Consider

- Asbestos-related pleural disease is most common etiology of pleural plaques
- Other lesions may produce multifocal pleural calcification; clinical history helps suggest alternate diagnoses

Image Interpretation Pearls

 Calcified pleural plaques in bilateral central hemidiaphragmatic pleura are diagnostic of asbestosrelated pleural disease

Reporting Tips

- Radiographic evidence of characteristic pleural plaques may be first sign of occupational asbestos exposure
 - Exposure history sometimes unknown or forgotten in asymptomatic patients given prolonged latency
- Occupational asbestos exposure: Well-established risk factor for developing lung cancer, CT may help detect early malignancy

SELECTED REFERENCES

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Pleural Plaques





(Left) PA chest radiograph of a patient with a history of occupational asbestos exposure shows sharply marginated pleural plagues that exhibit the characteristic holly leaf morphology 🖂 As with other pleural abnormalities, plaques exhibit the incomplete border sign on radiography 🛃. (Right) Graphic shows the typical distribution of pleural plaques involving the parietal pleura over the central tendinous portions of the hemidiaphragms, the paravertebral regions, and the undersurfaces of ribs.





(Left) Axial CECT of a patient with a history of asbestos exposure shows calcified pleural plaques involving the central tendinous portions of the hemidiaphragms ⊇ and right basilar pleural thickening ⊇. (Right) Axial CECT of a patient with a history of occupational asbestos exposure and bilateral calcified pleural plaques ⊇ shows bilateral subpleural reticulation ⊇, indicative of fibrosis related to asbestosis.





(Left) Axial CECT shows diffuse right pleural thickening , calcified pleural plaques ₽, and a right lower lobe subpleural mass \implies that exhibits the characteristic comet-tail swirling of bronchovascular structures typical of rounded atelectasis. (Right) Axial NECT of a patient with prior asbestos exposure shows diffuse bilateral pleural thickening \blacksquare and small pleural effusions 🔁. Bilateral parenchymal subpleural masslike lesions \supseteq with swirled bronchovascular structures are consistent with multifocal rounded atelectasis.

KEY FACTS

TERMINOLOGY

- Synonyms
 - Pleural fibrosis
 - o Fibrothorax
- Definition
 - Visceral and parietal pleural thickening and calcification with resultant volume loss

IMAGING

- Radiography
 - Dense circumferential pleural calcification
 - o Ipsilateral volume loss and mediastinal shift
 - o Narrow ipsilateral intercostal spaces
- CT
 - Continuous pleural thickening ± coarse calcification
 - Small volume pleural fluid between thick/calcified pleural surfaces
 - o Ipsilateral volume loss and narrow intercostal spaces
 - Hypertrophy of adjacent extrapleural fat

TOP DIFFERENTIAL DIAGNOSES

- Pleural metastases
- Asbestos-related pleural disease
- Malignant pleural mesothelioma

PATHOLOGY

- Etiology
 - o Infection
 - Hemothorax
 - o latrogenic

CLINICAL ISSUES

- Signs/symptoms
 - o Most asymptomatic; incidental finding
 - Dyspnea, dyspnea on exertion
 - Restrictive lung disease
- Treatment
 - Decortication in carefully selected symptomatic patients
 - o Fluid aspiration ineffective; no lung reexpansion

(Left) PA chest radiograph of a man who developed a leftsided fibrothorax following median sternotomy for coronary artery bypass grafting shows asymmetric narrow left intercostal spaces ➡ and low left lung volume due to restrictive left basilar pleural fibrosis and calcification 🔁. (Right) Axial CECT (bone window) of the same patient shows a thin rind of left-sided pleural fibrosis that manifests with coarse curvilinear calcification 🛃 and spares the mediastinal pleura. Note associated low left lung volume.





(Left) Axial CECT of a patient with prior tuberculous empyema shows right hemithorax volume loss as depicted by narrow right intercostal spaces \square and densely calcified visceral 🔁 and parietal \blacksquare pleural surfaces separated by a small volume of pleural fluid. Note associated pericardial calcification 🛃. (Right) Axial NECT of a patient with prior traumatic hemothorax shows unilateral, discontinuous right pleural calcification \blacksquare and adjacent hypertrophy of extrapleural fat 🖂





980

Synonyms

- Pleural fibrosis
- Fibrothorax

Definitions

• Abnormal pleural **thickening** and **calcification** with resultant **volume loss**

IMAGING

General Features

- Best diagnostic clue
 - Unilateral pleural thickening ± calcification with associated volume loss, mediastinal shift, and narrow intercostal spaces
- Location
 - Typically unilateral; may be bilateral
 - Often involves entire hemithorax; may be focal

Radiographic Findings

- Circumferential pleural thickening ± calcification
- Ipsilateral volume loss and mediastinal shift
- Ipsilateral narrow intercostal spaces

CT Findings

- Continuous pleural thickening ± coarse calcification
 - Typically **spares mediastinal pleura**
 - Often affects > 25% of pleural surface area
- Pleural fluid between calcified pleural surfaces common
 Variable attenuation; fluid, soft tissue
- Ipsilateral pulmonary volume loss
- Expansion/proliferation of adjacent **extrapleural fat**

Imaging Recommendations

- Best imaging tool
 - CT: Imaging modality of choice for assessment of the pleura and the adjacent lung
- Protocol advice
 - Intravenous contrast useful for excluding malignant enhancing soft tissue nodules

DIFFERENTIAL DIAGNOSIS

Pleural Metastases

- Nodular pleural thickening; can be circumferential
 Mediastinal pleural involvement helps differentiate malignant from benign etiology
- Pleural effusions common
- Calcification may occur: Osteosarcoma, mucinous adenocarcinoma

Asbestos-Related Pleural Disease

- Diffuse pleural thickening
 - Continuous pleural thickening involves costophrenic angles
 - Typically bilateral; can be asymmetric or unilateral
- Pleural plaque
 Dilatosal discontis
 - Bilateral discontinuous multifocal nodular pleural thickening; often with calcification
 - Parietal pleural involvement; typically spares apices and costophrenic angles

Malignant Pleural Mesothelioma

- Circumferential nodular pleural thickening
 - Preferential involvement of basilar pleura; may involve mediastinal pleura
- ± calcified pleural plaques, but not directly associated

PATHOLOGY

General Features

- Etiology
 - Infection: Bacterial empyema
 - Tuberculosis: Most common etiology
 - Hemothorax
 - Trauma: Penetrating or blunt injury
 - latrogenic
 - Typically after coronary artery bypass graft surgery; hemothorax
 - Talc pleurodesis; exaggerated fibrotic response to therapeutic pleural space obliteration
 - Immunologic disorders
 - Rheumatoid arthritis: Up to 50% of affected patients have pleural changes at autopsy
 - Systemic lupus erythematosus
 - Uremic pleuritis
 - May occur after years of hemodialysis
 - Drug reaction
 - Tyrosine kinase inhibitors: Immune-mediated complication in chronic myelogenous leukemia
 - Ergot derivatives, bromocriptine, cyclophosphamide
- Pathogenesis
 - Mesothelial cell release of inflammatory mediators (cytokines and growth factors)
 - o Disordered fibrin turnover and subsequent fibrosis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Most are **asymptomatic**; incidental finding
 - o Dyspnea, dyspnea on exertion
 - Restrictive lung disease

Natural History & Prognosis

- Chronic and non-progressive
- Not associated with malignant transformation

Treatment

- Decortication in carefully selected symptomatic patients
- Fluid aspiration ineffective: "Trapped lung" does not reexpand

DIAGNOSTIC CHECKLIST

Consider

• Fibrothorax in patients with unilateral diffuse pleural thickening ± calcification and ipsilateral volume loss

- Adrianza AM et al: Tyrosine kinase inhibitor-associated fibrothorax. Am J Respir Crit Care Med. 199(11):1432, 2019
- Hallifax RJ et al: State-of-the-art: radiological investigation of pleural disease. Respir Med. 124:88-99, 2017

Malignant Pleural Effusion

KEY FACTS

TERMINOLOGY

- Malignant pleural effusion (MPE)
- Exudate; neoplastic cells from pleural malignancy
- IMAGING

• Radiography

- Unilateral or bilateral MPE
- Variable size of pleural effusion
 - Small: Blunt costophrenic angle
 - Moderate: Obscured hemidiaphragm
 - Moderate to large: Opaque mid to inferior hemithorax
 - Massive: Opaque hemithorax
- Pleural effusion + smooth or nodular pleural thickening
- CT
 - Identification of pleural thickening/nodularity
 - Assessment of adjacent structures
- PET/CT
 - FDG avid pleura, pleural thickening/nodules

TOP DIFFERENTIAL DIAGNOSES

- Transudative pleural effusion
- Exudative pleural effusion
- Empyema

PATHOLOGY

- Metastatic lung and breast cancer: 50-65% of MPEs
- Lymphoma, gynecological malignancy, mesothelioma
- Diagnosis: Malignant cells in pleural fluid/tissue

CLINICAL ISSUES

- Mean age at presentation: 65 years
- Dyspnea, chest pain, constitutional symptoms
- Poor prognosis
- Palliative fluid drainage for symptom relief

DIAGNOSTIC CHECKLIST

• Consider MPE in patient with massive pleural effusion or pleural effusion with associated thickening/nodularity

(Left) PA chest radiograph of a 58-year-old woman with stage IV primary lung adenocarcinoma who presented with dyspnea shows a massive malignant right pleural effusion that manifests with an opaque right hemothorax. Note mediastinal shift to the left. (Right) PA chest radiograph of a 57-yearold woman with primary breast cancer shows a large right pleural effusion and associated pleural thickening, consistent with malignant pleural effusion secondary to stage IV breast cancer.





(Left) Axial CECT of the same patient shows a large right pleural effusion and enhancing right parietal pleural nodules $\overline{\square}$, consistent with solid pleural metastases. The imaging features are virtually diagnostic of malignant pleural disease. (Right) Graphic shows typical features of malignant pleural effusion. These are exudative pleural effusions of variable size. Identification of pleural nodularity 🔁 on imaging is consistent with malignant pleural effusion and solid pleural metastases.





Abbreviations

• Malignant pleural effusion (MPE)

Definitions

- Exudate; neoplastic cells from pleural malignancy
- Paramalignant effusion: Pleural effusion in malignancy

IMAGING

General Features

- Best diagnostic clue
- Pleural effusion with nodular pleural thickeningLocation
 - o Unilateral or bilateral

Radiographic Findings

- Small pleural effusion: Blunt costophrenic angle
- Moderate pleural effusion: Obscured hemidiaphragm
- Moderate to large pleural effusion: Opaque mid to inferior hemithorax; frequent ipsilateral relaxation atelectasis
- **Massive** pleural effusion: Opaque hemithorax; MPE is most common cause
- Pleural effusion + smooth or nodular pleural thickening

CT Findings

- High sensitivity for detection of pleural fluid • Variable size; free or loculated
- Fluid attenuation not reliable indicator of malignancy
- Direct visualization of parietal and visceral pleura
- CECT
 - Increased sensitivity for identification of pleural thickening/nodularity
 - Assessment of adjacent structures
 - Atelectasis, nodule, mass
 - Lymphadenopathy, metastases

MR Findings

• Identification of pleural fluid, thickening, nodules

Ultrasonographic Findings

- High sensitivity for detection of pleural fluid, pleural thickening/nodularity
- Guidance for diagnostic/therapeutic thoracentesis

Nuclear Medicine Findings

- PET/CT
 - Documentation of FDG-avid pleural thickening, nodules, &/or masses in malignant pleural effusion

Imaging Recommendations

- Best imaging tool
 - CECT for detection of pleural thickening and nodularity

DIFFERENTIAL DIAGNOSIS

Transudative Pleural Effusion

- May be indistinguishable from MPE
- Associated with heart failure and interstitial edema

Exudative Pleural Effusion

- Malignancy, infection, pulmonary infarction
- May be associated with pleural thickening

Empyema

- Signs and symptoms of infection
- Unilateral, loculated pleural effusion ± bronchopleural fistula or empyema necessitatis

PATHOLOGY

General Features

- Metastatic lung and breast cancer: 50-65% of MPEs
- Other: Lymphoma, gynecological malignancy, malignant mesothelioma
- Diagnosis
 - Fluid cytology: 46-49% sensitivity; 100% specificity
 - Ultrasound-guided biopsy: 61-90% sensitivity; 100% specificity
 - o CT-guided biopsy: 77-87% sensitivity; 100% specificity
 - o Medical/surgical thoracoscopy: 89-95% sensitivity; 100% specificity

Gross Pathologic & Surgical Features

- Hemorrhagic pleural fluid; exudate
- Pleural thickening or nodularity

Microscopic Features

- Exfoliated malignant cells in pleural fluid
- Demonstration of malignant cells in pleural tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dyspnea, chest pain, constitutional symptoms
 - Asymptomatic 15-25%

Demographics

• Mean age at presentation: 65 years

Natural History & Prognosis

• Poor prognosis; median survival of 3-12 months

Treatment

- Expectant management: Asymptomatic patients
- Therapeutic thoracentesis; may be repeated
- Chemical pleurodesis
- Indwelling tunneled pleural catheter: MPE with trapped lung or failed pleurodesis

DIAGNOSTIC CHECKLIST

Consider

 MPE in patient with massive pleural effusion or pleural effusion with associated thickening/nodularity

Image Interpretation Pearls

- 10% of MPEs are massive
 - o 70% of massive pleural effusions are malignant

- Jany B et al: Pleural effusion in adults-etiology, diagnosis, and treatment. Dtsch Arztebl Int. 116(21):377-86, 2019
- Kaul V et al: Contemporary approach to the diagnosis of malignant pleural effusion. Ann Am Thorac Soc. 16(9):1099-106, 2019
- Asciak R et al: Malignant pleural effusion: from diagnostics to therapeutics. Clin Chest Med. 39(1):181-93, 2018

KEY FACTS

TERMINOLOGY

• Definition: Secondary pleural malignancy; thickening, nodules, masses

IMAGING

- Radiography
 - Focal or multifocal pleural thickening/nodules/masses
 - Frequent pleural effusion; may obscure solid metastases
- CT
 - Pleural thickening, nodules &/or masses
 - Features of malignant pleural thickening: Circumferential (may involve fissures), nodular, thickness > 1 cm, mediastinal pleural involvement
 - Frequent associated pleural effusion
 - CT may underestimate extent of disease
- MR: Enhancing pleural thickening/nodules/masses
 - Diffusion-weighted imaging; identification of malignant pleural disease
- PET/CT: FDG-avid pleural fluid, nodules, masses

TOP DIFFERENTIAL DIAGNOSES

- Malignant pleural mesothelioma
- Localized fibrous tumor of pleura
- Pleural fibrosis and fibrothorax
- Asbestos-related pleural fibrosis

PATHOLOGY

- Metastases are most common pleural malignancy
- Visceral pleura more commonly involved than parietal
- Lung cancer, breast cancer, lymphoma, invasive thymoma

CLINICAL ISSUES

- Signs/symptoms: Dyspnea, chest pain, constitutional
- Poor prognosis; median survival of 3-12 months
- Treatment: Periodic thoracenteses, talc pleurodesis

DIAGNOSTIC CHECKLIST

• Nodular pleural thickening in association with pleural effusion is highly concerning for malignant pleural disease

(Left) Coronal CECT of a patient with metastatic lung cancer shows multiple enhancing pleural metastases and a right pleural effusion. Malignant pleural thickening is often > 1 cm in thickness, and involvement of mediastinal pleura is characteristic. (Right) Axial FDG PET/CT of a patient with stage IV breast cancer shows a large right pleural effusion and FDG-avid circumferential solid pleural metastases. Solid metastases associated with pleural effusion are virtually diagnostic of malignant pleural disease.





