Chronic Airspace Diseases

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Airspace disease can be acute or chronic and commonly present as consolidation or ground-glass opacity on chest imaging. Consolidation or ground-glass opacity occurs when alveolar air is replaced by fluid, pus, blood, cells, or other material. Airspace disease is considered chronic when it persists beyond 4-6 weeks after treatment. These can be secondary to certain infectious, inflammatory, or neoplastic conditions. Computed tomography of the chest is usually performed in this set of patients to identify characteristic imaging findings. Familiarity with the differential diagnosis and characteristic imaging findings for chronic airspace disease is very important for guiding patient's management in a timely fashion.
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Introduction

Lung consolidation and ground-glass opacity are common radiologic findings on chest imaging. These occur when alveolar air is replaced by fluid, pus, blood, cells, or other material. Airspace disease can be acute or chronic and have a wide range of differential diagnosis. If the disease persists beyond 4-6 weeks after treatment, differential diagnosis for chronic airspace disease should be considered. Certain types of infectious, inflammatory, and neoplastic conditions can result in chronic airspace disease (Table 1). Chest radiography is often the initial imaging modality but computed tomography (CT) scan is usually performed in this set of patients to identify characteristic imaging findings. Incorporating clinical manifestations and laboratory findings with radiologic findings can help in narrowing the differential diagnosis. In this review, we will discuss these diseases with emphasis on radiologic findings. Radiologists should be familiar with the differential diagnosis of chronic airspace disease, which would help in directing patient's management in a timely fashion.

Infectious Causes

Pulmonary Tuberculosis

Tuberculosis (TB) is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS). In 2016, there were an estimated 1.3 million TB deaths among HIV-negative people and an additional 374,000 deaths among HIV-positive people. An estimated 10.4 million people fell ill with TB in 2016.[1] Mycobacterium tuberculosis (*M. tuberculosis*) is the species responsible for the vast majority of cases and transmission of infection occurs via inhalation of droplet nuclei.[2] Reactivation or post primary or secondary TB results from reactivation of a dormant *M. tuberculosis* infection usually in the setting of decreased immunity. Patients typically present with insidious fever, cough, weight loss, and night sweats. Early diagnosis of TB is important not only to treat patients but also to prevent the spread of the infection in the community. The definitive diagnosis of pulmonary TB is established by isolating *M. tuberculosis* from a bodily secretion or tissues. Additional diagnostic tools include sputum acid-fast bacilli smear and nucleic acid amplification testing. Radiologic studies are important supportive diagnostic tools.[2]

Chest radiography is typically obtained initially to look for active disease but *CT* is considered more sensitive in determining disease activity.[3] Consolidation with or without cavitation, centrilobular nodules, and tree-in-bud opacities are the common imaging findings in reactivation TB (Fig. 1). The apical posterior segments of the upper lobes or the superior segment of the lower lobe of the lung are frequently involved due to reduced lymphatic clearance and increased oxygen tension in these regions.[4] Cavitary lesions are the radiologic hallmark of reactivation TB and may be evident radiographically in 20%-45% of patients.[5,6] Cavities are often seen within areas of consolidation and may be single or multifocal. Centrilobular nodules and tree-in-bud opacities indicate the presence of endobronchial spread of the infection

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Table 1 Chronic Airspace Diseases

Infectious causes	Pulmonary tuberculosis, Aspergillosis, mucormycosis
Inflammatory causes	Waxing and waning pattern: OP, CEP, Eosinophilic GPA
	GPA, alveolar sarcoidosis, PAP, lipoid pneumonia
	Treatment-related disease: radiation pneumonitis and drug-induced pneumonitis
Neoplastic causes	Primary lung adenocarcinoma, pulmonary lymphoma

Abbreviations: CEP, chronic eosinophilic pneumonia; GPA, granulomatosis with polyangiitis; OP, organizing pneumonia; PAP, pulmonary alveolar proteinosis.
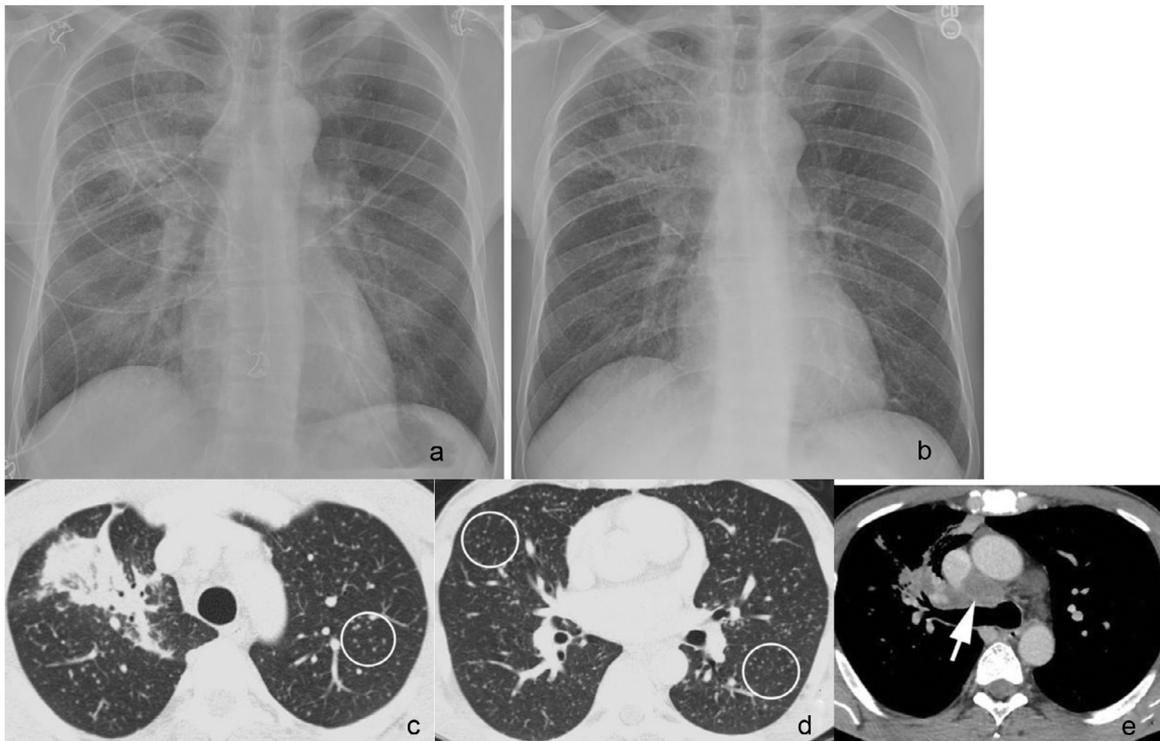

Figure 1 (a-e) Reactivation tuberculosis. Frontal chest radiograph (a) shows consolidation in the right upper lung which persisted on the follow-up radiograph (b) obtained 4 weeks after treatment with antibiotics. CT with lung window (c, d) shows consolidation in the right upper lobe and centrilobular nodules bilaterally (circles). CT with soft tissue window (e) shows mediastinal lymphadenopathy with central necrosis (arrow).

and are due to the presence of caseous necrosis and granulomatous inflammation filling the terminal and respiratory bronchioles and alveolar ducts. Tree-in-bud pattern is not specific to reactivation TB and can be seen with other infections. However, when seen in the appropriate clinical setting, this is considered a reliable marker for active TB.[7]

Pulmonary Aspergillosis

Aspergillosis is a mycotic disease caused by *Aspergillus* species, usually *Aspergillus fumigatus*, a saprophytic and ubiquitous airborne fungus.[8] The manifestations of pulmonary aspergillosis depend on the immunologic status of the host and the existence of an underlying lung disease. Pulmonary aspergillosis is traditionally classified into 4 categories[9]:

- Aspergilloma: fungus ball in pre-existing lung cavities usually resulting from old TB or fibrotic sarcoidosis.

