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RadioGraphics

Postoperative Complications of Lung Transplantation: Radiologic Findings along a Time Continuum[1]

CME FEATURE

See accompanying test at http://www.rsna.org/education/rg_cme.html

LEARNING OBJECTIVES FOR TEST 3

After reading this article and taking the test, the reader will be able to:

- Describe the pulmonary complications that may occur after lung transplantation.
- Identify the relevant imaging features of pulmonary complications.
- Recognize the temporal relationships and pathologic processes in pulmonary complications after lung transplantation.

TEACHING POINTS

See last page

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In the past decade, lung transplantation has become established as an accepted therapy for end-stage pulmonary disease. Complications of lung transplantation that may occur in the immediate or longer postoperative term include mechanical problems due to a size mismatch between the donor lung and the recipient thoracic cage; malposition of monitoring tubes and lines; injuries from ischemia and reperfusion; acute pleural events; hyperacute, acute, and chronic rejection; pulmonary infections; bronchial anastomotic complications; pulmonary thromboembolism; upper-lobe fibrosis; primary disease recurrence; posttransplantation lymphoproliferative disorder; and native lung complications such as hyperinflation, malignancy, and infection. Radiologic imaging—particularly chest radiography, computed tomography (CT), and high-resolution CT—is critical for the early detection, evaluation, and diagnosis of complications after lung transplantation. To enable the selection of an effective and relevant course of therapy and, ultimately, to decrease morbidity and mortality among lung transplant recipients, radiologists at all levels of experience must be able to recognize and understand the imaging manifestations of posttransplantation complications.

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Abbreviations: CMV = cytomegalovirus, COPD = chronic obstructive pulmonary disease, H-E = hematoxylin-eosin, RSV = respiratory syncytial virus

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Introduction

Since the first successful single-lung transplantation, which was performed in 1983 by the Toronto General Hospital group for treatment of pulmonary fibrosis (1), adult lung transplantation has become an established technique for the treatment of end-stage pulmonary diseases. Single lung transplantation is commonly performed, but double lung transplantation, which in the past was reserved primarily for patients with suppurative lung disease and pulmonary arterial hypertension, is currently the preferred option for all patients with end-stage pulmonary disease, because of better long-term survival (2,3). Overall survival after lung transplantation also has greatly improved because of advances in surgical technique, careful harvesting and preserving of donor organs, improvements in immunosuppressive therapy, and earlier recognition of complications with the use of various imaging techniques. The reported 1-, 5-, 10-, and 15-year survival rates are 75%, 50%, 35%, and 25%, respectively (3,4). The most common causes of mortality are bacterial infection in the first 6 months and chronic graft dysfunction thereafter (3).

Teaching Point

Postoperative complications may have nonspecific and sometimes confusing clinical and radiologic manifestations. To help reduce mortality and morbidity among lung transplant recipients, it is important that radiologists understand and recognize the various postoperative complications of lung transplantation. These complications are best classified in relation to the point at which they occurred along the postoperative time continuum, to help clinicians narrow the differential diagnosis.

The article describes the salient radiologic features of complications at postoperative chest radiography, computed tomography (CT), and high-resolution CT. Where appropriate, pathologic features also are described. Complications are classified and discussed according to the period in which they typically occur within a postoperative time continuum, as follows: immediate (<24 hours), early (24 hours to 1 week), intermediate (8 days to 2 months), primary late (2–4 months), and secondary late (≥4 months) (Table).

Immediate Complications (<24 Hours)

Malpositioned Monitoring Tubes and Lines

Complications associated with the malposition of a monitoring tube or line are evident radiographically in less than 24 hours. Accidental intubation of a main bronchus may result in rapid collapse of the contralateral lung, pneumomediastinum, pneumothorax, or pulmonary interstitial emphysema secondary to barotrauma from mechanical ventilation. Improper placement of a central venous catheter or a Swan-Ganz catheter may lead to pneumothorax, hemorrhagic events such as hemothorax and intra- and extrathoracic hematomas, perforation of the mediastinal vasculature, and cardiac dysrhythmias. Improper placement of a chest tube leads to inadequate or ineffective drainage of postoperative air and fluid from the thoracic cavity.

Donor-Recipient Size Mismatch

A size mismatch between the donor lung and the recipient thoracic cage may cause mechanical complications. Atelectasis and impaired ventilation may result from the implantation of a large donor lung in a thoracic cage that is too small. These complications are immediately evident on postoperative radiographs (5). In patients who undergo single lung transplantation for emphysema, the implantation of a small donor lung within a thoracic cage that is too large results in allograft compression by the hyperexpanded emphysematous native lung. Size differences of 10%–25% between a donor lung and a recipient thoracic cage have been reported to be acceptable (5).