(Left) Composite image with PA chest radiograph (left) and axial CECT (right) shows metastatic renal cell cancer that manifests with circumferential right nodular pleural thickening that is > 1cm thick and involves the mediastinal pleura, consistent with malignant pleural disease. (Right) Axial CECT of a patient with metastatic melanoma shows marked circumferential right pleural thickening by large lobulated heterogeneous solid pleural metastases that produce mass effect on the mediastinum.





Definitions

- Secondary pleural malignancy; thickening, nodules, masses
- Most common etiology of malignant pleural thickening

IMAGING

General Features

Best diagnostic clue
 Focal or multifocal pleural nodules/masses

Radiographic Findings

- Focal or multifocal pleural thickening/nodules/masses
- Frequent pleural effusion; may obscure solid metastases

CT Findings

- Pleural thickening, nodules &/or masses
 - o Focal or multifocal; unilateral or bilateralo May exhibit contrast enhancement
- Features of malignant pleural thickening: Circumferential (may involve fissures), nodular, thickness > 1 cm, mediastinal pleural involvement
- Frequent associated pleural effusion

MR Findings

- T1WI C+: Enhancing pleural thickening/nodules/masses
- Diffusion-weighted imaging; identification of malignant pleural disease

Nuclear Medicine Findings

• PET/CT

• FDG-avid malignant pleural fluid, nodules, masses

Imaging Recommendations

- Best imaging tool
 - Chest CT is imaging modality of choice
 - o MR and PET may show extent of involvement

DIFFERENTIAL DIAGNOSIS

Malignant Pleural Mesothelioma

- Most common primary pleural neoplasm
- May be indistinguishable from metastases

Localized Fibrous Tumor of Pleura

- Focal pleural nodule or mass
- Benign and malignant types indistinguishable on imaging

Pleural Fibrosis and Fibrothorax

- Fibrous obliteration of pleural space; usually unilateral
- Hemothorax, tuberculous empyema
- Spares mediastinal pleura; extensive calcification

Asbestos-Related Pleural Fibrosis

- Bilateral or unilateral
- May be indistinguishable from malignant pleural thickening

Pleurodesis

- High-attenuation pleural thickening
- FDG-avidity may mimic malignancy

Thoracic Splenosis

• Unilateral post traumatic pleural splenic implants

• Tc-99m sulfur colloid or Tc-99m-damaged erythrocyte scintigraphy

PATHOLOGY

General Features

- Etiology
 - Metastases are most common pleural malignancy
 - Mechanisms of pleural involvement: Hematogenous, direct invasion, lymphatic dissemination, drop pleural metastases
- Pleural metastatic disease from primary abdominal malignancies usually results from hepatic metastases
- Lung cancer, breast cancer, lymphoma, invasive thymoma

Staging, Grading, & Classification

• Pleural metastases represent stage IV disease

Gross Pathologic & Surgical Features

- Visceral pleura more commonly involved than parietal pleura
- Associated pleural effusion thought to be secondary to obstruction of pleural lymphatics by tumor
- Solid pleural metastases may only be visible at surgery

Microscopic Features

• Malignant tumor cells in pleural tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Dyspnea, chest pain, constitutional symptoms

Natural History & Prognosis

• Poor prognosis; median survival of 3-12 months

Treatment

- Expectant management of asymptomatic patients
- Drainage of associated pleural effusion, pleurodesis

DIAGNOSTIC CHECKLIST

Consider

- Video-assisted thoracoscopic surgery (VATS) enables visualization of pleural space, diagnosis of pleural abnormalities, and cytoreduction of metastases
- Pleurodesis may be performed at time of VATS
- Importance of preprocedural planning in multidisciplinary environment

Image Interpretation Pearls

- Visualization of nodular pleural thickening in association with pleural effusion is highly concerning for malignant pleural disease
- Pleural effusion in setting of malignancy should raise suspicion for pleural metastases even in absence of pleural thickening or nodularity
- CT may underestimate disease extent

- Hallifax RJ et al: State-of-the-art: radiological investigation of pleural disease. Respir Med. 124:88-99, 2017
- 2. Shroff GS et al: Imaging of metastases in the chest: mechanisms of spread and potential pitfalls. Semin Ultrasound CT MR. 38(6):594-603, 2017

KEY FACTS

TERMINOLOGY

Malignant pleural mesothelioma (MPM)
 Most common primary pleural neoplasm

IMAGING

• Radiography

- Pleural effusion
- Circumferential nodular pleural thickening
- Loss of volume of affected hemithorax
- CT
 - Pleural effusion
 - Nodular &/or lobulated pleural thickening
 - Loss of volume of affected hemithorax
 - o Chest wall, mediastinal, diaphragmatic invasion
 - o Mediastinal/thoracic lymphadenopathy
 - o Calcified pleural plaques in 25% of cases
- MR and FDG PET/CT more sensitive than CT for identification of local invasion
- FDG PET/CT for staging, restaging, and surveillance

TOP DIFFERENTIAL DIAGNOSES

- Solid pleural metastases
- Invasive thymoma
- Localized fibrous tumor of pleura
- Pleural fibrosis and fibrothorax
- Asbestos-related diffuse pleural thickening

PATHOLOGY

• Strong association with asbestos exposure

CLINICAL ISSUES

- Predominantly men (85-90%); 50-70 years of age
- Symptoms: Nonpleuritic chest wall pain, dyspnea
- Prognosis: Mean survival time is 12 months

DIAGNOSTIC CHECKLIST

• Consider MPM in differential diagnosis of symptomatic patients with unilateral circumferential nodular pleural thickening

(Left) Graphic shows the morphologic features of malignant pleural mesothelioma, including circumferential nodular pleural thickening that involves the fissures 🔁, the mediastinal pleura 乏, and the diaphragmatic pleura 🛃 with encasement of the affected hemithorax. (Right) Coronal CECT of a patient with mesothelioma demonstrates a multiloculated right pleural effusion and extensive right pleural thickening and nodularity 🔁. Note involvement of the mediastinal pleura.





(Left) Axial CECT of a patient with persistent right pleuritic chest pain demonstrates a large right pleural effusion but no evidence of pleural thickening or nodularity. Subsequent thoracentesis revealed the presence of malignant cells consistent with malignant pleural mesothelioma. (Right) Axial CECT of a patient previously treated for left malignant pleural mesothelioma shows a new left pleural mass \supseteq that directly invades the adjacent left chest wall 🖂, consistent with tumor recurrence.





Abbreviations

• Malignant pleural mesothelioma (MPM)

Definitions

- Most common primary pleural neoplasm
- Strong association with **asbestos exposure**: Long latency period between exposure and MPM

IMAGING

General Features

- Best diagnostic clue
 - Pleural effusion ± circumferential nodular pleural thickening
- Location
 - Parietal > visceral pleura; basilar pleura

Radiographic Findings

- Radiography
 - o Pleural effusion: Unilateral > bilateral
 - $\circ \ {\rm Circumferential} \ {\rm nodular} \ {\rm pleural} \ {\rm thickening}$
 - Fissural pleural thickening
 - Loss of volume of affected hemithorax
 - o Evidence of asbestos-related pleural disease

CT Findings

- Pleural effusion
- Nodular &/or lobulated pleural thickening: Circumferential;
 > 1 cm thick
- Loss of volume of affected hemithorax
- Chest wall, mediastinal, diaphragmatic invasion
- Mediastinal/thoracic lymphadenopathy
- Calcified pleural plaques in 25% of cases

MR Findings

- T1WI
 - Hyperintense to muscle
- T2WI
 - Isointense or hyperintense to muscle
- T1WIC+
- Tumor enhances with gadolinium
- MR is more sensitive than CT for detection of local invasion

Nuclear Medicine Findings

- PET/CT
 - Intense FDG uptake within tumor and metastases
 - o Sensitive for detection of local invasion and metastases

Imaging Recommendations

- Best imaging tool
 - o CT is optimal modality for evaluating extent of disease
 - MR and FDG PET/CT more sensitive than CT for evaluation of chest wall, mediastinum, and diaphragm invasion
 - FDG PET/CT for staging, restaging, and surveillance

DIFFERENTIAL DIAGNOSIS

Solid Pleural Metastases

- May be indistinguishable from MPM
- Lower association with pleural effusion

• Involvement of visceral pleura more common

Invasive Thymoma

- Prevascular mediastinal mass
- Drop pleural metastases; multifocal pleural nodules, circumferential pleural thickening

Localized Fibrous Tumor of Pleura

- Small lesions: Homogeneous, obtuse margins
- Large lesions: Heterogeneous, acute margins

Pleural Fibrosis and Fibrothorax

- Fibrous obliteration of pleural space
- Hemorrhagic and tuberculous effusions, empyema
- Mediastinal pleura spared in 88%
- May demonstrate extensive calcification

Asbestos-Related Diffuse Pleural Thickening

- Bilateral pleural thickening involving 25% of chest
- Unilateral thickening involving 50% of chest
- Pleural thickening > 5 mm at any site

Pleurodesis

- Thickening of parietal and visceral pleura
- Hyperattenuation on CT due to talc deposition
- FDG-avid

PATHOLOGY

General Features

- Etiology
 - Strong association with **asbestos exposure**
 - Carcinogenicity of asbestos fibers proportional to aspect ratio (length:width) and durability in tissue
 - Higher aspect ratio, greater tumorigenicity
 - $\circ \ \ \uparrow \ risk$ of MPM with exposure duration and intensity

Staging, Grading, & Classification

- TNM Staging
 - IA: T1 N0 M0
 - o IB: T2-T3 N0 M0
 - o II: T1-T2 N1 M0
 - o IIIA: T3 N1 M0
 - o IIIB: T1-T3 N2 M0, T4 N0-2 M0
 - o IV: Any T4, Any N, M1

Gross Pathologic & Surgical Features

- Parietal pleura > visceral pleura
- Right hemithorax > left hemithorax
- Coalescence into sheet-like or confluent pleural masses
- Pleural effusion in 60% at diagnosis
- Metastases in > 50% at autopsy
- Asbestos-related pleural plaques; not premalignant

Microscopic Features

- Difficult differentiation between mesothelioma, metastatic adenocarcinoma, asbestos-related pleural fibrosis, and reactive pleural hyperplasia
- MPM: Greater nuclear atypia than adenocarcinoma
- Diagnostic yield of pleural fluid cytology is low; imageguided and surgical biopsies preferred
 - Image-guided core biopsy: Sensitivity (86%), needle track seeding (4%)

8th International Association for the Study of Lung Cancer TNM Staging for Malignant Pleural Mesothelioma

TNM Definitions Т ТΧ Primary tumor cannot be assessed Т0 No evidence of primary tumor T1 Tumor limited to ipsilateral parietal &/or visceral pleura Т2 Tumor involving ipsilateral pleura (parietal or visceral) and involvement of at least one of following: Diaphragm Extension into lung Т3 Locally advanced, potentially resectable tumor involving all ipsilateral pleura (parietal and visceral) and involvement of at least one of following: Endothoracic fascia Mediastinal fat/chest wall soft tissues Pericardium Τ4 Locally advanced unresectable tumor involving ipsilateral pleura (parietal and visceral) and at least one of following: Chest wall (multifocal masses ± rib destruction) Peritoneum (via direct transdiaphragmatic extension) Contralateral pleura, mediastinal organs, or spine Pericardium (transmural invasion ± pericardial effusion) or myocardium Ν NX Regional lymph nodes cannot be assessed N0 No regional lymph node metastases Metastases to ipsilateral intrathoracic lymph nodes (bronchopulmonary, hilar, mediastinal) N1 N2 Metastases to contralateral mediastinal, ipsilateral or contralateral supraclavicular lymph nodes М MO No distant metastasis M1 Distant metastases

- Thoracoscopy/thoracotomy and biopsy: Sensitivity (94% and 100%); needle track seeding (22% combined)
- 3 histologic categories
 - Epithelioid (55-65%)
 - Uniform cuboidal cells with eosinophilic cytoplasm, central nuclei, and distinct nucleoli
 - Difficult to distinguish from lung adenocarcinoma and adenocarcinoma metastases
 - Sarcomatoid (10-15%)
 - Spindle cells with nuclear atypia
 - Difficult to distinguish from true sarcoma
 - Biphasic (20-35%)
 - Elements of epithelioid and sarcomatoid cell types
 - Intermediate transitional areas common
- Asbestos body: Hallmark of asbestos exposure

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Nonpleuritic chest wall pain, dyspnea
- Other signs/symptoms
 - Weakness, fatigue, cough, weight loss; less common
 - Dullness to percussion and decreased breath sounds

Demographics

- Age
 - o 50-70 years

- Sex
 - Predominantly men (85-90%)
- Epidemiology
 - o 80% of patients with MPM had asbestos exposure
 - o 10% of patients exposed to asbestos develop MPM

Natural History & Prognosis

- Mean survival time: 12 months
- Longer survival: Disease limited to parietal pleura
- Reduced survival: Thoracic lymph node and distant metastases, advanced pleural involvement

Treatment

- Palliative pleurectomy to relieve chest wall pain
- Pleurectomy or pleurodesis for recurrent effusion
- Curative extrapleural pneumonectomy in absence of lymph node and distant metastases
- Prolonged survival with combination of surgery, chemotherapy, and radiation therapy

DIAGNOSTIC CHECKLIST

Consider

• MPM in differential diagnosis of patients with unilateral circumferential nodular pleural thickening

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(Left) Fused axial FDG PET/CT of a patient with malignant pleural mesothelioma demonstrates extensive FDGavid nodular right pleural thickening that involves the mediastinal pleura \square and encases the right lung. (Right) Whole-body FDG PET of a patient with newly-diagnosed . malignant pleural mesothelioma shows extensive FDG-avid tumor in the right hemithorax that extends into the upper abdomen ⊇. FDG PET/CT is the imaging modality of choice for mesothelioma staging, restaging, and surveillance.