- Allergic bronchopulmonary aspergillosis: hypersensitivity reaction to Aspergillus in asthma patients.
- Chronic pulmonary aspergillosis (Semi-invasive aspergillosis): mildly immunocompromised patients.
- Invasive (angioinvasive or airway-invasive) aspergillosis; immunocompromised patients with severe neutropenia.

Only 2 of these categories typically show chronic lung consolidation as a prominent radiologic finding: chronic pulmonary aspergillosis and angioinvasive aspergillosis.

Chronic Pulmonary Aspergillosis

Chronic pulmonary aspergillosis (semi-invasive aspergillosis or chronic necrotizing aspergillosis) is usually seen in patients with mildly impaired immune status such as diabetes mellitus, chronic obstructive pulmonary disease, chronic renal failure, chronic malnutrition, alcoholism, or chronic

steroid therapy. It is also seen in patients with underlying chronic lung disease, usually chronic obstructive pulmonary disease or old TB. Clinical presentation is nonspecific with long-standing fever, cough, and malaise. Radiologic manifestations include upper lobe predominant consolidation progressing to cavitation. Intracavitary soft tissue (necrotic tissue with fungus) can be seen. Multiple small nodular opacities and pleural thickening may appear adjacent to consolidative lung. Radiologically, it can be challenging to differentiate this from reactivation TB.[10,11]

Angioinvasive Aspergillosis

Angioinvasive aspergillosis is the most aggressive type of *Aspergillus* infection and almost exclusively seen in severely immunocompromised patients, especially with severe neutropenia in the setting of stem cell transplantation, solid-organ transplantation, immunosuppressive chemotherapy, and prolonged high-dose steroid.[8,12] Symptoms are nonspecific, so a high index of suspicion is required for early diagnosis and to reduce the high mortality rate.

The radiological findings on CT are nodules and areas of peripheral wedge-shaped consolidation surrounded by ground-glass opacity ("halo sign")[12] (Fig. 2). Surrounding ground-glass opacity is due to alveolar hemorrhage. The "halo sign" is not specific to aspergillus infection but is highly suggestive of invasive aspergillosis in a patient with neutropenia and fever. The occurrence of cavitation within a nodule or a consolidation is usually seen in the late phase of the infection (2-3 weeks after initiation of treatment) and coincides with the recovering of neutropenia. Separation of the necrotic lung fragment from the adjacent lung parenchyma results in an "air crescent sign."[12,13]

Mucormycosis

Mucormycosis is caused by fungi of the class Zygomycetes and order Mucorales.[14] It is a relatively uncommon and aggressive angioinvasive infection, which often leads to pulmonary infarction. It occurs mostly in immunocompromised patients such as those with hematological malignancies, diabetes mellitus, transplant recipients, and chronic steroid therapy. Radiological findings on initial CT include consolidation and nodules/masses with "halo sign" and peripheral distribution. Sequential follow-up CT may show "reverse halo sign" (central ground-glass opacity with surrounding dense consolidation),
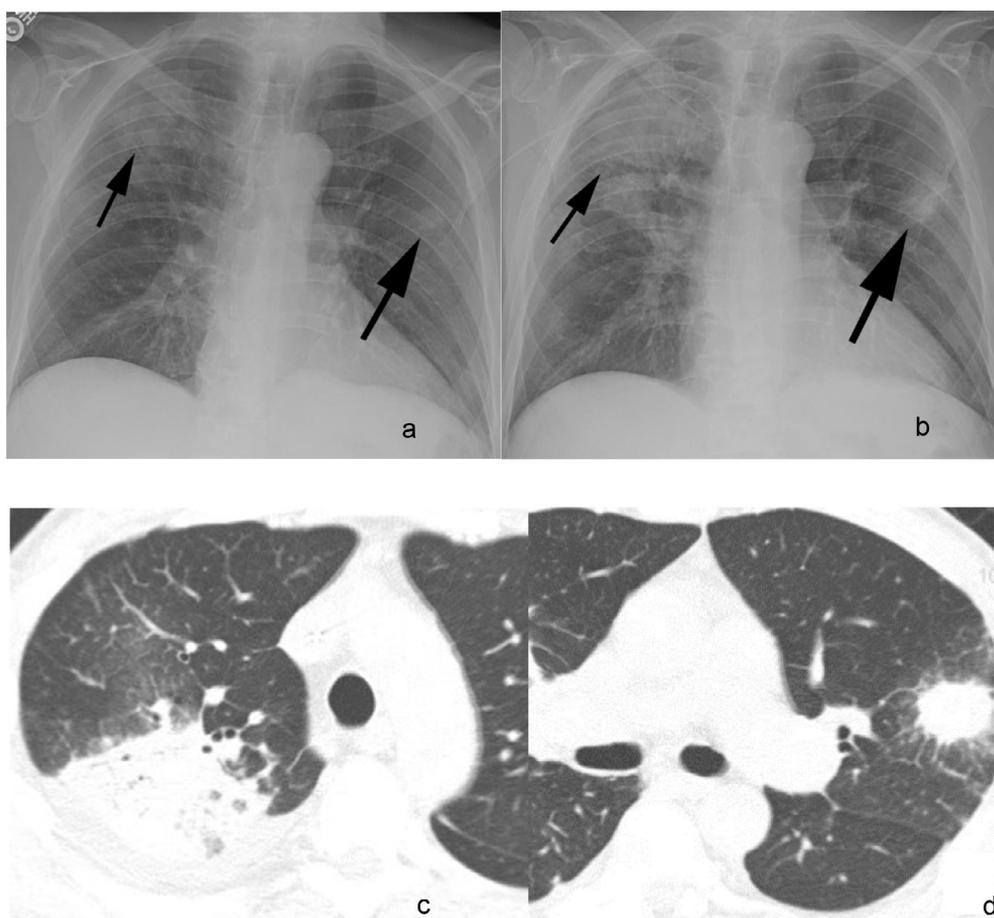