Hyperacute Rejection

The presence of preformed antibodies to donor organ–specific HLA or ABO antigens is thought to play a central role in hyperacute rejection, which is a fulminant, rapidly evolving, fatal clinical syndrome that may occur immediately after transplantation (6). Radiographically, hyperacute

Postoperative Complications of Lung Transplantation and Time of Occurrence

Time of Occurrence and Type of Complication	Common Radiologic Features
Immediate (<24 h)	
Abnormality due to malposition of postoperative lines and tubes	Pneumothorax, hemothorax, hemomediastinum, lung collapse, barotrauma
Size mismatch between donor lung and recipient thoracic cage	Atelectasis or hyperinflation
Hyperacute rejection	Massive infiltration of the allograft parenchyma
Early (24 h to 1 wk)	
Reperfusion injury	Perihilar haze, peribronchial thickening
Pleural complications	Hemothorax, pneumothorax, empyema
Intermediate (8 d to 2 mo)	
Acute rejection	Ground-glass opacities with intra- and interlobular septal thickening
Bronchial dehiscence	Perianastomotic air leak or flap and bronchial wall irregularity
Pneumonia due to *Candida* infection	Miliary nodules, ground-glass and airspace opacities
Primary late (2–4 mo)	
CMV infection	Nodules, ground-glass opacities and consolidation
Aspergillus infection	Irregular nodules with surrounding halos, consolidation
Pulmonary embolism	Filling defects
Bronchial stenosis	Abnormal airway narrowing and air trapping
Native lung abnormality	Hyperinflation, infection
Secondary late (≥4 mo)	
Mycobacterial infection	Multiple small nodules, ground-glass and tree-in-bud opacities, consolidation, pleural effusions, low-density adenopathy
Organizing pneumonia	Consolidation, bronchial wall thickening
Chronic rejection	Bronchiectasis, bronchial wall thickening, nodular and linear branching opacities, mosaic lung attenuation and air trapping
Posttransplantation lymphoproliferative disorder	Multiple or solitary pulmonary nodules or lymphadenopathy
Primary disease recurrence	Pulmonary nodules in sarcoidosis
Upper-lobe fibrosis	Architectural distortion
Bronchogenic carcinoma	Noncalcified spiculated nodule or mass

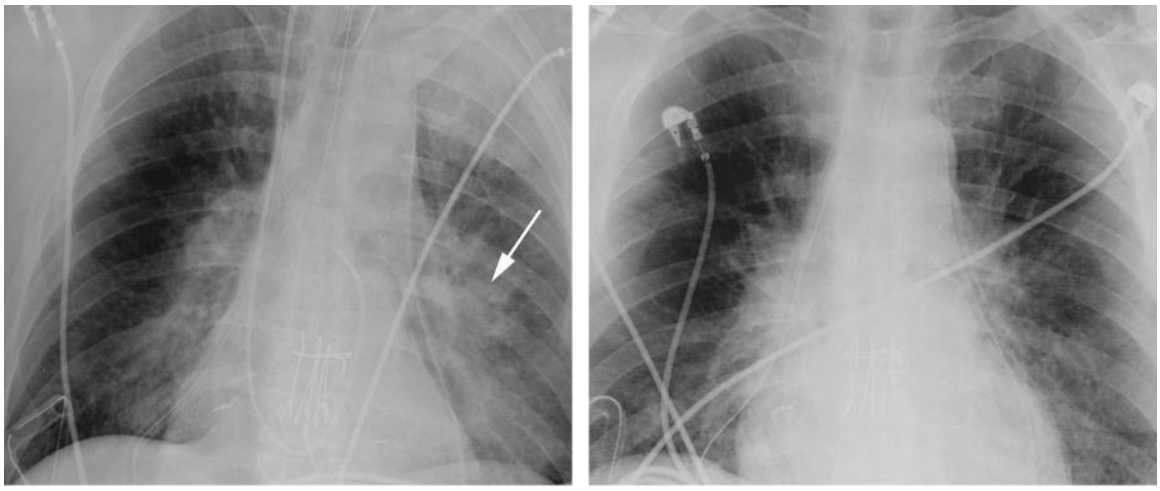
rejection appears as diffuse homogeneous infiltration of the entire allograft (6).

Early Complications (24 Hours to 1 Week)

Ischemia-Reperfusion Injury (Reperfusion Edema)

Teaching Point

Ischemia-reperfusion injury is a noncardiogenic pulmonary edema that typically occurs more than 24 hours after transplantation, peaks in severity on postoperative day 4, and generally improves by the end of the 1st week. This condition also is referred to as a pulmonary reimplantation response. The edema may continue up to 6 postoperative months; however, in most lung transplant recipients, it has cleared completely by 2 months. Ischemia-reperfusion injury has many possible causes, including surgical trauma, donor lung ischemia, interruption of the bronchial circulation or lymphatic flow, and denervation of the donor lung (7). The radiographic and CT features are nonspecific and may include perihilar ground-glass opacities, peribronchial and perivascular thickening, and reticular interstitial or airspace opacities located predominantly in the middle and lower lung lobes (7,8) (Fig 1).



a. b.