(Left) Axial fused FDG PET/CT of a patient with mesothelioma shows FDG-avid tumor 🔁 abutting the liver and invading the right hemidiaphragm ₽ and FDGavid metastases \implies in the liver. PET/CT can differentiate between benign and malignant pleural disease with a sensitivity of 96.8% and a specificity of 88.5%. (Right) Fused axial FDG PET/CT of a patient with malignant pleural mesothelioma shows FDG avid pleural thickening in the right hemithorax and direct focal invasion of the adjacent right chest wall 🛃.





(Left) Axial fused FDG PET/CT of a patient with a persistent right pleural effusion that represented malignant pleural mesothelioma treated with talc pleurodesis shows FDGavid linear pleural thickening Axial NECT of the same patient demonstrates regions of high attenuation \supseteq within the pleural thickening that represented talc deposition. Sequela of talc pleurodesis should not be misinterpreted as residual/recurrent malignancy on FDG PET/CT.
•

TERMINOLOGY

• Localized fibrous tumor of pleura (LFTP)

IMAGING

- Radiography
 - Pleural nodule or mass; variable size
 - Abuts pleura; incomplete border sign
- CT
 - Well-defined lobulated contours
 - Heterogeneous peripheral mass without local invasion or lymphadenopathy
 - Low-attenuation foci: Cystic change, hemorrhage, necrosis
- MR
 - Exclusion of local invasion
 - Heterogeneous signal on T1WI and T2WI
 - o Low signal on T2WI: Fibrous septa, tumor capsule
 - High signal on T2WI: Cystic change, hemorrhage, necrosis

PATHOLOGY

- Origin from submesothelial connective tissue
- Most arise from visceral pleura
- Often pedunculated (50%)
- Lobular mass with whorled fibrous appearance
- Low-grade neoplasm; variable histologic appearance

CLINICAL ISSUES

- Wide age range; 6th and 7th decades of life
- Asymptomatic in up to 50% of affected patients
 - Large LFTP typically symptomatic
 - Cough, dyspnea, chest pain/discomfort
 - Systemic complaints
 - Paraneoplastic syndromes
- Therapy and prognosis
 - Complete excision is typically curative
 - Favorable prognosis
 - Long-term imaging follow-up recommended

(Left) PA chest radiograph of an asymptomatic 65-year-old woman with an incidentally discovered localized fibrous tumor shows a left-sided peripheral elongate soft tissue mass that exhibits the incomplete border sign with a sharply marginated medial border 🔁 and an ill-defined lateral border ⊇, consistent with its extrapulmonary location. (Right) Axial CECT of the same patient shows a homogeneously enhancing left pleural soft tissue mass that forms obtuse angles \bowtie with the adjacent pleura.





(Left) Axial FDG PET/CT of the same patient shows characteristic absence of FDG avidity in the tumor and FDG uptake similar to that of blood pool. (Right) Graphic shows the gross features of localized fibrous tumor. The mass is attached to the visceral pleura by a pedicle \implies and exhibits a whorled, nodular appearance and foci of necrosis on cut section. Obtuse angles with the adjacent pleura 🖂 are characteristic, but large lesions often form acute angles D with the adjacent pleura on cross-sectional imaging.





Abbreviations

• Localized fibrous tumor of pleura (LFTP)

Synonyms

- Solitary fibrous tumor of pleura (SFTP)
 - Term "solitary" inaccurate; multifocal lesions rarely reported

Definitions

- 2nd most common primary pleural neoplasm
- < 5% of pleural neoplasms
- Neoplasms of similar histology reported in lung, mediastinum, pericardium, breast, other organs/locations
- Term "localized mesothelioma" inaccurate
 LFTP originates in submesothelial tissues
- Term "benign fibrous tumor" inaccurate
 10-15% of LFTP are malignant

IMAGING

General Features

- Best diagnostic clue
 - Peripheral soft tissue nodule/mass; incomplete border sign
 - Fissural soft tissue nodule/mass without associated pleural effusion
 - Positional change in lesion shape/location; implies presence of pedicle
 - Large intrathoracic mass without local invasion or lymphadenopathy
 - No chest wall involvement
- Location
 - Abuts pleura
 - Predilection for mid/inferior hemithorax
- Size
 - Variable size; slow growth

Radiographic Findings

- Small LFTP
 - Well-defined peripheral nodule or mass
 - Abuts pleura
 - May exhibit incomplete border sign
 - May exhibit fissural location
- Large LFTP
 - Pleural location may not be evident; may mimic pulmonary or mediastinal mass
 - Mass effect on adjacent structures
 - May occupy entire hemithorax
- Pedunculated LFTP may exhibit positional changes
- Predilection for mid and inferior hemithorax
 May mimic diaphragmatic elevation/eventration

CT Findings

- Soft tissue nodule or mass (rarely multicentric)
 - Variable size, well-defined lobulated contours
 - o Whorled fibrous cross-sectional appearance
 - Low attenuation: Cystic change, hemorrhage, necrosis
 - Calcification (up to 26%): Punctate, linear, coarse
 - Mass effect without local invasion
 - Rare visualization of tumor pedicle

- Although obtuse angles with adjacent pleura are considered typical, acute angles are more frequent
 - Smoothly tapered margin with adjacent pleura
 - Obtuse angles often seen with small LFTP
 - Acute angles often seen with large LFTP
- Ipsilateral pleural effusion in 25%; more common in malignant LFTP
- Rarely adjacent focal skeletal sclerosis
- NECT
 - Small lesions often exhibit homogeneous attenuation
 - Large/malignant LFTP often exhibit heterogeneous
 - attenuation
- CECT
 - Small lesions may enhance homogeneously
 - Heterogeneous enhancement is typical
 - Increased conspicuity of heterogeneity and lowattenuation areas
 - Geographic, rounded, or linear
 - More frequent in malignant LFTP
 - Cystic change, hemorrhage, necrosis, myxoid degeneration
 - Visualization of enhancing intratumoral vessels
 - 3D CT angiography; evaluation of vascular supply

MR Findings

- Documentation of intrathoracic location of juxtadiaphragmatic LFTP
- Exclusion of local invasion (diaphragm, chest wall)
- Heterogeneous signal intensity on T1WI and T2WI
 - Intermediate signal intensity in T1WI
 - Heterogeneous low signal intensity on T2WI: Hypocellular fibrous tissue with abundant collagen
 - Increase in signal on T2WI compared to T1WI
- High signal intensity on T2WI: Cystic change, hemorrhage, necrosis, myxoid degeneration, hypercellular areas
- Heterogeneous contrast enhancement

FDG PET/CT

- Not FDG-avid; FDG avidity suggests alternate diagnosis
- Differentiation of LFTP from other malignant pleural neoplasms

Angiographic Findings

- Preoperative angiography to identify vascular supply from aorta, internal mammary, phrenic, or bronchial arteries
- Preoperative embolization may be of value for large LFTP

Imaging Recommendations

- Best imaging tool
 - CECT considered imaging study of choice
 - Multiplanar MR for exclusion of local invasion
- Protocol advice
 - Prone imaging may document tumor mobility and presence of pedicle
 - CECT for evaluation of extent of central necrosis and vascular supply

DIFFERENTIAL DIAGNOSIS

Chest Wall Lipoma

- Peripheral nodule/mass with incomplete border sign
- CT/MR diagnostic: Fat attenuation/signal

Pleural Metastasis

- Rarely solitary pleural nodule or mass
- Solid pleural nodules/masses, pleural effusion, both

Chest Wall Metastasis

- Peripheral nodule/mass with incomplete border sign
- Skeletal destruction &/or soft tissue involvement

Thymoma

- Prevascular mediastinal location
- Mediastinal pleura LFT may mimic thymoma

Neurogenic Neoplasm

- Paravertebral nodule/mass with benign pressure erosion of adjacent ribs/vertebrae
- Paravertebral LFT may mimic neurogenic neoplasm

Lung Cancer

- Peripheral lung cancer may mimic LFTP
- Local invasion, lymphadenopathy, metastases

PATHOLOGY

General Features

- Etiology
 - o Unknown
 - No association with exposure to asbestos, cigarette smoke, or other carcinogens

Gross Pathologic & Surgical Features

- Well-marginated lobulated soft tissue mass
- Variable size; range: 1-39 cm
- Typically arises from visceral pleura
- Frequent fibrovascular pedicle (up to 50%)
- Grayish-white whorled or nodular cut surface
- Necrosis, hemorrhage, cystic degeneration; typically in large or malignant LFTP

Microscopic Features

- Origin in submesothelial connective tissue
- Low-grade neoplasm; variable histologic appearance
 Ovoid or spindle-shaped cells, round to oval nuclei
 - Faint cytoplasm, indistinct cell borders
 - Variable amounts of collagen
- Haphazardly arranged tumor cells (patternless pattern)
- Hypercellular zones with large staghorn-like vessels (hemangiopericytoma pattern)
- Criteria for malignancy
 - High cellularity
 - o Pleomorphism
 - o > 4 mitoses/10 high-power fields
- Immunoreactive with CD34 and Bcl-2

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Up to 50% of patients asymptomatic; small LFTP
 - Large LFTP typically symptomatic
 - Cough, dyspnea, chest pain/discomfort
- Other signs/symptoms
 - Systemic complaints
 - Chills, sweats

- Weakness
- Weight loss
- Paraneoplastic syndromes, typically with large LFTP
 - Hypoglycemia (5%)
 - Doege-Potter syndrome: Postulated production of insulin-like growth factor II
 - Hypertrophic osteoarthropathy (20%)
 - Pierre Marie-Bamberger syndrome: Postulated production of growth hormone-like substance
 - Digital clubbing

Demographics

- Age
- Wide age range; 6th and 7th decades
- Sex
 Slightly more common in women

Natural History & Prognosis

- Favorable prognosis; 66.9-97.5% 10-year survival
 - Complete excision is best prognostic indicator
 - Pedunculated LFTP less likely to recur
 - o 12% of patients die of recurrent or unresectable LFTP
- Recurrence of 23-30%; more likely with malignant and sessile LFTP
 - o Most recurrences within 24 months after resection
 - Recurrence typically in ipsilateral pleura; rarely in lung
- Malignant LFTP may produce distant metastases

Treatment

- Complete excision typically curative
 - Sessile LFTP may require en bloc wide excision of adjacent lung, pleura, chest wall
 - Video-assisted thoracoscopic surgery for small LFTP
 - Thoracotomy for large LFTP
- Resection of recurrent LFTP
- Role of adjuvant therapy not established
 May be used for malignant sessile LFTP

Imaging Follow-Up

- Long-term follow-up recommended; rate of recurrence highest within first 24 months
- CT follow up every 6 months for first 2 years; annual followup CT thereafter

DIAGNOSTIC CHECKLIST

Consider

- LFTP in focal lesions that exhibit incomplete border sign
- LFTP in focal large peripheral thoracic masses without local invasion or lymphadenopathy

Image Interpretation Pearls

• Features that favor malignant LFTP: Symptomatic patient, large tumor size, sessile morphology, necrosis, cystic change, pleural effusion, multifocality

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- Raafat E et al: Solitary fibrous tumour of the pleura presenting as a giant intrathoracic mass. BMJ Case Rep. 2017, 2017
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(Left) Composite image with PA chest radiographs of an asymptomatic 89-year-old man shows growth of a right apical localized fibrous tumor \implies over the course of 5 years. In spite of its large size, the lesion was histologically benign at surgical resection. (Right) Composite image with axial (left) and coronal (right) CECT of a 66-year-old man with a benign localized fibrous tumor shows a soft tissue mass in the right major fissure. Note the beak-like morphology \supseteq of the tumor along the adjacent interlobar fissure.





(Left) Coronal CECT shows a large left basilar localized fibrous tumor with intrinsic enhancing vessels 🔁, a large left pleural effusion, and left lung atelectasis *⊡*. Large lesion size and pleural effusion are features concerning for malignancy. (Right) Coronal CECT of a 61-year-old man with a right basilar localized fibrous tumor shows an ovoid lobulated mass that abuts the right hemidiaphragm with enhancing vessels that were derived from adjacent phrenic arteries. Large basilar tumors may mimic diaphragmatic elevation on radiography.





(Left) Axial contrast-enhanced T1WI FS MR of a 60-year-old woman who presented with Doege-Potter syndrome shows a left basilar localized fibrous tumor that exhibits avid contrast enhancement. Note the medially located blood vessels \supseteq that supply the tumor and typically course through a pedicle. (Right) Axial T2WI FS MR of the same patient shows that the tumor abuts the pleura and exhibits heterogeneous signal intensity. High signal intensity foci \supseteq within the lesion may represent cystic changes or necrosis.