Figure 2 (a-d) Angioinvasive aspergillosis. Frontal chest radiograph (a) shows consolidation in the right upper lung (short arrow) and a nodule in the left midlung (long arrow) which increased in size on follow-up chest radiograph performed 1 week later (b). CT shows consolidation in the right upper lobe and a nodule in the left upper lobe with surrounding ground glass opacity ("halo sign").
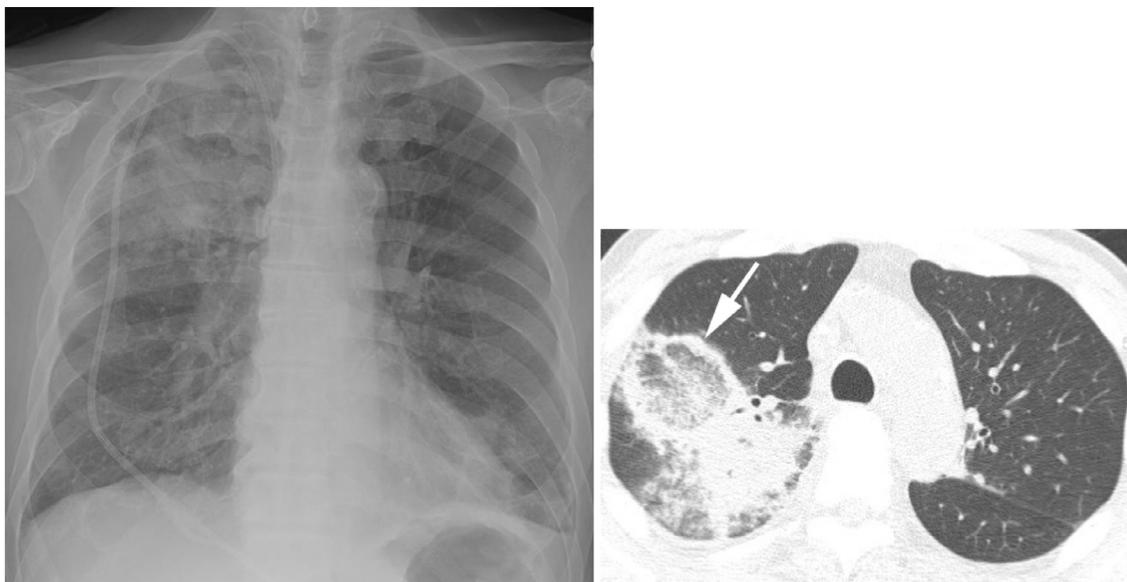
Figure 3 Mucormycosis. Chest radiograph shows consolidation in the right upper lobe. CT shows consolidation with central ground glass opacity, "reverse halo sign" (arrow).

central necrosis, cavitation and "air crescent sign" with recovery of neutrophil counts (Fig. 3). It is challenging to differentiate mucormycosis from angioinvasive pulmonary aspergillosis on the basis of radiological findings. "Reverse halo sign" is not pathognomonic for mucormycosis but highly suggestive of this entity in the appropriate clinical setting. Definitive diagnosis is made with biopsy.[15,16]

Inflammatory Causes

Waxing and Waning Pattern

Waxing and waning pattern is defined as regression of some abnormalities either spontaneously or with treatment and appearance of new abnormalities at different sites on follow-up imaging. This pattern has been described with organizing pneumonia, chronic eosinophilic pneumonia (CEP), and eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome).

Organizing pneumonia is a pattern of lung injury, which can be secondary to a wide range of etiologies or idiopathic, known as cryptogenic organizing pneumonia.[17] Common secondary causes of organizing pneumonia include infection, collagen vascular disease, drug reaction, radiation therapy, inhalation of toxic gas, or transplant rejection. cryptogenic organizing pneumonia affects males and females equally, usually in the fifth or sixth decade. Clinical presentation is subacute and common symptoms are cough, dyspnea, fever, and malaise. Histologically, organizing pneumonia is characterized by the presence of granulation tissues in the alveolar spaces and mild interstitial inflammation.[17,18]

The most common radiologic findings are patchy consolidation or ground-glass opacities in the peripheral and peri-bronchovascular distribution. Consolidation or ground-glass

opacity may show migratory pattern[18,19] (Fig. 4). Radiologically, it is difficult to differentiate this from CEP. Peripheral or bronchoalveolar lavage (BAL) eosinophilia and clinical history can help to differentiate CEP from organizing pneumonia. Another radiologic finding, which is suggestive of organizing pneumonia is the "reverse halo sign" or "atoll sign." This is defined as a central area of ground-glass opacity with peripheral crescent or ring of consolidation (Figs. 4 and 5). Differential diagnosis for "reverse halo sign" includes Granulomatosis with polyangiitis (GPA), sarcoidosis, mucormycosis, paracoccidioidomycosis, TB, and pulmonary infarction.[19,20]

The other less common findings are solitary or multiple nodules, perilobular consolidation in an arcade-like pattern around the secondary pulmonary lobules, radial bands of consolidation with air bronchogram, and subpleural curvilinear bands of consolidation. A subset of patients can progress to fibrotic disease showing peripheral reticulation and architectural distortion resembling fibrotic nonspecific interstitial pneumonia pattern of interstitial lung disease.[18,21] Although radiologic findings are not pathognomonic, these are highly suggestive of organizing pneumonia when used in combination with clinical presentation and history.

CEP is an idiopathic condition characterized by infiltration of the lungs with eosinophils. Peripheral blood eosinophilia is usually mild or moderate but can be severe occasionally. The most important finding is the increased percentage of eosinophils in the BAL fluid.[22] Patients are usually middle aged and found more commonly in women than in men. Typical clinical manifestations include chronic cough and dyspnea. Asthma can be seen in approximately 50% of the patients.[22]

Typical radiographic findings are peripheral consolidation, predominantly in the upper lobes. This has been described as "photographic negative of pulmonary edema." However, this classic radiographic pattern is seen in less than 50% of the
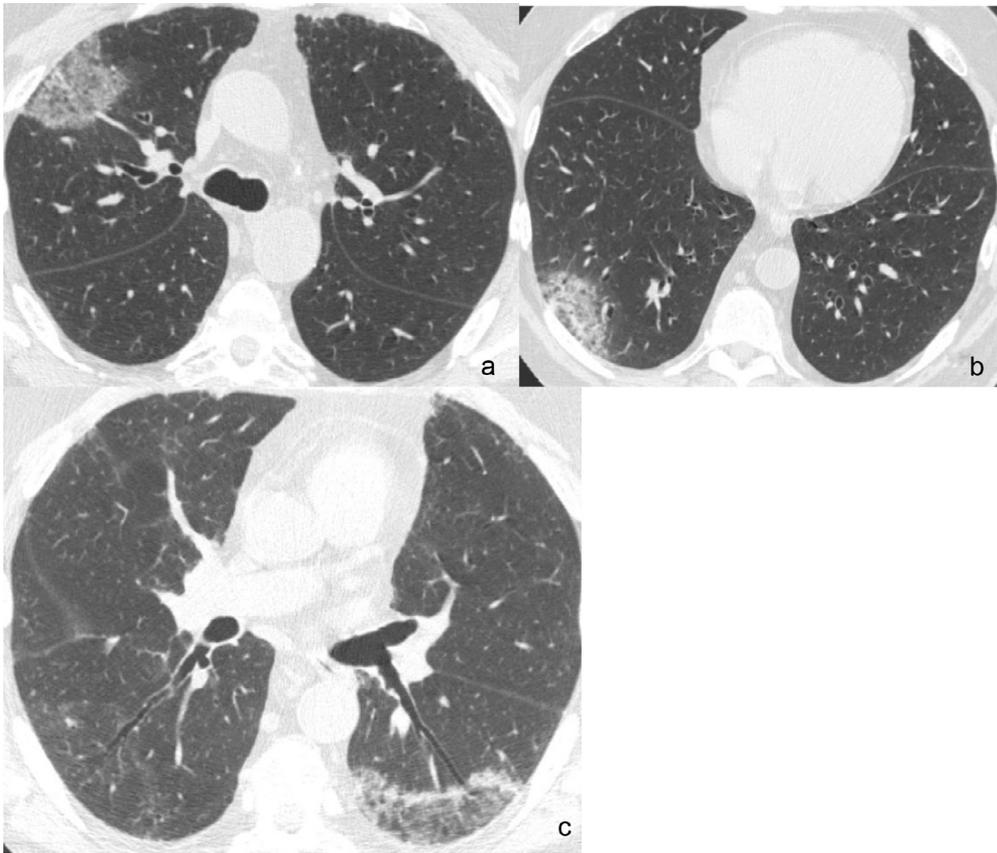
Figure 4 (a-c) Cryptogenic organizing pneumonia. CT (a, b) shows peripheral areas of ground glass opacities in the right upper and lower lobes. Follow-up CT after 3 months shows resolution of previously seen ground glass opacities (not shown) and a new area of peripheral ground glass opacity with surrounding crescentic consolidation, "reverse halo sign" or "atoll sign" (c).

cases. CT shows peripheral nonsegmental consolidation or ground-glass opacities with upper lobe predominance. These opacities can show a migratory pattern. The other less common findings are nodules and reticulation, which are usually seen in the later stage of disease.[22,23] CEP responds very well to steroids and the opacities usually resolve 7-10 days after initiation of steroid therapy.[23]
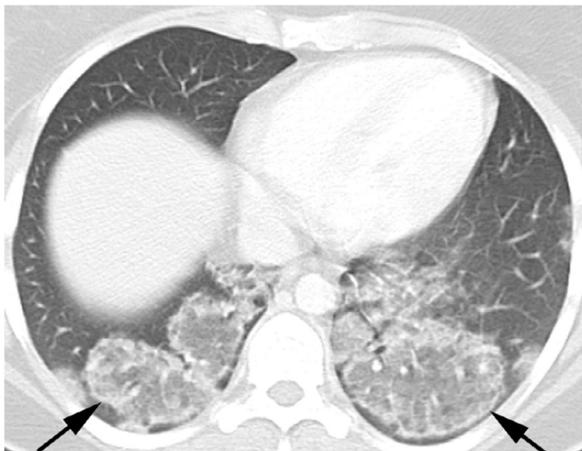

Figure 5 Cryptogenic organizing pneumonia. CT shows peripheral areas of ground glass opacities surrounded by crescentic consolidation (arrows), "atoll sign."

Eosinophilic granulomatosis with polyangiitis (eosinophilic GPA) is antineutrophil cytoplasmic autoantibody-associated systemic vasculitis characterized by asthma, hypereosinophilia, and necrotizing vasculitis. The lungs are the most common site of involvement. Histopathology shows granulomatous necrotizing vasculitis of the small arteries and eosinophil tissue infiltration.[24] The most common radiologic findings on CT are bilateral consolidation or ground-glass opacities with peripheral predominance. Air space opacities may be transient or migratory. The other less common findings include peribronchial nodular opacities, bronchial wall thickening, and centrilobular nodules due to eosinophilic infiltration of the airways.[24,25] The imaging findings are similar to CEP or organizing pneumonia. Patients with CEP do not have extra thoracic manifestations. Patients with organizing pneumonia do not have history of asthma and BAL fluid do not show increased eosinophil counts.

Granulomatosis With Polyangiitis

GPA, previously known as Wegener's granulomatosis, is antineutrophil cytoplasmic autoantibody-associated multisystemic small-vessel vasculitis that commonly affects adult between 30 and 50 years of age without sex predilection.[26]
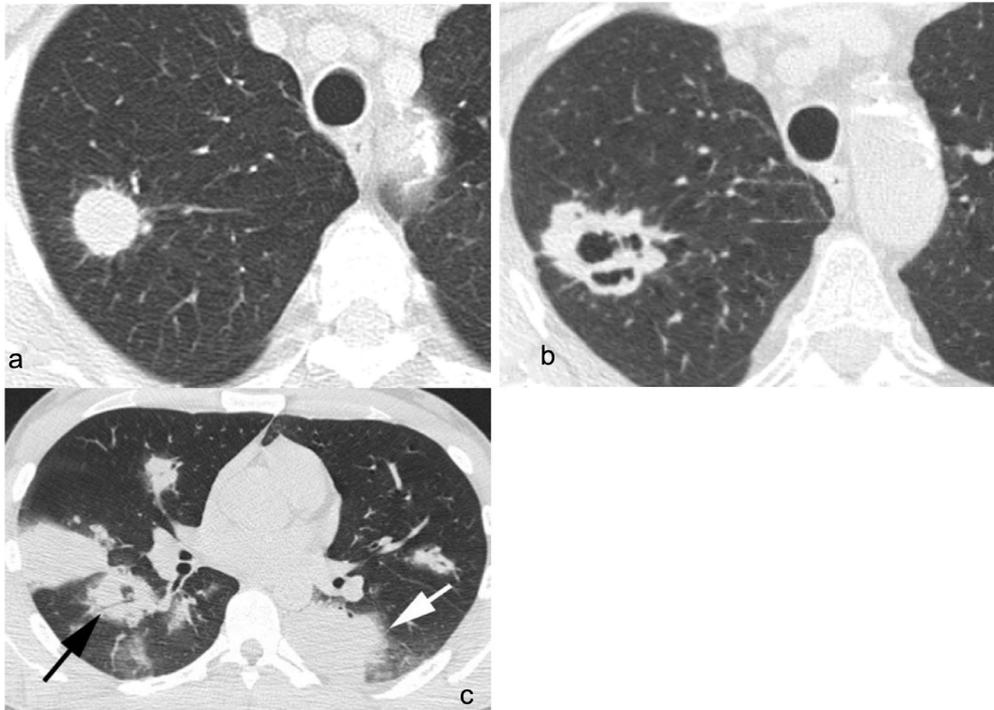
Figure 6 (a-c) Granulomatosis with polyangiitis. CT shows a nodule in the right upper lobe (a). Follow-up CT after 1 month shows increased size of the nodule and new cavitation (b). CT in a different patient shows bilateral multifocal consolidations. Right lower lobe consolidation (black arrow please move arrow back on image (c) shows central cavitation and left lower lobe consolidation shows peripheral ground glass opacity, "halo sign" (white arrow).