SECTION 13 Chest Wall and Diaphragm

Introduction and Overview Approach to Chest Wall and Diaphragm

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Chest Wall

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Introduction

Chest Wall

The chest wall consists of multiple tissue components (muscles, nerves, fat, bone, cartilage, and vessels) that surround and protect the lungs and pleura and that are in turn enveloped by the skin. These mesenchymal, vascular, osseous, and cartilaginous tissues may be affected by a wide range of disease processes, for which detection, localization, and characterization may be challenging. Chest radiography is useful for the initial assessment of chest wall deformities, osteocartilaginous lesions, and chest wall neoplasms. Chest wall masses characteristically exhibit the **incomplete border sign** on radiography, which, together with radiographic documentation of skeletal &/or soft tissue involvement, allows lesion localization to the chest wall and the formulation of a differential diagnosis. Cross-sectional imaging with computed tomography (CT) and magnetic resonance (MR) enables more precise assessment of the extent of chest wall involvement, lesion characterization, and evaluation of adjacent structures for evidence of involvement or invasion. In some instances, advanced imaging with chest CT &/or MR will enable a definitive diagnosis (e.g., chest wall lipoma). CT and MR have complementary roles for imaging chest wall disorders. CT provides higher spatial resolution and shows calcification and bone erosion and destruction more readily than MR. The advantages of MR include its multiplanar capabilities, improved contrast resolution, and the availability of flow-sensitive pulse sequences.

Diaphragm

The diaphragm is a muscular partition between the thoracic and abdominal cavities and plays an important role in the process of respiration. Diaphragmatic contraction and relaxation allow alterations in intrathoracic pressure and facilitate respiration.

Image Interpretation

The symmetric arrangement of the chest wall structures allows side-to-side comparison on radiography and crosssectional imaging. Any asymmetry should prompt consideration of congenital or acquired disorders. Correlation with clinical history is vital in constructing a reasonable differential diagnosis. A history of recent trauma, for instance, should prompt consideration of acute abnormalities (e.g., fractures, dislocations), whereas chronic and progressive chest wall pain would suggest subacute etiologies (e.g., tumor, infection, inflammatory process). Important anatomic regions to evaluate on CT and MR include the supraclavicular fossae, axillae, paravertebral regions, and the parasternal-internal mammary zones.

The diaphragmatic contours are well visualized on orthogonal PA and lateral chest radiographs. However, because of its horizontal orientation and dome-like configuration, it may be difficult to fully assess the diaphragm on axial CT or MR, but it is optimally evaluated on coronal &/or sagittal images.

Chest Wall Disorders

The chest wall may be affected by a variety of disease processes, including congenital, infectious, inflammatory, traumatic, and neoplastic conditions. Patients with chronic chest wall pain may be difficult to assess on radiography or cross-sectional imaging studies, which often show normal findings. It has been suggested that these patients may benefit from nuclear scintigraphy for anatomic localization of the source of symptoms. Cross-sectional imaging of scintigraphic abnormalities can then be tailored for assessment of the affected area(s).

Infection

Infections may reach the chest wall hematogenously or as a result of direct extension of diseases of the lung, pleura, or mediastinum. These may manifest as soft tissue &/or fluidattenuation lesions and may contain intrinsic gas. Associated findings may include soft tissue stranding of the adjacent fat &/or osseous involvement, which may manifest with periostitis &/or bone destruction. Imaging allows characterization of these lesions and identification of associated pulmonary, mediastinal, or pleural abnormalities.

Neoplasms and Tumors

Chest wall lipoma is the most common benign chest wall neoplasm and exhibits characteristic and diagnostic CT and MR features. Significant soft tissue components within an otherwise fatty chest wall lesion should raise the possibility of malignancy. Other benign mesenchymal tumors may involve the skeletal structures &/or soft tissues. Elastofibromas are cytologically bland fibrous lesions that have a propensity to occur near the inferior scapula, may be bilateral, and may recur if excised. Fibrous dysplasia, enchondroma, and aneurysmal bone cyst may manifest with rib expansion. Neurogenic neoplasms may produce characteristic benign pressure erosion along the rib and vertebral margins.

Metastatic disease is the most common chest wall malignancy and is often secondary to common malignancies, such as primary lung cancer, breast cancer, and prostate cancer. Chondrosarcoma is the most common primary malignant chest wall neoplasm. Other primary chest wall malignancies include multiple myeloma, undifferentiated pleomorphic sarcoma (also known as malignant fibrous histiocytoma), and lymphoma. Rib destruction and a growing chest wall soft tissue mass in an adult should prompt consideration of secondary or primary malignancy as the underlying cause. In young adults and children diagnostic considerations include Ewing sarcoma family of tumors and metastatic neuroblastoma.

Diaphragmatic Abnormalities

The diaphragm may be abnormal in its contour (e.g., eventration) or its lack of excursion (e.g., paralysis), or it may be affected by blunt or penetrating trauma. Normal and abnormal apertures in the diaphragm permit a variety of herniations to occur. Diaphragmatic apertures may enlarge in older and obese patients and in patients with emphysema. Acquired hiatal hernias are very common, especially in the older adult population, and allow intrathoracic herniation of the stomach and other abdominal contents through a widened esophageal hiatus. Posterior Bochdalek hernias (posterolateral vertebrocostal triangle) and anterior Morgagni hernias (sternocostal hiatus) are also common and typically allow intrathoracic herniation of abdominal fat, but also abdominal organs and hollow viscera.

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Approach to Chest Wall and Diaphragm

Chest Wall Lipoma



Chest Wall Chondrosarcoma



Breast Cancer and Metastatic Melanoma

(Left) Composite image with PA chest radiograph (left) and coronal NECT (right) shows a left chest wall lipoma manifesting as a lenticular opacity 🔁 with incomplete borders on radiography and as a homogeneous fatattenuation mass \implies on CT. (Right) Composite image with PA (left) and lateral (middle) chest radiographs and sagittal MR (right) shows a chondrosarcoma of the right 6th costochondral junction. The tapering obtuse margins of the tumor \bowtie manifest as incomplete borders on both orthogonal radiographs.

Lymphoma



(Left) Axial CECT of a patient with mediastinal Hodgkin lymphoma demonstrates a heterogeneous prevascular mediastinal soft tissue mass that directly invades the adjacent right anterior chest wall A. (Right) Composite image with axial CECT shows a primary breast cancer (left) manifesting as a right breast lobulated mass $rac{2}{and}$ and metastatic melanoma (right) manifesting as an infiltrative heterogeneous soft tissue mass 🔁 in the right anterior chest wall involving the supraclavicular, subpectoral, and axillary regions.

Hiatus Hernia



Bochdalek Hernia



(Left) Coronal CECT demonstrates thoracic herniation of colon and mesentery within a large hiatus hernia 🔁. Hiatus hernias often manifest on radiography as air-containing bowel (typically stomach) within a retrocardiac opacity. (Right) Composite image with lateral chest radiograph (left) and axial CECT (right) shows a Bochdalek hernia that manifests as a left posterior diaphragmatic contour $abnormality \ge$ and contains the left kidney \square and retroperitoneal fat 🔁

Chest Wall Infections

KEY FACTS

TERMINOLOGY

• Definition: Infection involving chest wall bones and soft tissues

IMAGING

- Radiography
 - o Skeletal involvement: Bone destruction, periostitis
 - Subcutaneous gas; necrotizing infection or fistula
 - o Displaced sternal wires suggest dehiscence
 - ± lung consolidation, pleural effusion
- CT
 - Chest wall edema, fluid, mass, gas, bone destruction, periostitis, osteomyelitis
 - Sternoclavicular joint septic arthritis
 - Pleural effusion, empyema necessitatis
 - Evaluation of suspected sternotomy infection
 - ± lung consolidation/abscess
- **MR**: More sensitive than CT for early bone involvement • Bone, soft tissue, and fascial plane edema

TOP DIFFERENTIAL DIAGNOSES

- Actinomycosis
- Tuberculosis
- Sternotomy infection
- Necrotizing soft tissue infection
- Chest wall malignancy

CLINICAL ISSUES

- Etiology
 - Hematogenous; direct extension from lung infection
 - Complication of trauma or surgery
- Symptoms/signs
 - Fever and chest wall pain
 - o Palpable chest wall lesion; abscess, edema
 - Cutaneous fistulas
- Treatment
 - Abscess drainage and antimicrobial therapy
 - Surgical debridement for severe infection

(Left) Axial CECT of a patient with fever and left chest pain shows a left pleural effusion and pleural thickening \square and adjacent chest wall involvement 🔁, consistent with empyema necessitatis, and transdiaphragmatic splenic invasion \boxtimes secondary to actinomycosis, in this case. (Right) Axial CECT of an immunocompromised patient with invasive aspergillosis who presented with fever shows right lung consolidations and direct invasion of the adjacent chest wall 🔁. Identification of chest wall asymmetry helped establish the diagnosis.





(Left) Axial T2WI MR of a man with tuberculosis shows T2hyperintense signal in the left anterior chest wall \supseteq and a small left pleural effusion 🔁. *MR is the preferred modality* to evaluate extent of chest wall infection, and is particularly superior to CT in evaluating extent of bone marrow involvement. (Right) Axial T1 C+ MR of a patient with human immunodeficiency virus and Cryptococcal pneumonia shows enhancing, inflamed left paravertebral soft tissues 🔁 with involvement of the posterior chest wall 🔁 and a rib 🔁.





Definitions

• Infection of chest wall skeletal structures and soft tissues

IMAGING

Radiographic Findings

- Skeletal involvement: Bone destruction, periosteal reaction
- Subcutaneous gas; necrotizing infections or fistulas
- Displaced sternotomy wires suggest dehiscence
- ± lung consolidation, pleural effusion

CT Findings

- Chest wall: Edema, fluid collection, soft tissue mass, gas, skeletal destruction, periostitis, osteomyelitis
- Sternoclavicular joint septic arthritis: Fluid, erosions, bone sclerosis; may result in abscess or mediastinitis
- Pleural effusion, empyema necessitatis
- ± pulmonary involvement

MR Findings

- More **sensitive** than CT for early bone/joint involvement
- Bone, soft tissue, and fascial plane edema
- Use of contrast for determination of disease extent

Nuclear Medicine Findings

• Skeletal scintigraphy: Sensitive and specific for osteomyelitis

Imaging Recommendations

- Best imaging tool
 - CT: Optimal evaluation of chest wall (soft tissue and skeletal) involvement, fistulous tracks

DIFFERENTIAL DIAGNOSIS

Actinomycosis

- Mouth flora; aspiration after dental manipulation or in patients with dental disease
- Lung consolidation/abscess with chest wall involvement

Nocardiosis

- Gram-positive bacterium; immunocompromised host
- Consolidation or cavitary nodules; rare chest wall involvement

Tuberculosis

- Chest wall mass or cutaneous fistula
- Rib involvement more common in IV drug users
- Tuberculous spondylitis (Pott disease); hematogenous infection
- Empyema necessitatis involves adjacent chest wall

Streptococcus Pneumonia

- Most common gram-positive pneumonia
- Chest wall invasion rare

Sternotomy Infection

- 0.3-5% of median sternotomy cases
- Mortality rates range: 14-47%
- Risk factors: Diabetes, obesity, chronic obstructive pulmonary disease, smoking

• Most common pathogens: *Staphylococcus aureus* (29%), *S. epidermidis* (22%), and *Pseudomonas aeruginosa*

Necrotizing Soft Tissue Infection

- Most frequent in postoperative setting
- Predisposing condition: Chest wall malignancy
- High mortality; early surgical intervention required

Chest Wall Malignancy

- Peripheral locally invasive lung cancer may mimic chest wall infection
- Mesothelioma may invade chest wall
- Primary chest wall neoplasms
 - o Rare: Chondrosarcoma, osteosarcoma, lymphoma
- Secondary chest wall neoplasms
 Lung, breast, prostate, renal cell cancers; melanoma

PATHOLOGY

General Features

- Etiology
 - Hematogenous dissemination of infection
 - Direct extension from adjacent lung infection
 - Complication of trauma or surgery

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 Fever, chest wall pain
 - Palpable chest wall lesion; abscess, edema
- Other signs/symptoms
 Cutaneous fistulas

Demographics

- Epidemiology
 - Incidence of mediastinal and chest wall infection after cardiac surgery range: 0.3-5%

Diagnosis

• Biopsy may be warranted to exclude chest wall malignancy

Treatment

- Abscess drainage and culture-tailored antimicrobial therapy
- Necrotizing or severe chest wall infection: Early and aggressive surgical debridement

DIAGNOSTIC CHECKLIST

Consider

• Chest wall infection in febrile patient with palpable chest wall mass ± adjacent lung consolidation

Image Interpretation Pearls

• Subcutaneous gas may be absent in cases of necrotizing chest wall infection

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Discitis

KEY FACTS

TERMINOLOGY

• **Disc space infection** that characteristically involves adjacent vertebral bodies

IMAGING

- Radiography
 - Earliest finding: **Disc space narrowing**
 - Endplate sclerosis develops after 8 weeks
- CT
 - Disc space narrowing
 - Irregularity, erosion, or destruction of vertebral endplates
 - Paravertebral inflammatory fat stranding, soft tissue, or fluid collection
 - MR
 - Early findings: Disc space narrowing, subtle endplate enhancement; may mimic degenerative disc disease
 - Affected disc and adjacent vertebrae hypointense on T1WI; hyperintense on T2WI due to edema

- Enhancement of disc, adjacent vertebrae, paravertebral soft tissue/ fluid, epidural abscess
- Epidural involvement, optimally assessed with MR

TOP DIFFERENTIAL DIAGNOSES

- Degenerative disc disease
- Spinal metastases

PATHOLOGY

- Etiology
 - Bacterial infection; *Staphylococcus aureus* in > 50%
 - o Granulomatous infection
 - Tuberculosis, brucellosis, fungal infection

CLINICAL ISSUES

- Focal back pain not relieved by rest
- Fever, chills, malaise
- Neurologic compromise
- Intravenous antibiotic therapy for at least 6 weeks

(Left) Graphic shows findings of discitis, including disc space destruction and narrowing, erosion of adjacent vertebral body endplates \implies , extension of infection into the epidural space with epidural abscess formation \square , resultant narrowing of the spinal canal, and involvement of paravertebral tissues \implies . (Right) Axial NECT of a patient with Staphylococcus aureus thoracic spondylodiscitis shows paravertebral fluid 🖂 and fat stranding \square from inflammatory changes and erosions rightarrow 2 of the adjacent vertebral endplate.











Synonyms

- Spondylodiscitis
- Diskitis

Definitions

• **Disc space infection** that characteristically involves adjacent vertebral bodies

IMAGING

General Features

- Best diagnostic clue
 - Disc space narrowing
 - o Erosion/irregularity of adjacent vertebral body endplates
- Location
 - Lumbar spine > thoracic spine
 - Single disc typically involved

Radiographic Findings

- Radiography may be normal in first 2 weeks after onset of symptoms
- Earliest finding: Disc space narrowing
- Indistinctness, irregularity, or destruction of adjacent vertebral body endplates
- Endplate sclerosis develops after 8 weeks
- Lateral displacement of paravertebral stripes by adjacent soft tissue infection
- ± pulmonary consolidation; pneumonia may be source of hematogenous spread of infection

CT Findings

- Disc space narrowing
 - Best appreciated on sagittal reformatted images
- Irregularity or destruction of vertebral body endplates
- Endplate skeletal sclerosis
- Paravertebral inflammatory fat stranding, soft tissue, or fluid collection
- Epidural involvement, optimally assessed with MR

MR Findings

- Imaging modality of choice
- Early findings: Disc space narrowing, subtle endplate enhancement; may mimic degenerative disc disease
- Affected disc and adjacent vertebrae are **hypointense on T1WI**, **hyperintense on T2WI** due to edema
- Enhancement of disc and adjacent affected vertebrae, paravertebral soft tissues &/or fluid collection, epidural abscess

Imaging Recommendations

- Best imaging tool
 - MR with and without contrast; highly sensitive (97%) and specific (93%)
 - Allows optimal evaluation of adjacent soft tissue and epidural involvement
- Protocol advice
 - T1WI MR with contrast and fat suppression
 - **Sagittal** imaging for optimal visualization of disc height loss

DIFFERENTIAL DIAGNOSIS

Degenerative Disc Disease

- Disc space narrowing with no endplate destruction or disc enhancement
- Characteristic multilevel involvement, unlike discitis

Spinal Metastases

- Involvement of multiple vertebral bodies
- Spared intervertebral disc; preserved disc height

PATHOLOGY

General Features

- Etiology
 - Bacterial infection; *Staphylococcus aureus* in > 50%
 - Granulomatous infection
 - Tuberculosis, brucellosis, fungal infection
 - Involvement of adjacent paravertebral soft tissues &/or vertebral bodies
 - Relative sparing of disc space
 - Hematogenous dissemination of infection
 - Respiratory tract, urinary tract
 - Direct inoculation of infection
 - Surgery, discography, penetrating trauma
 - Local extension of adjacent infection
 - Retroperitoneum, abdomen, thorax
 - Retropharyngeal abscess, infected aortic graft

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Focal back pain not relieved by rest
 - Fever, chills, malaise
- Other signs/symptoms
 - Neurologic compromise
 - Elevated erythrocyte sedimentation rate (ESR)

Demographics

- Epidemiology
 - Risk factors: Recent spine surgery, bacteremia, immunosuppression, diabetes, intravenous drug use
 M > F

Natural History & Prognosis

• Mortality: 2-20%

Treatment

• Intravenous antibiotic therapy for at least 6 weeks

DIAGNOSTIC CHECKLIST

Consider

• Discitis in patients with back pain and evidence infection

Image Interpretation Pearls

• Review sagittal reformatted CT images to assess disc height and adjacent vertebral endplate abnormalities

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TERMINOLOGY

• Liposarcoma (LS)

IMAGING

- Lipoma: Homogeneous fatty mass, well-defined margins
 Should follow fat signal intensity on all MR sequences
 May exhibit thin soft tissue septa (< 2 mm)
- LS: Fatty mass with thick soft tissue septa or nodules
- Soft tissue nodules > 1 cm suspicious for aggressive subtypes
- Calcification does not reliably differentiate LS from lipoma
- MR is preferred modality to evaluate fatty mass
- Contrast-enhanced imaging preferable

TOP DIFFERENTIAL DIAGNOSES

- Pleural lipoma
- Lipoblastoma/lipoblastomatosis
- Hibernoma

PATHOLOGY

- Lipoma: Composed of mature adipocytes
- LS: 5 subtypes in 3 major categories

CLINICAL ISSUES

- Lipoma: Most common soft tissue neoplasm
 - Rarely symptomatic, may grow slowly
 - More common in obese patients
 - Deep chest wall lipomas: 30-60 years of age
- Only 10% of LS occur in chest wall
 - o Usually painful, rapidly growing mass
 - o 50-70 years of age

DIAGNOSTIC CHECKLIST

- Homogeneous, fatty chest wall mass ± thin, nonenhancing septa may be confidently diagnosed as lipoma
- Thick septa (> 2 mm) and soft tissue nodules in fatty mass should raise suspicion for LS
- Biopsy should be directed to nonlipomatous components

(Left) Coned-down PA chest radiograph shows a lobulated mass at the right apex. Obtuse margins \bowtie with the adjacent pleural surface suggest an extrapulmonary location (pleura or chest wall). (Right) Axial CECT of the same patient shows a right chest wall lipoma manifesting as a fat-attenuation chest wall mass 🔁 at the intercostal space with intrathoracic extension. A chest wall homogeneous fatty mass without soft tissue septa or solid components may be confidently diagnosed as a lipoma.





(Left) Transverse ultrasound of a palpable chest wall mass demonstrates a large, homogeneously hyperechoic mass \supseteq without through transmission or internal regions of cystic or solid components. Subsequent biopsy confirmed chest wall lipoma. (Right) Fused axial FDG PET/CT of a patient with a right posterolateral chest wall lipoma shows a fatcontaining mass \blacksquare with few thin internal septations and no FDG avidity. Regions of increased FDG uptake in fatty masses should raise concern for malignancy.





Abbreviations

- Liposarcoma (LS)
 - Atypical lipomatous tumor (ATL)
 - o Well-differentiated liposarcoma (WDL)
 - Dedifferentiated liposarcoma (DDL)

Definitions

- Lipoma: Benign neoplasm composed of adipose tissue
- LS: Rare malignant neoplasm arising in fat cells

IMAGING

General Features

- Best diagnostic clue
 - Lipoma: Homogeneous fatty mass
 - Well-defined margins
 - May exhibit thin soft tissue septa (< 2 mm) &/or thin capsule
 - LS: Fatty mass with thick soft tissue septa or nodules
 - May invade adjacent structures
- Location
 - Lipoma: Superficial or deep (intra- or intermuscular)
- Size
 - Lipoma: < 5 cm in 80% of cases
 - < 1% of lipomas > 10 cm
 - Deep lipomas larger than superficial lipomas
- Morphology
 - Lipoma: Thin fibrous capsule may be present
 - Intramuscular lipoma may be unencapsulated and appear striated or infiltrative

Radiographic Findings

- Radiography
 - o Lipoma
 - Fat density when large
 - Small or deep lipomas may not be visible
 - Obtuse margin with adjacent pleura/chest wall suggests extrapulmonary location
 - Chondroid or osteoid mineralization uncommon
 - o LS
 - Heterogeneous
 - May produce osseous destruction

CT Findings

- CECT
 - o Lipoma
 - Homogeneous, fat attenuation (-60- to -120-HU) mass with well-defined margins
 - ± thin soft tissue septa (< 2 mm)
 - Intramuscular lipomas may be poorly-defined
 - o LS
 - Fatty mass with thick soft tissue septa (> 2 mm)
 - Soft tissue nodules > 1 cm suggest dedifferentiation
 - Calcification not reliable to distinguish from lipoma
 - Necrosis and hemorrhage in aggressive subtypes

MR Findings

- T1WIFS
 - Chemical fat saturation of T1-hyperintense mass

- T2WI
- Myxoid LS may have high T2 signal intensity
- T1WI C+ FS • Lipoma: Thin capsule may enhance, thin septa usually do
- o LS: Enhancing soft tissue components
- Lipoma: MR signal characteristics identical to subcutaneous fat on all sequences
 - May exhibit T1- and T2-hypointense thin septa
 - o Thin capsule, when present, also T1 and T2 hypointense
 - Striated or interdigitated appearance of intramuscular lipoma may help to differentiate it from LS

Ultrasonographic Findings

- Lipoma: Hyperechoic without through transmission
- LS
 - Solid components may be hypervascular
 - Necrotic tumors may exhibit cystic areas
 - Hemorrhage and shadowing calcification may be visible

Imaging Recommendations

- Best imaging tool
 - MR is preferred imaging modality for evaluation
 - T1WI, T1WI FS, and T1WI C+ FS sequences are most important for diagnosing lipoma
 - CT helpful for detection of calcification and assessing extent of tumor
- Protocol advice
 - Contrast-enhanced imaging for optimal assessment

DIFFERENTIAL DIAGNOSIS

Pleural Lipoma

- May represent lipomas arising deep to parietal pleura or from adjacent mediastinal fat; not of pleural origin
- Pleural, subpleural, or diaphragmatic

Lipoblastoma/Lipoblastomatosis

- Infants and children
- May be indistinguishable from lipoma/LS
- May exhibit thick soft tissue septa and local infiltration

Hibernoma

- Benign tumor composed of brown fat
- Often hypervascular
- Most patients 30-40 years of age
- Often periscapular or in supraclavicular fossa

Lipomatosis

- Rare in adults
- Infiltrative fat overgrowth, often in shoulder girdle, neck, and back

Parosteal Lipoma of Rib, Scapula, or Clavicle

- Very rare benign tumor associated with periosteum
- Often associated with reactive changes of underlying bone

PATHOLOGY

General Features

- Genetics
 - o Multiple lipomas familial in 30% of cases
 - Usually men; lipomas usually superficial

• Associated abnormalities

• Multiple lipomas associated with Cowden syndrome, Frohlich syndrome, and Proteus syndrome

- High proportion of soft tissue elements usually indicates higher grade tumors
- p16, CDK4, and MDM2 may differentiate benign adipocytic tumors from WDL

Staging, Grading, & Classification

- Several benign variants of lipoma: Chondroid lipoma, osteochondroma, angiolipoma, infarcted lipoma
 Spindle cell lipoma
 - Predilection for shoulder and neck
 - M>F
- LS: 5 subtypes in 3 major categories based on molecular/genetic testing
 - ALT/WDL and DDL
 - Most common category of tumors (50% of LS)
 - May represent morphological and behavioral spectrum of same disease
 - WDL subtype most common in chest wall
 - Sclerosing variant of well-differentiated subtype more likely to dedifferentiate
 - o Myxoid and round cell tumors
 - Usually affect young adults
 - Probably continuum of same tumor type
 - Round cell component proportional to gradePleomorphic tumors
 - Least common, highly aggressive
 - Usually affect older adults

Gross Pathologic & Surgical Features

• May have thin capsule

Microscopic Features

• Lipoma: Composed of mature adipocytes • Scant fibrous connective tissue in septa

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Lipoma is rarely symptomatic
 - When symptomatic, manifests with soft, pliable massCharacteristically no or very slow growth
 - LS usually manifests as painful, rapidly growing mass

Demographics

- Age
 - o Deep chest wall lipomas: 30-60 years of age
 - LS: 50-70 years of age
- Sex
 - o Lipoma: M > F
- Epidemiology
 - Lipoma: Most common soft tissue neoplasm
 Lipomas more common in obese patients
 - LS: Most common mesenchymal malignancy
 Only 10% of LS occur in chest wall

Natural History & Prognosis

Lipomas may grow slowly
 May recur after excision

- LS: 5-year survival 60%
 - Recurrence rates high for most subtypes
 - Most subtypes metastasize to liver and lung
 - o 15-20% of DDL metastasize
 - Myxoid subtype metastasizes to paraspinal tissues, bone, retroperitoneum, and opposite extremity

Treatment

- Options, risks, complications
 - Lipoma: Surgical resection recommended for symptomatic lesions
 - Enables definitive diagnosis
 - Local recurrence in 4-5%
 - More frequent with deep or intramuscular lipomas
 Few case reports of malignant transformation
 - Controversial, may be attributed to sampling error or initial misdiagnosis
 - LS: Subtotal surgical resection considered palliative in most cases
 - ALT may be cured by complete resection
 - Adjuvant chemotherapy/radiation controversial
 - Adjuvant radiation may be used when resection margins positive for residual tumor
 - May be beneficial in large tumors (> 5 cm) or for very aggressive subtypes
 - □ Myxoid LS may be sensitive to therapies that target *FUS-DDIT3* (FUS-CHOP) fusion oncogene

DIAGNOSTIC CHECKLIST

Consider

- Homogeneous, fatty chest wall mass without septations or with few, thin, nonenhancing septa may be confidently diagnosed as lipoma
 - Age > 60, size > 10 cm; atypical for lipoma
 Biopsy may be required
- Lipoma should follow fat signal intensity on all MR sequences
- Thick septa (> 2 mm) and soft tissue nodular components should raise suspicion for LS
 - Calcification does not reliably differentiate LS from lipoma

Image Interpretation Pearls

- Intramuscular lipomas may be striated or interdigitated
- In postoperative surveillance imaging LS, scrutinize soft tissue components for growth
- Most subtypes metastasize to liver and lung
- Aggressive subtypes of LS may have little or no visible fat
 Soft tissue nodules > 1 cm should raise suspicion for DDL or more aggressive subtypes

Reporting Tips

• Biopsy should be directed to sample nonfatty components

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(Left) Axial CECT of a patient with a palpable left posterior chest wall mass demonstrates a predominantly fatcontaining lesion \supseteq with only scattered thin soft tissue septa \blacksquare , consistent with a benian lipoma. (Right) Axial CECT of a patient with an enlarging mass in the right posterolateral chest wall shows a large well-defined mass \square of predominant fat attenuation with an ill-defined soft tissue component anteriorly 🔁. Subsequent biopsy revealed liposarcoma.





(Left) Axial CECT of a patient with a palpable mass in the right anterior chest wall demonstrates a fat-containing mass 🔁 with a medial cystic component 🖾. Surgical biopsy confirmed the diagnosis of myxoid liposarcoma. (Right) Axial T1WI MR of a patient with progressive left chest wall pain shows a large heterogeneous mass 🔁 that represented a liposarcoma. The internal regions of high signal intensity \boxtimes represent fat.