Clinical presentation depends upon the organ affected. Lungs are involved in up to 90% of cases and patients may clinically present with dyspnea, cough, and hemoptysis.[26] Histopathology shows necrosis, vasculitides, and granulomatous inflammation.

Pulmonary nodules or masses are the most common radiologic findings of active GPA[27] (Fig. 6). Central cavitation may be noted in up to 50% of nodules, which are larger than 2 cm in diameter.[27,28] Cavities are usually thick walled and characterized by an irregular inner margin. Ground-glass opacity around the nodules or masses (halo sign) may be seen. Consolidation or ground-glass opacity are also noted in about 30% of patients, which may result from alveolar hemorrhage[27,28] (Fig. 6).

Sarcoidosis

Sarcoidosis is a multisystem disorder of unknown etiology characterized by noncaseating epithelioid cell granulomas, which may affect almost any organ. Thoracic involvement is seen in more than 90% of patients at some time during the course of the disease.[29] Although sarcoidosis can affect patients of any age, it typically occurs in young adults less than 40 years of age with a slightly higher prevalence in women. African-Americans and Scandinavians are known to have the highest prevalence worldwide.

Clinical manifestations are nonspecific and common symptoms are cough, chest pain, and dyspnea. Some patients can also present with constitutional symptoms such as fever,

fatigue, night sweats, weight loss, or skin rash (erythema nodosum). Up to 50% of patients with sarcoidosis are asymptomatic at the time of diagnosis and abnormalities are incidentally detected on chest radiography.[29,30]

Sarcoidosis can present with a wide spectrum of radiologic findings, bilateral hilar lymphadenopathy with or without right paratracheal lymphadenopathy being the most common finding seen in about 95% of patients with thoracic involvement.[29,31] A perilymphatic distribution of micronodules (less than 5 mm) with upper lobes predominance is the most common parenchymal abnormality in patients with pulmonary sarcoidosis.[29,31] Several atypical radiologic manifestations of sarcoidosis have been described including alveolar form which shows consolidation and patchy ground-glass opacities[29,31,32] (Fig. 7). This can mimic other airspace disease processes such as pneumonia, TB, organizing pneumonia, or neoplasms. Airspace disease in sarcoidosis reflects coalescence of numerous micronodules, which compress or encroach on the alveolar spaces.[29] Consolidation is seen in up to 20% of patients with sarcoidosis. It is usually bilateral and symmetric in the upper and mid lungs with predominantly peribronchovascular distribution.[29] Patchy ground-glass opacities are seen in up to 40% of patients and often accompanied by other parenchymal abnormalities. "Revere halo sign" can be seen with the alveolar form of sarcoidosis.[31]

Pulmonary Alveolar Proteinosis

Pulmonary alveolar proteinosis (PAP) is a rare disease characterized by intra-alveolar accumulation of periodic acid-Schiff-
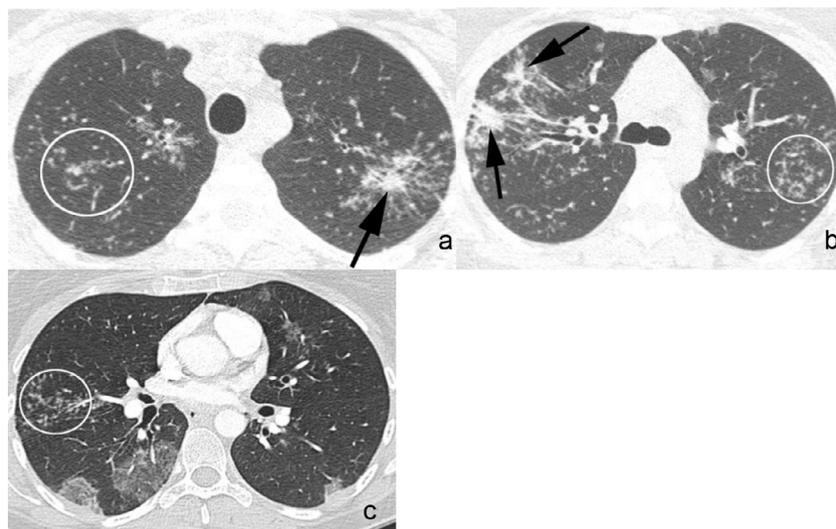
Figure 7 (a-c) Sarcoidosis. CT (a, b) shows nodular consolidations (arrows) and perilymphatic nodules (circles). CT in a different patient (c) shows patchy ground glass opacities and perilymphatic nodules (circle).

positive lipo-proteinaceous material due to impaired clearance by the alveolar macrophages or overproduction of surfactant by type 2 pneumocytes. Three distinct forms have been described: primary (idiopathic), secondary, and congenital. The primary (idiopathic) form is the most common, seen in about 90% of the patients.[33] Secondary and congenital forms are exceedingly rare. Granulocyte-monocyte colony-stimulating factor antibodies play a central role in the pathogenesis of the primary subtype while the secondary type is seen in various pulmonary infections, hematological malignancies, immunodeficiency disorders, and industrial dust exposure such as silica, aluminum, cement, or nitrogen dioxide. Clinical presentation varies from mild progressive dyspnea to respiratory failure. Although PAP affects patients of all ages, it is commonly seen in young patients in the third-fourth decade with male predominance (M:F ratio 2-4:1). Strong association with smoking has been described, approximately 75% of patients are smokers.[33,34]

The most common CT finding is the "crazy-paving" pattern, defined as a network of septal thickening on the background of ground-glass opacity (Fig. 8). This pattern was first described with PAP and is highly suggestive of the diagnosis, being present in up to 80% of the patients.[35] These areas are typically bilateral and geographic with sharp demarcation from surrounding normal lung parenchyma. The other less common findings include patchy areas of consolidation, nodules, mediastinal/hilar lymphadenopathy, and pleural effusion. Although the CT finding of crazy-paving is highly suggestive of alveolar proteinosis, it has also been described in several other conditions including pulmonary edema, alveolar hemorrhage, pneumocystis pneumonia, primary lung adenocarcinoma, lymphangitic carcinomatosis, diffuse alveolar damage, radiation- or drug-induced pneumonitis, and lipoid pneumonia.[33,35]

Although definitive diagnosis is made with lung biopsy, BAL may be diagnostic. BAL fluid has a milky appearance due to the presence of lipo-proteinaceous material and shows

characteristic finely periodic acid-Schiff-positive granular eosinophilic material with rare macrophages or inflammatory cells. The prognosis of idiopathic PAP is very good with 95%-100% 5-year survival. The main treatment is sequential therapeutic whole-lung lavage and repeat treatment is usually necessary, with a mean interval of 15 months.[34]