(Left) Axial T2WI FS MR of the same patient shows heterogeneous high signal intensity within the mass. (Right) Axial T1WI FS C+ MR of the same patient demonstrates marked enhancement of most of the mass. When internal thick septations, soft tissue components, &/or enhancement are identified in a fat-containing chest wall mass, liposarcoma should be strongly suspected.

TERMINOLOGY

- Elastofibroma: Fibroelastic pseudotumor typically in subscapular region of older adult patients
- Fibromatosis: Locally aggressive connective tissue malignancy

IMAGING

- CT
 - Elastofibroma: Ill-defined, lenticular, heterogeneous soft tissue mass; characteristic bilateral subscapular location
 - Fibromatosis: Poorly-defined soft tissue mass; variable attenuation and enhancement
- MR
 - Elastofibroma: Lenticular unencapsulated mass of intermediate signal intensity; linear strands of signal intensity similar to fat; heterogeneous enhancement
 - Fibromatosis: Heterogeneous; T1- and T2- hypointense non-enhancing linear bands

TOP DIFFERENTIAL DIAGNOSES

- Soft tissue sarcomas
- Ewing sarcoma family of tumors
- Chest wall metastasis

CLINICAL ISSUES

- Symptoms and signs
 - Elastofibroma: > 50% asymptomatic; pain or clicking with scapular movement
 - Fibromatosis: Symptoms vary with location; painless mass vs. pain and functional impairment
- Elastofibroma: Older adult patients; F:M = 5-13:1; surgery curative, rare recurrence
- Fibromatosis: 15-60 years of age; more common in women; variable treatment options

DIAGNOSTIC CHECKLIST

• Consider elastofibroma in older adult patient with asymptomatic bilateral subscapular soft tissue masses

(Left) Axial CECT of an asymptomatic patient demonstrates a heterogeneous mass in the right chest wall composed of both soft tissue and fat \supseteq consistent with elastofibroma. This benign lesion most commonly occurs in the subscapular region and is often bilateral. (Right) Axial T1WI MR of the same patient shows heterogeneous signal intensity with most of the lesion similar to that of skeletal muscle in the adjacent chest wall but with linear regions of high signal intensity corresponding to fat 🖂.





(Left) Axial T1WI C+ FS contrast-enhanced MR of the same patient demonstrates heterogeneous enhancement \Longrightarrow within the lesion, which is a characteristic MR imaging finding. (Right) Axial T2 FS MR of the same patient shows a few linear foci of high signal intensity within the mass \square that correspond to fat. Note that most of the lesion has signal intensity similar to that of skeletal muscle. Although regions of internal fat may be present, the soft tissue components are typically similar to skeletal muscle.





Synonyms

- Elastofibroma dorsi
- Desmoid fibromatosis or desmoid tumor

Definitions

- Elastofibroma: Fibroelastic pseudotumor typically in subscapular region of older adult patients
- Fibromatosis: Locally aggressive connective tissue malignancy

IMAGING

General Features

- Best diagnostic clue
 - Elastofibroma: Subscapular mass deep to serratus anterior; **99% subscapular**, 10-66% bilateral
 - o Fibromatosis: Chest wall origin in 10-28% of cases

CT Findings

- Elastofibroma
 - Poorly-defined, lenticular, heterogeneous soft tissue mass
 - Linear low-attenuation streaks from internal fat; multilayered appearance
 - Similar attenuation to muscle in majority of mass
 - o Characteristic location and bilaterality suggest diagnosis
 - Rarely rib erosion
- Fibromatosis
 - Well- or poorly-defined soft tissue mass
 - Variable attenuation and enhancement

MR Findings

- Elastofibroma
 - Lenticular unencapsulated mass, intermediate signal intensity (majority of mass of signal similar to that of skeletal muscle)
 - o T1WI and T2WI: Linear strands of signal intensity similar to that of fat (hyperintense on T1WI and T2WI)
 - Heterogeneous enhancement
- Fibromatosis
 - Heterogeneous signal intensity
 - o T1- and T2- hypointense non-enhancing linear bands

Ultrasonographic Findings

- Elastofibroma
 - Crescent-shaped subscapular mass between extrinsic back muscles and costal plane
 - Striated, multilayered mass with alternating hypoechoic (fatty tissue) and echogenic bands (fibroelastic tissue)
 - Little or no flow on color Doppler
 - Optimal visualization in prone patient with abducted ipsilateral upper extremity

Image-Guided Biopsy

• Elastofibroma: Biopsy unnecessary in most cases with classic imaging appearance and location

Nuclear Medicine Findings

- PET/CT
 - Elastofibroma: Variable FDG uptake; none to marked
 Uptake less than that of liver (55%)

- Uptake equal to that of liver (33%)

DIFFERENTIAL DIAGNOSIS

Soft Tissue Sarcomas

- Fibrosarcoma, undifferentiated pleomorphic sarcoma
- Similar CT and MR appearances
- May invade adjacent osseous structures

Ewing Sarcoma Family of Tumors

• Large chest wall mass with rib destruction, pleural thickening/effusion, lung invasion

Chest Wall Metastasis

- Direct invasion, hematogenous or lymphatic dissemination
- Often multifocal involvement

PATHOLOGY

General Features

- Etiology
 - Elastofibroma: Postulated reaction to repetitive microtrauma; friction between scapula and chest wall
 - Fibromatosis: Rare monoclonal locally aggressive sporadic or familial tumor

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Elastofibroma: **> 50% asymptomatic**
 - Pain, scapular clicking/snapping with movement
 - Fibromatosis: Symptoms vary with location; painless mass vs. pain and functional impairment

Demographics

- Age
 - Elastofibroma: Older adult patients (mean age: 65-70 years)
 - Fibromatosis: 15-60 years of age
- Sex
 - o Elastofibroma: F:M = 5-13:1
 - Fibromatosis: More common in women
- Epidemiology
 - o Elastofibroma
 - 2% prevalence based on CT series of 258 patients (age > 60 years) imaged for other reasons
 - Fibromatosis: Rare; 2-4/million population

Natural History & Prognosis

- Elastofibroma: Slow growth over time, no reports of malignant degeneration
- Fibromatosis: Unpredictable behavior

Treatment

- Elastofibroma: Surgery curative; rare recurrence
- Fibromatosis: Surveillance, surgery, radiotherapy, systemic therapy

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- Ganeshan D et al: Current update on desmoid fibromatosis. J Comput Assist Tomogr. 43(1):29-38, 2018

(Left) Axial CECT of an asymptomatic patient demonstrates a heterogeneous mass \supseteq in the right chest wall composed of soft tissue and fat, consistent with an elastofibroma. (Right) Axial NECT shows bilateral heterogeneous subscapular soft tissue masses \supseteq typical of fibroelastomas. Note low attenuation within the masses that represents intrinsic fat. On CT, fibroelastoma typically shows attenuation similar to that of skeletal muscle, but low-attenuation streaks from internal fat may also be present.





(Left) Coronal T2WI MR shows low signal intensity of the fibrous portions 🔁 and high signal intensity of the fatty portions $rac{1}{2}$ of an elastofibroma. A crescentic mass located between the lower scapula and the ipsilateral costal plane containing both fat and fibrous signal intensity on MR is typical. (Right) Coronal T2WI MR of a patient with bilateral elastofibromas shows welldefined subscapular lenticular soft tissue masses 🔁 with heterogeneous areas of increased and decreased signal intensity.





(Left) Axial CECT of an asymptomatic patient demonstrates a heterogeneous mass in the right subscapular region composed of soft tissue and fat ⊇. (Right) Fused axial FDG PET/CT of the same patient shows low-grade FDG uptake within the mass ⊇. Elastofibromas demonstrate variable FDG uptake, which ranges from none to marked.





Elastofibroma and Fibromatosis





(Left) Axial CECT of an asymptomatic patient demonstrates bilateral elastofibromas 🖂 (Right) Fused axial FDG PET/CT of the same patient shows low-grade FDG uptake within the bilateral subscapular masses ■. On FDG PET/CT, elastofibromas demonstrate variable FDG uptake. The most common pattern is FDG uptake that is less that of the liver, and the second most common pattern is FDG uptake equal to that of the liver.





(Left) Axial CECT of a patient who presented with right anterior chest wall pain and a palpable mass ⇒ shows a soft tissue mass in the right breast. Biopsy revealed fibromatosis. (Right) Axial T1WI FS MR of a patient with fibromatosis shows a homogeneous mass in the left anterior chest wall ⇒. Fibromatosis typically exhibits heterogeneous signal intensity on MR.





(Left) Axial T1WI C+ FS MR of the same patient shows diffuse intense enhancement throughout the mass and helps confirm the locally invasive behavior \square of the lesion. (Right) Axial T2WI MR of the same patient demonstrates high signal intensity (relative to the adjacent skeletal muscle) within the mass. Note the internal bands of low signal intensity \supseteq within the lesion, which did not enhance following the administration of intravenous contrast.

TERMINOLOGY

- Metastatic disease involving chest wall
- Most common chest wall malignancy

IMAGING

• Radiography

- Incomplete border sign should suggest chest wall or pleural lesion
- Osseous destruction is most specific sign
- **CT**: Direct chest wall evaluation for metastases
- MR
 - Modality of choice for assessment of chest wall involvement
 - o Typically T1 hypointense
 - Melanoma may be T1 and T2 hyperintense
- **Bone scan**: High sensitivity for skeletal metastases; wholebody imaging
- **PET/CT**: Staging of malignancy

TOP DIFFERENTIAL DIAGNOSES

- Chest wall infection
- Healing traumatic fractures
- Primary chest wall neoplasms
- Neurofibromatosis

PATHOLOGY

- Patterns of metastatic spread to chest wall
 Disast subastics
 - Direct extension
 - Hematogenous/lymphatic dissemination
- Common primaries: Lung, breast, prostate

CLINICAL ISSUES

- Localized pain is most frequent symptom
- Poor prognosis: Lung cancer, recurrent breast cancer

DIAGNOSTIC CHECKLIST

• CT- or ultrasound-guided biopsy for diagnosis confirmation and for metastases from unknown primary malignancies

(Left) Axial CECT of a patient with metastatic melanoma shows multiple skin lesions that follow lymphatic pathways, so-called in-transit lesions. In this case, a primary melanoma 🔁 exhibits intransit lesions \blacksquare toward the right axilla. There were also lung, lymph node, and pleural metastases. (Right) Axial NECT of a patient with multiple myeloma and multiple lytic and expansile rib and sternal lesions shows a large lytic expansile metastasis \overline{rad} in the sternal body, which exhibits cortical discontinuity and irregular margins.





(Left) Axial CECT of a patient with a large locally invasive primary lung cancer shows a heterogeneously enhancing left upper lobe mass that directly invades the adjacent pleura, ribs, and chest wall soft tissues. (Right) Coronal CECT of the same patient shows direct invasion of the apical chest wall by this Pancoast tumor 🔁. Pancoast tumors are lung cancers that directly involve the adjacent apical chest, including the pleura, chest wall muscles, ribs, and the lower trunks of the brachial plexus.





Chest Wall Metastases

TERMINOLOGY

Definitions

- Metastatic disease involving chest wall
- Most common chest wall malignancy
- Typically in terminal stages of malignancy

IMAGING

General Features

- Best diagnostic clue
 - Rib/bone destruction or expansion most specific finding
 - Solitary/multiple chest wall masses, aggressive features (ill-defined, infiltrative, locally invasive)
- Location
 - o Supraclavicular lymph nodes
 - Breast and lung cancer most common
 - Left-sided metastases 5x more frequent than right in abdominal/pelvic malignancies
 - High frequency: Ovarian, stomach, head and neck, thyroid cancers
 - Axillary lymph nodes: Breast cancer and lymphoma most common
 - Skin and subcutaneous tissues
 - Chest most common site of skin metastases
 - Typically: Lung, breast, colon cancers and melanoma
 - o Muscle metastases rare; melanoma most common
 - o Skeletal metastases: Direct invasion or hematogenous
 - Hematogenous spread most common to red marrow: Vertebrae, proximal ribs
 - Sternum: Breast and melanoma most common; renal, thyroid, gastric less common
 - Ribs (16% of metastases): Lung, breast, prostate, thyroid cancers most common
- Morphology
 - o Imaging features depend on primary malignancy
 - Osseous: Optimally evaluated on CT
 - Sclerotic lesions: Breast and prostate cancers
 - □ Lytic/expansile: Thyroid and renal cell cancers
 - Lytic or permeative: myeloma
 - Soft tissue: Denote extensive metastases, poor prognosis
 - Intense enhancement on CECT: Melanoma, thyroid and renal cell cancers, most sarcomas, choriocarcinoma

Radiographic Findings

- 20% of lesions visible
- Soft tissue mass
 - **Incomplete border sign**: Discrepant margin visualization on orthogonal images; suggests chest wall or pleural lesion
 - Crosses fissural boundaries
- Osseous cortical destruction: Most specific sign

 ± pathologic fracture, soft tissue mass
- ± pleural effusion, rare calcification

CT Findings

• Direct chest wall visualization; assessment of lesion origin and disease extent

- Optimal evaluation of calcification and osseous destruction
- Frequent contrast enhancement, particularly melanoma and sarcoma

MR Findings

- T1WI
 - Typically T1 hypointense
 - Melanoma may be T1 hyperintense
 - Fat in liposarcoma metastases; T1 hyperintense
- T2WI
- o Typically T2 hyperintense relative to skeletal muscle
- T1WIC+
 - Most chest wall metastases enhance
 - Post treatment: Identification of residual or recurrent disease
- Optimal modality for assessment of extent of soft tissue involvement and direct chest wall invasion
- Multiplanar imaging for optimal evaluation of invasive superior sulcus tumors

Nuclear Medicine Findings

- Bone scan
 - More sensitive than radiography for detecting bone metastases
 - o Extensive osseous metastases may result in superscan
 - Widely available whole-body imaging
- PET/CT
 - Staging of primary malignancies

Image-Guided Biopsy

• CT- or ultrasound-guided biopsy often required to confirm diagnosis of metastatic disease

Imaging Recommendations

- Best imaging tool
 - MR and CT are complementary in evaluating chest wall involvement
 - PET/CT optimal for staging malignancy
- Protocol advice
 - o Contrast may improve detection of small lesions