Lipoid Pneumonia

Lipoid pneumonia is an uncommon condition that results from accumulation of lipids in the alveoli and can be either exogenous or endogenous. Exogenous lipoid pneumonia is caused by inhalation or aspiration of animal fat or vegetable or mineral oil. Endogenous lipoid pneumonia is usually associated with bronchial obstruction.[36]

Exogenous lipoid pneumonia can be acute or chronic. The acute form is rare and is caused by aspiration of a large quantity of a petroleum-based product, typically occurring in children due to accidental poisoning, but also seen in fire-eaters who use liquid hydrocarbons for flame blowing.[36,37]

Chronic exogenous lipoid pneumonia results from repeated aspiration or inhalation of small quantities of oils over an extended period of time. It typically occurs in older patients, but has been reported in children with a predisposition to aspiration. Repeated aspiration of mineral oil for the treatment of chronic constipation in elderly patient is a frequently observed clinical scenario.[37]

Patients with chronic lipoid pneumonia may be asymptomatic or may present with progressive dyspnea and cough. The most characteristic radiologic appearance on CT is the presence of fat attenuation (<-10 HU) areas within the consolidation which is usually seen in the dependent portions of the lungs (Fig. 9). The other radiologic findings which can be seen with chronic exogenous lipoid pneumonia include "crazy-paving" pattern or nodules or masses with or without fat. Radiologically, this can mimic bacterial pneumonia or lung cancer. Fat attenuation area within the consolidation or
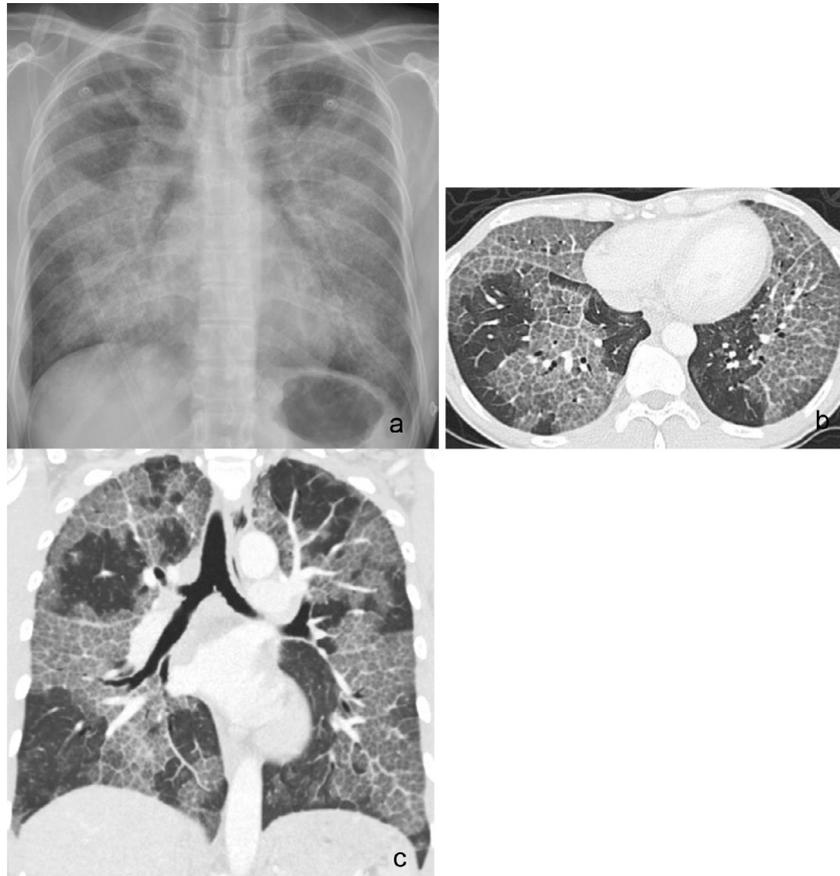
Figure 8 (a-c) Pulmonary alveolar proteinosis. Chest radiograph (a) shows diffuse airspace and reticular opacities. CT axial (b) and coronal reformation (c) images show geographic areas of ground glass opacities with septal thickening (crazy-paving). Diagnosis was confirmed with bronchoalveolar lavage (BAL) which showed milky fluid rich in periodic acid-Schiff (PAS)-positive lipoproteinaceous material.
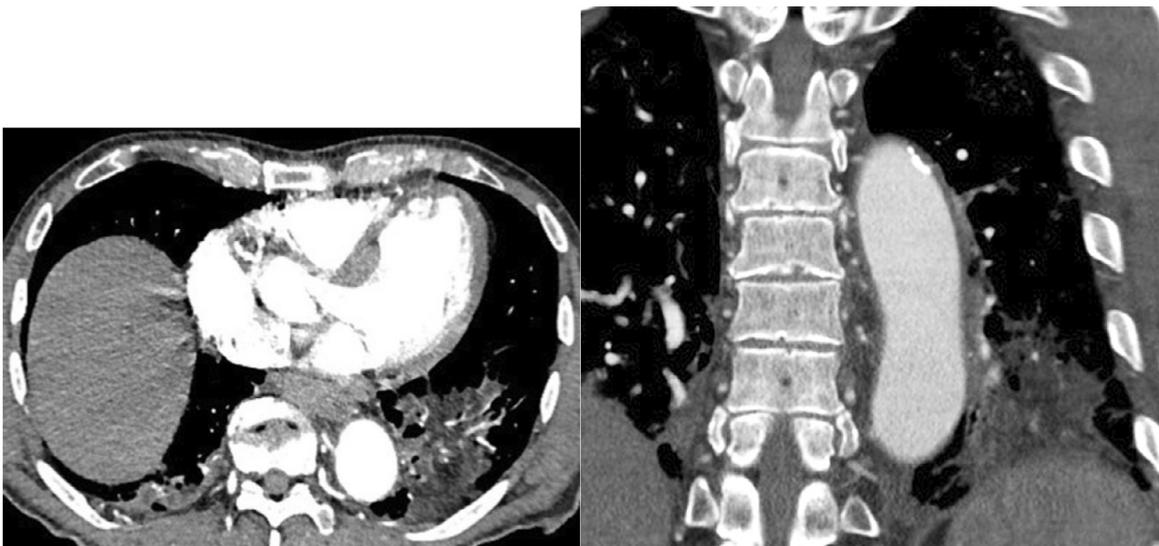

Figure 9 (a, b) Lipoid pneumonia. CT axial (a) and coronal reformation (b) images show areas of fat attenuation within the left lower lobe consolidation.

mass-like consolidation, when present, is diagnostic of lipoid pneumonia.[36-38]

Treatment-Related Diseases

Drug-induced pneumonitis comprises a wide spectrum of radiologic manifestations, which are nonspecific with no characteristic imaging pattern. Various imaging patterns which have been described in drug-induced pneumonitis include hypersensitivity pneumonitis, organizing pneumonia, acute eosinophilic pneumonia, nonspecific interstitial pneumonia, and diffuse alveolar damage[39,40] (Fig. 10). Infection and progression of underlying disease must be excluded before making the diagnosis of drug-induced pneumonitis. Clinical manifestations are nonspecific and there are no pathognomonic laboratory or pathologic findings to make the specific diagnosis of drug-induced pneumonitis. Establishing the temporal relationship between the onset of clinical symptoms, radiologic findings, administration of a suspected drug, and exclusion of other causes helps in making the diagnosis of drug-induced pneumonitis.

It is common to see the lung injury after therapeutic irradiation of lung and chest wall malignancies, mainly for lung and breast cancers. Conventional radiation techniques result in the delivery of therapeutic radiation doses to a wide area, outside the primary tumor margins. As a result, greater quantity of normal lung tissue is radiated and the risk of radiation injury increases. This also limits the maximum radiation dose that can be delivered to the tumor volume. Newer techniques such as stereotactic body radiation therapy have been developed over the past decade to reduce the toxic effects and improve the efficacy of radiation therapy.[41]

Radiation-induced lung injury is classified into 2 categories: acute radiation pneumonitis, which usually occurs 1-6 months after the completion of radiation therapy, and chronic radiation fibrosis, which usually occurs 4-12 months to years after the completion of radiation therapy. Radiologically, acute radiation pneumonitis manifests as ground-glass opacities and consolidation in the irradiated area. Nodules

within the treatment plan have also been reported. Occasionally, an ipsilateral pleural effusion can develop at the time of radiation pneumonitis. The radiological abnormalities of acute radiation pneumonitis may gradually resolve over 6 months without sequelae when the injury to the lung is limited. In cases of more severe injury, this usually progresses to radiation fibrosis, which manifests radiologically as volume loss, focal areas of consolidation, architectural distortion, and traction bronchiectasis.[41,42] Awareness of the treatment timelines, radiation technique, and treatment plan help in accurately interpreting the radiologic findings of radiation lung injury.

Neoplastic Causes
Lung Adenocarcinoma

Adenocarcinoma is the most common histologic type of lung cancer worldwide. A new classification of adenocarcinoma of the lung was published in 2011 by an international multidisciplinary committee sponsored by the International Association for the Study of Lung Cancer, the American Thoracic Society, and the European Respiratory Society.[43] This new classification has provided uniform terminology and the latest understanding of the various pathologic subtypes of adenocarcinoma of the lung. The majority of the pathologic subtypes of adenocarcinoma present as solid or subsolid (pure ground glass or part solid nodule) nodules on imaging. Radiologic presentations of various subtypes of adenocarcinoma show overlap. Invasive mucinous adenocarcinoma, previously called mucinous bronchoalveolar carcinoma, is the most common histologic subtype, which can present as a consolidation with air bronchogram on imaging. Invasive mucinous adenocarcinoma can have a wide spectrum of presentation on imaging ranging from subsolid nodules to solid nodules to consolidation.[44,45] Adenocarcinoma can be solitary or multifocal and can mimic pneumonia or organizing pneumonia radiologically (Fig. 11).
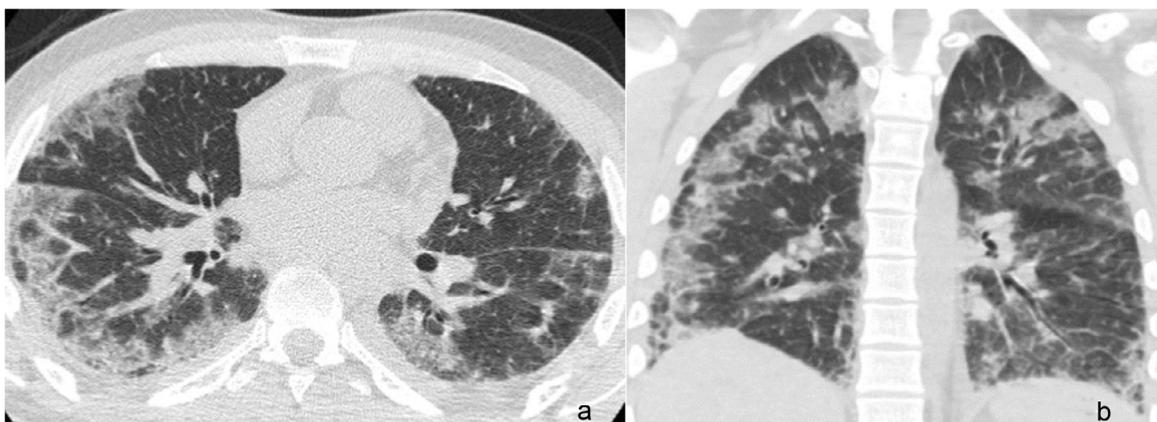