DIFFERENTIAL DIAGNOSIS

Chest Wall Infection

- Direct extension from pulmonary infection
 - Pyogenic infection, actinomycosis, nocardiosis, tuberculosis, fungal disease
- Empyema necessitatis (73% from tuberculosis)
 Primary infection, postoperative/post-traumatic,
- hematogenous in bacteremia

Bone Disease

- Fibrous dysplasia
- Metabolic bone disease: Hyperparathyroidism, rickets, scurvy
- Paget disease: Ribs and clavicle least common sites involved
- Langerhans cell histiocytosis with bone involvement

Chest Wall Trauma

• Healing rib fractures and hematomas may mimic malignancy

Elastofibroma Dorsi

- Benign lesion, unknown etiology
- Soft tissue mass with linear streaks of fat
- Sub- or infrascapular, often bilateral

Primary Chest Wall Neoplasms

• Rare

- Multiple myeloma (plasmacytoma), chondrosarcoma, enchondroma
- Neurogenic neoplasms: Neurofibroma, schwannoma, malignant peripheral nerve sheath tumor, neuroblastoma, ganglioneuroblastoma, ganglioneuroma
- Mesenchymal neoplasms: Lipoma, fibromatosis, malignant fibrous histiocytoma, fibrosarcoma
- Ewing sarcoma family of tumors

Neurofibromatosis

- Multiple neurogenic neoplasms along neurovascular bundles
- Pressure erosion of ribs/vertebrae (50%)
- Malignant peripheral nerve sheath tumor (rare)

Vascular Lesions

• Arteriovenous malformation, aneurysm, hemangioma

Desmoid-Type Fibromatosis/Aggressive Fibromatosis

- Locally aggressive soft tissue mass(es), invade surrounding structures
- No metastatic potential, high recurrence rate

PATHOLOGY

General Features

- Rare calcification: Osteosarcoma, treated lymphoma
- Patterns of metastatic spread
 - Direct extension
 - Lung cancer (Pancoast tumor), inflammatory pseudotumor, carcinosarcoma
 - Breast cancer
 - Malignant thymic neoplasm, lymphoma, other mediastinal tumors
 - Malignant pleural mesothelioma
 - Hematogenous spread: Melanoma, thyroid, renal, hepatocellular cancers
 - Lymphatic spread: Lung cancer, breast cancer, lymphoma

Staging, Grading, & Classification

- Lung cancer
 - Direct chest wall invasion: At least T3
 - o Scalene or supraclavicular lymph node metastases: N3
 - o Hematogenous chest wall metastases: M1b
- Breast cancer
 - Axillary, subpectoral, supraclavicular, internal thoracic lymph node metastases
 - o Direct invasion of ribs, sternum, chest wall
 - o Hematogenous rib, sternum, vertebral metastases
 - Local recurrence in resection margin or scar
- Melanoma
 - Regional lymph nodes: 70%
 - o Skin, subcutaneous fat, muscle: 70%

- o Bone: 23-49%
- Prostate cancer
 - Vertebrae > sternum > pelvis > ribs

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Local pain, palpable mass
 - Chronic infection or ulceration
 - Symptoms related to primary malignancy
 - o < 25% asymptomatic
 - B symptoms in lymphoma

Demographics

- Epidemiology
 - Most common primaries: Lung, breast, prostate, renal, colon cancers and melanoma
 - Less common primaries: Ovarian, thyroid cancers
 - o Chest wall invasion in 5-8% of patients with lung cancer
 - Seeding of biopsy tracts in lung cancer and mesothelioma
 - Seeding of pleural drainage tracts in malignant pleural effusions
 - Metastases from unknown primary: Often melanoma, breast and colon cancers

Natural History & Prognosis

- Lung cancer
 - N3 disease: Approximately 9% 5-year survival
 - o M1 disease: Approximately 13% 5-year survival
- Breast cancer chest wall recurrence in 5-20%; poor prognostic indicator

Treatment

- Chemotherapy and radiation therapy most common
- Surgical resection may be considered
 - Isolated metastases, locally recurrent breast cancer
 - Resection of isolated rib involvement may be considered
 - Palliation: Pain, chronic ulceration, infection
 - Omental flaps, muscular flaps, prosthetic material for reconstruction
 - Depending on resection margin, histology, smoking history
 - Sarcomas and melanoma have poor prognosis after resection

DIAGNOSTIC CHECKLIST

Consider

• CT- or ultrasound-guided biopsy for diagnosis confirmation and for metastases from unknown primary malignancies

Image Interpretation Pearls

- Rib/bone destruction: Most specific imaging findings of chest wall metastases
- CT and MR complementary when evaluating direct extension of malignancy

- McCann MR et al: Smooth muscle conditions of the chest: a clinical, radiologic, and pathologic review. J Thorac Imaging. 36(5):263-78, 2021
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Chest Wall Metastases





(Left) Axial CECT of a patient with aggressive fibromatosis shows soft tissue infiltration of the chest wall musculature \mathbf{E} , which is subtle on chest CT, unless there is gross structural distortion of normal tissues (poorly visualized in this case). (Right) Axial T1W C+ FS MR of the same patient allows visualization and characterization of multifocal high signal intensity enhancing soft tissue lesions 🛃 in the chest wall musculature. MR imaging allows documentation of extent of soft tissue infiltration and involvement.





(Left) Axial CECT shows multifocal osteoblastic metastases involving the ribs, vertebrae, and sternum. Note soft tissue component of the right anterior rib metastasis, which may exhibit the incomplete border sign on radiography. The ribs and vertebrae are the most common sites of skeletal metastases from prostate cancer. (Right) Axial CECT of a patient with metastatic renal cell cancer shows a heterogeneously enhancing left supraclavicular metastasis \square , consistent with coalescent metastatic lymphadenopathy.





(Left) Axial CECT of a patient with metastatic melanoma to the left breast shows a diffusely infiltrative heterogeneously enhancing soft tissue mass ⇒ that replaces the normal left breast soft tissues. Such lesions may mimic primary breast cancer. (Right) Axial CECT of a patient with advanced breast cancer shows metastatic right axillary ⇒ and right internal mammary [≥] lymphadenopathy.

TERMINOLOGY

• Malignant cartilage-forming tumor of bone IMAGING

Dadiogram

- Radiography • Anterior chest wall mass
 - Sternum, costochondral junction (first five ribs)
 - Incomplete border sign
 - Soft tissue cartilaginous calcifications
 - Bone destruction
- CT
 - Well-circumscribed anterior chest wall mass
 - Soft tissue components, chondroid calcifications
 - Bone destruction
- MR
 - T2WI: High signal intensity, low signal intensity foci represent calcification
- Bone scan: > 80% show increased activity
- FDG PET/CT: High SUV correlates with high-grade tumors

TOP DIFFERENTIAL DIAGNOSES

- Chest wall metastasis
- Ewing sarcoma family of tumors (Askin)
- Osteosarcoma
- Chest wall lymphoma

PATHOLOGY

• Most common primary chest wall malignancy

CLINICAL ISSUES

- Palpable painful anterior chest wall mass
- 4th-7th decades of life
- Male > female
- Treatment: Complete surgical resection with wide margins; refractory to chemotherapy and radiation therapy

DIAGNOSTIC CHECKLIST

• Consider chondrosarcoma in adult with anterior chest wall mass with chondroid calcifications

(Left) Axial CECT (bone window) of a 52-year-old man shows a lobulated partially calcified mass ₽ involving a left anterior rib with calcified chondroid matrix \blacksquare , which is a typical feature of chondrosarcoma. (Right) Axial NECT (soft tissue window) of a 63-year-old woman shows a low-attenuation right anterior chest wall mass with scattered calcifications 🔁. High-grade chondrosarcomas tend to exhibit large areas of noncalcified tumor matrix, as in the case.





(Left) Axial CECT (soft tissue window) of a 64-year-old woman with anterior chest wall pain shows a well-defined mass with prominent chondroid matrix calcification ightarrow arising from the posterior sternum 🛃 and extending into the mediastinum. (Right) Axial fused FDG PET/CT of the same patient shows FDG avidity within the mass. High metabolic activity on PET/CT correlates with high-grade tumors. Distant metastases are present in 10% of patients at initial staging and can be *identified on PET/CT.*





Definitions

• Malignant cartilage-forming tumor of bone

IMAGING

General Features

- Best diagnostic clue
 - o Chest wall mass + bone destruction + chondroid matrix
- Location
 - Sternum and costochondral junction (first five ribs)
- Size
 - Variable size; often palpable
- Morphology
 Well-circumscribed lobulated soft tissue mass

Radiographic Findings

- Anterior chest wall mass
 Sternum, costochondral junction
- Incomplete border sign
- Soft tissue ± cartilaginous calcifications
- Endosteal scalloping, cortical disruption, bone destruction

CT Findings

- NECT
 - o Well-circumscribed anterior chest wall mass
 - Soft tissue component
 - Chondroid calcifications; rings, arcs, stippled
 - Aggressive behavior: Endosteal scalloping, cortical disruption, bone destruction, extension to soft tissue

MR Findings

- T1WI: Variable signal intensity
- T2WI: High signal intensity; low signal intensity foci correspond to calcification

Imaging Recommendations

- Best imaging tool
 - CT is imaging modality of choice

Nuclear Medicine Findings

- Bone scan
 - o > 80% of lesions show increased activity
- PET/CT
 - FDG-avid: High SUV suggests high-grade tumor
 - Useful in detecting distant metastases

DIFFERENTIAL DIAGNOSIS

Chest Wall Metastasis

- Most common malignant chest wall neoplasm
- Common primaries: Lung, breast, and prostate cancers
- Multiple myeloma; painful lytic plasmacytoma

Ewing Sarcoma Family of Tumors (Askin)

- Young adults
- Osteolytic or osteoblastic skeletal involvement
- Frequent distant metastases

Osteosarcoma

- Osteoid matrix
- Frequent distant metastases

Chest Wall Lymphoma

- Soft tissue mass
- Surrounds rather than destroys adjacent bones

PATHOLOGY

General Features

- Etiology
 - Primary chondrosarcoma arises de novo
 - Secondary chondrosarcomas may occur in preexisting benign enchondroma or osteochondroma
- Up to 10% of chondrosarcomas are radiation-induced
- Chondrosarcoma: Most common primary chest wall malignancy
- Central chondrosarcomas arise in medullary cavity
- Peripheral chondrosarcoma arises from preexistent chondroma or osteochondroma

Staging, Grading, & Classification

• Histologic grades 1-3 based on mitotic activity, staining pattern, nuclear size, cellularity

Gross Pathologic & Surgical Features

- Gray lobulated mass
- Intrinsic calcification and central necrosis
 - o Well-organized calcific rings with low-grade tumors

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Palpable painful anterior chest wall mass

Demographics

- Age
- 4th-7th decades of life
- Sex
 - o Male > female

Natural History & Prognosis

- 10% of patients present with lung metastases
- Poor prognosis with high-grade tumors and metastases
- Lesion size and location do not predict outcome

Treatment

- Complete surgical resection with wide margins
- Refractory to chemotherapy and radiation therapy

DIAGNOSTIC CHECKLIST

Consider

• Chondrosarcoma in adult with palpable anterior chest wall mass with chondroid calcifications

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TERMINOLOGY

- Solitary plasmacytoma of bone (SPB)
- Extramedullary plasmacytoma (EMP)
- Multiple myeloma (MM)

IMAGING

- SPB and MM: Axial skeleton
- EMP: Upper aerodigestive tract

Radiography

- Small lesions may be occult
- Osseous destruction; lytic lesions
- Soft tissue mass; incomplete border sign
- CT
 - SPB: Lytic bone lesion ± soft tissue mass
 - MM: Multiple lytic lesions
 - CT superior to MR for cortical destruction
 - Soft tissue attenuation similar to muscle
 - Variable enhancement of soft tissue mass

- MR
 - Untreated: T1 hypointense; T2/STIR hyperintense; diffuse enhancement
 - Treated: Variable appearance
 - No active disease: T1 hyperintense; T2/STIR hypointense; no enhancement
- PET/CT
 - Disease extent and treatment response

TOP DIFFERENTIAL DIAGNOSES

- Chest wall metastases
- Cartilaginous and osseous neoplasms

CLINICAL ISSUES

- Treatment
 - SPB: Lowest recurrence with surgery and radiation
 - MM: Chemotherapy, selective transplantation
- Progression to MM: 50% SPB, 15% EMP
- Survival: EMP > SPB > MM; younger > older

(Left) Axial CECT of a patient with left posterior chest wall pain demonstrates a large heterogeneous mass \supseteq in the left posterior chest wall. Internal regions of low attenuation represent necrosis 🔁 Biopsy revealed solitary plasmacytoma of bone. (Right) Fused axial FDG PET/CT of the same patient shows FDG avidity in the majority of the lesion and decreased FDG $uptake \ge$ in the necrotic areas. FDG PET/CT can be used to assess disease burden, extramedullary involvement, and response to therapy.





(Left) Whole-body FDG PET of a patient with multiple myeloma demonstrates innumerable profuse foci of increased FDG uptake representing myelomatous lesions 🔁 (Right) Axial NECT (bone window) of the same patient shows lytic lesions in a right posterior rib \square and thoracic vertebral body 🔁. Whole-body low-dose CT is superior to skeletal survey for identification of lesions, assessment of risk of pathologic fracture, and evaluation of extramedullary disease.