Figure 10 (a, b) Organizing pneumonia pattern secondary to bleomycin toxicity. CT axial (a) and coronal reformation (b) images show peripheral predominant ground glass opacities and mild septal thickening. Belomycin was discontinued and the patient responded to steroids.
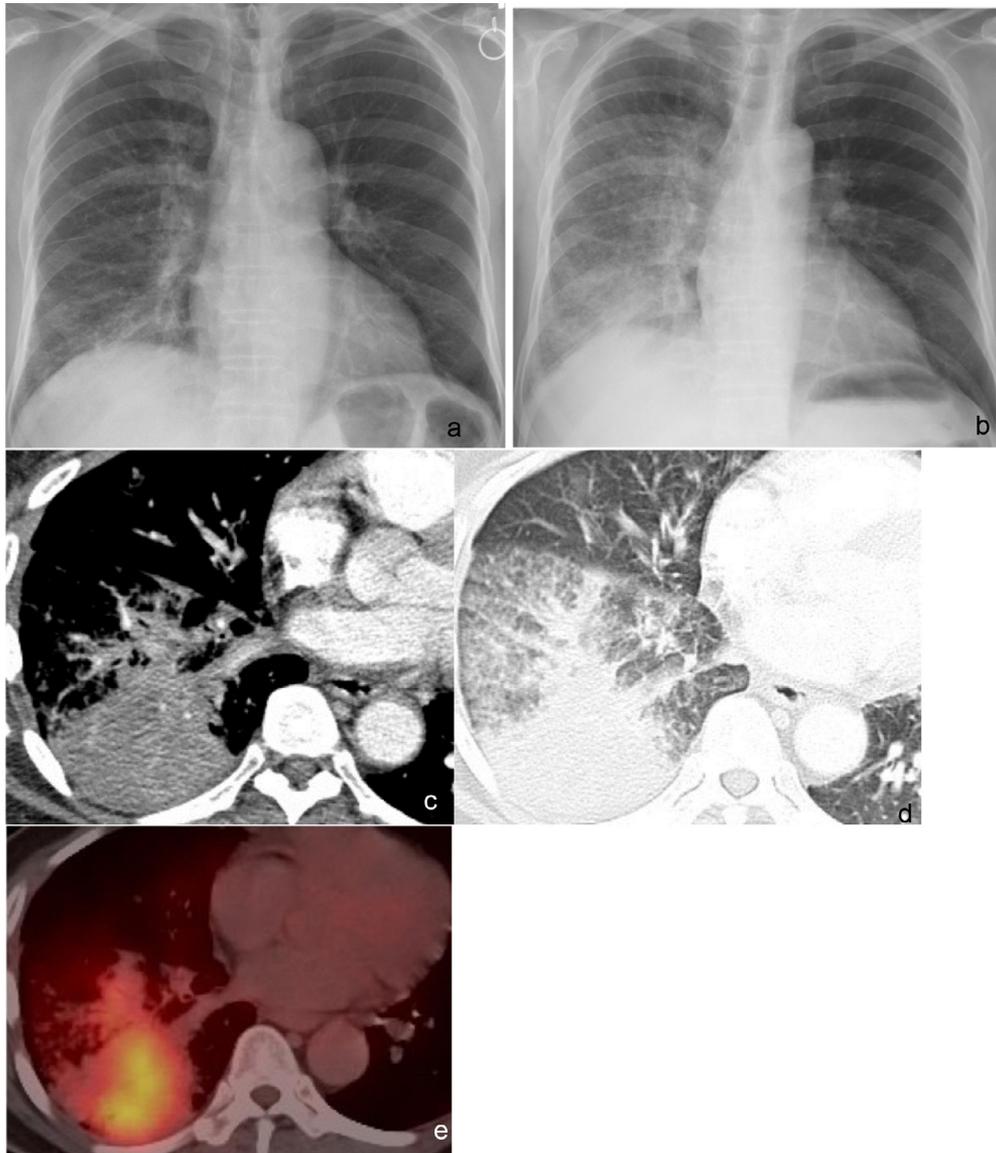
Figure 11 (a-e) Invasive mucinous adenocarcinoma. Chest radiograph (a) shows consolidation in the right infrahilar region and lung base. Follow-up chest radiograph (b) obtained 6 weeks later shows worsening of right lung consolidation. CT (c, d) shows mass-like consolidation and ground glass opacity in the right lower lobe. fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT (e) shows increased metabolic activity in the consolidation. Diagnosis of mucinous adenocarcinoma was made on lung biopsy.

Pulmonary Lymphoma

Pulmonary lymphoma can be primary or secondary. Primary pulmonary lymphoma is rare representing less than 1% of primary lung malignancies and approximately 4% of extranodal lymphoma.[46,47] Primary lymphoma is defined as a clonal proliferation of lymphoid tissue affecting lung parenchyma or bronchi with or without mediastinal lymphadenopathy and absence of extra thoracic dissemination for at least 3 months following initial diagnosis. Mucosa-associated lymphoid tissue (MALT) lymphomas are the most common form of primary pulmonary lymphoma, representing 60%-90% of primary pulmonary lymphomas.[46,47] Patients with MALT lymphoma are usually asymptomatic and the prognosis is good. Diffuse large B-cell lymphoma, another common histology of primary pulmonary lymphoma, is seen in immunocompromised patients who are symptomatic and the prognosis is poor. Hodgkin lymphoma (HL) is the least common form of primary pulmonary lymphoma.

Radiologic findings of MALT lymphoma are diverse and include single or multiple nodules, masses and/or consolidation, which tend to be peribronchovascular in distribution. The air bronchograms within these lesions may be dilated. Hilar/mediastinal lymphadenopathy is present in approximately 30% of cases.[46-48] Diffuse large B-cell lymphoma usually presents with solitary or multiple nodules or masses; cavitation is frequently seen.
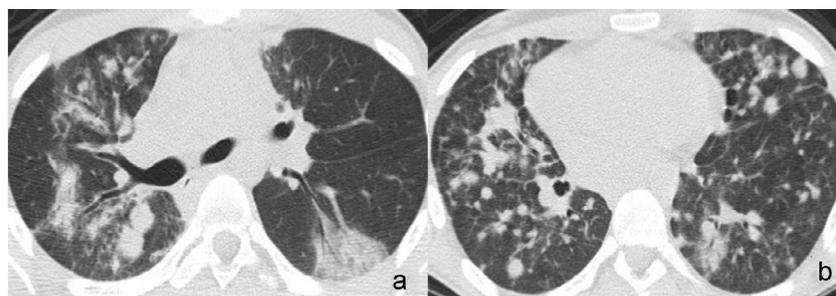
Figure 12 (a, b) Non-Hodgkin lymphoma with lung involvement. CT shows bilateral peribronchovascular consolidations and well-defined nodules along the bronchovascular bundles.
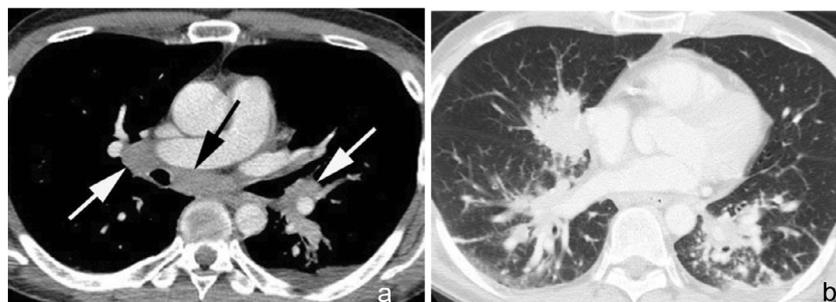

Figure 13 (a, b) Hodgkin lymphoma with lung involvement. CT with soft tissue window (a) shows mediastinal (black arrow) and hilar lymphadenopathy (white arrows). CT with lung window (b) shows peribronchovascular consolidations in the right middle and both lower lobes.

Secondary pulmonary lymphoma is much more common than primary pulmonary lymphoma. Approximately 80%-90% cases of secondary pulmonary lymphoma are non-HL (NHL) and 10%-15% are HL.[47,48] Pulmonary parenchymal involvement is more common with HL (38%) compared to NHL (24%).[47] Radiologically, 3 different patterns of parenchymal involvement have been described with secondary pulmonary lymphoma: interstitial, nodular, and alveolar. Mass-like consolidation and nodules are more common with NHL and the interstitial pattern is usually seen with HL (Fig. 12). Parenchymal involvement with HL is almost always due to contiguous extension of the disease from hilar/mediastinal lymphadenopathy (Fig. 13). Isolated parenchymal involvement may be seen in NHL.[47,48]

Conclusion

Chronic airspace disease has a wide range of differential diagnosis and can represent a diagnostic challenge. Persistent or nonresolving consolidation on chest radiography should alert the radiologists for further assessment with CT. Characteristic imaging appearance along with clinical information helps in narrowing the differential diagnosis.

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