Abbreviations

- Solitary plasmacytoma of bone (SPB)
- Extramedullary plasmacytoma (EMP)
- Multiple myeloma (MM)

Definitions

- SPB: Solitary plasma cell tumor of bone
- EMP: Solitary plasmacytoma arising in soft tissues
- MM: Neoplastic proliferation of plasma cells
- o Monoclonal gammopathy; multiple bone lesions

IMAGING

General Features

- Best diagnostic clue
 - Lytic bone lesion(s)
 - o Soft tissue mass(es)
- Location
 - SPB and MM: Bones with active hematopoiesis
 - Skull, thoracic skeleton, vertebral bodies
 - Pelvis, proximal humeri and femora
 - EMP: Upper aerodigestive tract

Radiographic Findings

- Radiographically occult if small
- Chest wall soft tissue mass; incomplete border sign
- Osseous destruction: Lytic bone lesions; may be advanced on skeletal survey

CT Findings

- NECT
 - SPB: Expansile lytic bone lesion ± soft tissue mass
 - EMP: Soft tissue attenuation similar to muscle
 - MM: Multiple lytic lesions
 - Whole-body low-dose CT superior to skeletal survey
 - More accurate (sensitivity of 70%, specificity of ~ 90%)
 Better for assessing risk of pathologic fracture,
 - extramedullary disease
- CECT
 - o Variable enhancement of soft tissue component

MR Findings

- T1WI
 - SPB: Hypo- to isointense
 - MM: Homogeneously hypointense (untreated)
 - Heterogeneous (treated)
 - Hyperintense (no active disease)
- T2WI
 - SPB: Iso- to hyperintense to muscle
 - MM: Hyperintense (untreated)
 - Heterogeneous (treated)
 - Hypointense (no active disease)
- T1WIC+
 - SPB: Variable enhancement
 - MM: Diffuse enhancement (active disease); no enhancement (no active disease)

Nuclear Medicine Findings

- Bone scan
 - o Sensitivity less than skeletal survey

• PET/CT

- Assessment of disease burden, extramedullary involvement, monitoring therapy
- o Successful treatment: Decreased or absent FDG uptake

DIFFERENTIAL DIAGNOSIS

Chest Wall Metastases

- Variable appearance according to primary malignancy
 Sclerotic lesions: Prostate cancer, breast cancer
- Lytic lesions: Renal cell cancer, thyroid cancer
- MR: T1 hypointense, T2 hyperintense

Cartilaginous and Osseous Neoplasms

- Chondrosarcomas: Soft tissue mass ± matrix
 MR: T1 isointense to muscle; T2 hyperintense to fat
- Osteosarcomas: Neoplastic new bone, disorganized
 ossification
 - MR: T1 hyperintense; T2 iso-/hyperintense (to muscle)

PATHOLOGY

Staging, Grading, & Classification

- Durie-Salmon PLUS system
 - o Imaging criteria
 - IA: Limited disease or single plasmacytoma
 - IB: < 5 focal lesions; mild diffuse disease
 - IIA, IIB: 5-20 focal lesions; moderate diffuse disease
 - IIIA, IIIB: > 20 focal lesions; severe diffuse disease
- International staging system: No imaging criteria

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - SPB: Focal pain at site of lesion
 - o EMP: Epistaxis, rhinorrhea, nasal obstruction
 - o MM: Bone pain, renal failure, anemia

Demographics

- Age
 - o SPB, EMP: 50 years; MM: 50-70 years
- Sex

o **2/3 M**; 1/3 F

- Epidemiology
 - SPB, EMP: 5-10% of malignant plasma cell tumors
 MM: 10% of hematologic tumors; 1% overall

Natural History & Prognosis

- Progression to MM: 50% SPB, 15% EMP
- SPB: 25-40% disease free at 10 years
- MM: Median survival 44.8 months
- Survival: EMP > SPB > MM; younger > older

Treatment

- SPB: Lowest recurrence with surgery and radiation
 Development of MM in 3 years with radiation alone
 Adjuvant chemotherapy delays conversion to MM
- MM: Chemotherapy, selective transplantation

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TERMINOLOGY

IMAGING

• Radiography

- Diaphragmatic elevation on frontal chest radiography
- Anterior diaphragmatic elevation on lateral chest radiography (focal eventration)
- Preservation of anterior &/or posterior costophrenic angles: HH:APD ratio > 0.28

• Fluoroscopy

• Eventration: Negative sniff test with inspiratory lag followed by delayed downward motion

• CT

o Useful when radiography is inconclusive or when eventration mimics mass

TOP DIFFERENTIAL DIAGNOSES

- Diaphragmatic paralysis
- Diaphragmatic tear
- Morgagni diaphragmatic hernia
- Subpulmonic pleural effusion

PATHOLOGY

- Congenital failure of fetal diaphragm to muscularize
- Thin diaphragmatic tendon and membranous muscle; decreased muscle fibers
- Permanent diaphragmatic elevation
- Usually unilateral, rarely bilateral

CLINICAL ISSUES

- Adults over 60 years of age
- Women typically affected
- Characteristic benign course with good prognosis

(Left) Graphic demonstrates the characteristic morphology of diaphragmatic eventration characterized by hump-like elevation of the anterior hemidiaphragm. Note that the posterior costophrenic angle is normally located. (Right) PA chest radiograph of a patient with right diaphragmatic eventration shows elevation of the right hemidiaphragm \square and adjacent subsegmental atelectasis. Atelectasis is more commonly seen in the context of diaphragmatic paralysis but may also occur in cases of severe diaphragmatic eventration.





(Left) Lateral chest radiograph of the same patient shows marked elevation of the right hemidiaphragm \square , which exhibits a hump-like morphology. Note that the *right posterior costophrenic* angle \square is preserved, and at a similar level when compared to the left. This feature is helpful in differentiating diaphragmatic eventration from diaphragmatic paralysis. (Right) Coronal NECT of the same patient shows elevation of the right hemidiaphragm →. Note associated adjacent right basilar subsegmental atelectasis 🔁





Definitions

• Congenital nonparalytic weakening and thinning of anterior portion and dome of hemidiaphragm

IMAGING

General Features

- Best diagnostic clue
 - Lobulated elevation or smooth hump-like morphology of anteromedial hemidiaphragm
 - **Preservation of posterior costophrenic angle** on lateral chest radiography
- Location
 - Right hemidiaphragm usually affected
 - Typically **anteromedial** portion of hemidiaphragm

Radiographic Findings

- Radiography
 - o Diaphragmatic elevation on frontal chest radiography
 - Anterior diaphragmatic elevation on lateral chest radiography (focal eventration)
 - Preservation of anterior &/or posterior costophrenic angles: HH:APD ratio> 0.28
 - HH = hemidiaphragm height
 - APD = anteroposterior diameter
 - May mimic intrathoracic mass

Fluoroscopic Findings

- Chest fluoroscopy
 - Sniff test
 - Technique: Rapid and forced inhalation through nose with closed mouth
 - Normal: Sharp brief downward displacement of both hemidiaphragms
 - Eventration: Negative sniff test with inspiratory lag followed by delayed downward motion
 - Total eventration: May be indistinguishable from diaphragmatic paralysis; false-positive sniff test

CT Findings

- Useful when radiography is inconclusive or when eventration mimics mass
- Intact but thinned diaphragmatic muscle and tendon
- Coronal/sagittal reformatted images help confirm diaphragmatic integrity

MR Findings

- Similar to CT findings
- Intact but thinned diaphragmatic muscle and tendon Respiratory gating or real-time imaging necessary for
- accurate characterization

Ultrasonographic Findings

- Evaluation of real-time diaphragmatic motion
- Can be performed at bedside

Imaging Recommendations

- Best imaging tool
 - Chest radiography is typically diagnostic
 - Fluoroscopy (sniff test) &/or CT may be useful in equivocal cases

DIFFERENTIAL DIAGNOSIS

Diaphragmatic Paralysis

- Positive sniff test
- Anterior and posterior costophrenic angles often elevated: HH:APD ratio < 0.28

Diaphragmatic Tear

- History of high-energy blunt or penetrating chest trauma
- Associated fracture, hemothorax, pneumothorax, pulmonary contusion
- Indentation of abdominal viscera &/or bowel at site of laceration (collar or waist sign)

Morgagni Diaphragmatic Hernia

- Right cardiophrenic angle, obscures right heart border
- Contains variable amounts of omental fat and bowel

Subpulmonic Pleural Effusion

- Lateral decubitus radiography demonstrates free fluid
- Ultrasound shows subpulmonic pleural fluid

PATHOLOGY

General Features

- Etiology
- Congenital failure of fetal diaphragm to muscularize
 Associated abnormalities
- Usually unilateral, rarely bilateral
 Rare association with Poland syndrome: Unilateral
- absence of chest wall muscles on one side of body and abnormally short, ipsilateral hand webbed fingers

Gross Pathologic & Surgical Features

- Permanent diaphragmatic elevation
- Thin diaphragmatic tendon and membranous muscle; decreased muscle fibers
- Preservation of diaphragmatic continuity and costal attachments

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Adults: Often asymptomatic
 - Children: Cardiopulmonary distress

Demographics

- Age
 - Adults over 60 years of age
- Sex
 - Women typically affected

Natural History & Prognosis

• Characteristically benign course; good prognosis

Treatment

- Asymptomatic adults do not require treatment
- Surgical repair: Extreme cases, symptomatic children

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TERMINOLOGY

- Extreme form of diaphragmatic weakness
- Decreased strength of diaphragmatic musculature

IMAGING

- Radiography
 - Diaphragmatic elevation
 - Hemidiaphragm height (HH)/anteroposterior diameter (APD) < 0.28
- Fluoroscopy (sniff test)
 - Diagnostic study of choice
 - Paralysis; absent or paradoxical upward motion
- CT
 - Diaphragmatic elevation
 - Identification of etiology of paralysis
- Ultrasound
 - o Absent caudal movement on inspiration
 - Paradoxical movement on sniff test

TOP DIFFERENTIAL DIAGNOSES

- Diaphragmatic eventration
 - o Congenital failure of muscular development
- Negative sniff test
- Subpulmonic pleural effusion
 - May simulate diaphragmatic elevation
 - Free pleural fluid on decubitus radiography

CLINICAL ISSUES

- Signs/symptoms
 - Unilateral paralysis; asymptomatic in 50%
 - Orthopnea, tachypnea, chest pain, cough
 - o Bilateral paralysis; more severe symptoms
- Treatment
 - o Unilateral: Usually no treatment required
 - Bilateral: Mechanical ventilation, tracheostomy
- Prognosis
 - Poor if paralysis is bilateral or associated with myopathy

(Left) NECT AP chest scout view of a patient with right diaphragmatic paralysis shows moderate elevation of the right hemidiaphragm 🔁 and a normal left hemidiaphragm. Diaphragmatic elevation is a nonspecific sign that can also be present in eventration and subpulmonic pleural effusion. (Right) Coronal NECT of the same patient shows nonspecific elevation of the right hemidiaphragm. CT is helpful in depicting potential structural abnormalities that *may produce diaphragmatic* paralysis (e.g., superior sulcus tumor).

(Left) AP fluoroscopic spot chest radiograph during inspiration demonstrates elevation of the left hemidiaphragm. (Right) AP fluoroscopic spot chest radiograph during sniff test (expiration) shows normal excursion of the right

of motion of the left hemidiaphragm. The

diaphragmatic eventration

with COPD and in weak, debilitated patients.









Diaphragmatic Paralysis

TERMINOLOGY

Synonyms

- Diaphragmatic **palsy**
- Diaphragmatic **paresis**
- Diaphragmatic weakness

Definitions

- Extreme form of diaphragmatic weakness
- Decreased strength of diaphragmatic musculature

IMAGING

General Features

- Best diagnostic clue
 - Absent or paradoxical diaphragmatic motion on chest fluoroscopy (**sniff test**)

Radiographic Findings

- Normal findings
 - Right hemidiaphragm typically higher than left
 - Equal heights of right and left hemidiaphragms in 9%
 Overlap in range of motion of normal compared to
 - paralyzed hemidiaphragm
- Diaphragmatic elevation without paralysis
 Bilateral elevation from low lung volume
 - Pulmonary fibrosis
 - o Unilateral elevation from relaxation atelectasis
- Diaphragmatic paralysis
 - Diaphragmatic elevation
 - Identification of associated thoracic malignancy or infection
 - **HH/APD** = Ratio of hemidiaphragm height (HH) to anteroposterior diameter (APD)
 - APD = Distance from anterior to posterior diaphragmatic insertions on lateral radiography
 - **HH** = Perpendicular height from APD to dome
 - HH/APD < 0.28 suggests diaphragmatic paralysis

CT Findings

- Diaphragmatic elevation
- Identification of etiology of diaphragmatic paralysis

MR Findings

- Real-time diaphragm imaging; only considered when other methods are inconclusive
- May be useful for long-term follow-up and monitoring of therapeutic interventions

Ultrasonographic Findings

- Absent caudal diaphragm movement on inspiration
- Paradoxical diaphragmatic movement on sniff test during M (motion) mode

Imaging Recommendations

- Best imaging tool
- Chest fluoroscopy
 - Normal diaphragmatic dome excursion: 3-5 cm
 - Sniff test
 - Technique: Rapid forced inhalation through nose with closed mouth
 - Normal: Sharp brief downward motion of both hemidiaphragms

- Paralysis: Absent or paradoxical upward motion
- False-positive sniff test: COPD, weak, debilitated patients

DIFFERENTIAL DIAGNOSIS

Diaphragmatic Eventration

- Congenital failure of diaphragm muscle development
 Thin membranous hemidiaphragm
 - Decreased muscle fibers
- Asymptomatic adults, respiratory distress in infants
- Imaging clues
 - Negative sniff test
 - Absence of relaxation atelectasis
 - HH/APD > 0.28

Subpulmonic Pleural Effusion

- May simulate diaphragmatic elevation
- Free pleural fluid on lateral decubitus radiography
- Ultrasound demonstration of subpulmonic fluid

PATHOLOGY

General Features

- Etiology
 - o Trauma, postsurgical
 - Nerve root compression or invasion from malignancy
 - o Inflammatory
 - Neuropathic
 - o Idiopathic, minority of cases

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - o Unilateral paralysis; more common than bilateral
 - Asymptomatic in 50% of cases
 - Orthopnea, tachypnea, chest pain, cough
 - Inward motion of abdomen during inspiration
 - Bilateral paralysis; more severe symptoms
 - Exertional dyspnea, orthopnea
 - Cor pulmonale
 - Increased incidence of pneumonia
 - Decreased oxygenation and vital capacity on supine position, worse with bilateral paralysis
 - Restrictive pattern on pulmonary function tests

Natural History & Prognosis

 Poor prognosis if paralysis is bilateral or associated with myopathy, chronic demyelinating condition, or coexistent COPD or pulmonary fibrosis

Treatment

- Unilateral: Usually no treatment required; surgical plication and phrenic pacing in selected cases
- Bilateral: Mechanical ventilation &/or tracheostomy

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