Figure 1. Ischemia-reperfusion injury in a patient with bilateral lung transplants for idiopathic pulmonary hypertension. **(a)** Chest radiograph, obtained 24 hours after lung transplantation, demonstrates bilateral lower-lobe heterogeneous airspace opacities (arrow) with peribronchial and perivascular thickening. **(b)** Chest radiograph, obtained more than 48 hours after transplantation, demonstrates interval resolution. Although the findings are nonspecific, the temporal relationship with regard to lung transplantation and the rapid resolution of the abnormal radiographic features are suggestive of this diagnosis.

Acute Pleural Complications

Pneumothorax, hemothorax, pleural effusion, empyema, and persistent or temporary air leaks usually are seen in the early postoperative period, with a reported frequency of 22% (Fig 2). The most common pleural complication is pneumothorax (9). Postoperative effusion tends to resolve by 2 weeks. Air leaks are due to various factors, including airway ischemia and bronchial dehiscence. A persistent air leak, defined as continuous leakage for more than 7 days, manifests as persistent pneumothorax, pneumomediastinum, or subcutaneous emphysema. These leaks and empyema are associated with increased mortality (9).

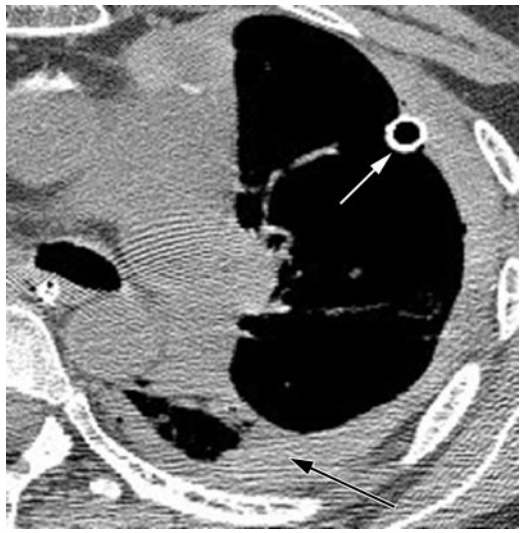


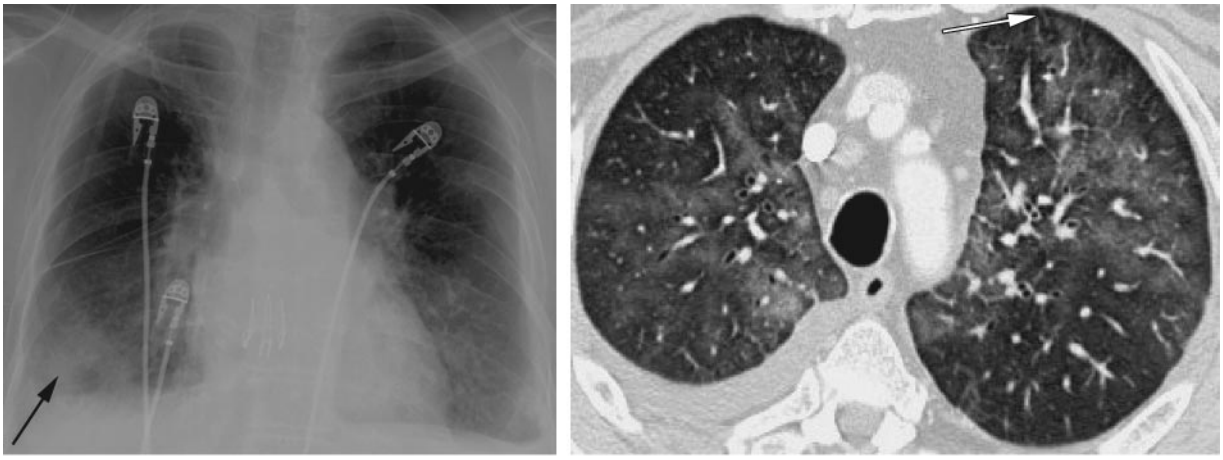
Figure 2. Hemothorax in a patient with bilateral lung transplants for idiopathic pulmonary hypertension. Axial chest CT image (soft-tissue window), obtained more than 5 days after lung transplantation, demonstrates a moderate-sized high-attenuating collection of blood (40 HU) that extends into the major fissure (black arrow). A thoracostomy tube also is visible (white arrow).

Intermediate Complications (8 Days to 2 Months)

Acute Rejection

Acute rejection due to a cell-mediated immune response commonly occurs in the 2nd postoperative week (10). Repeated episodes of acute rejection are considered a predisposing factor for chronic rejection or bronchiolitis obliterans syndrome (10). Chest radiographic features suggestive of (although not specific for) acute rejection include perihilar and lower-lobe opacities, interlobular septal thickening, and pleural effusions (Fig 3a, 3b) (10).

High-resolution CT features also are relatively nonspecific and may include ground-glass opacities (often with basal distribution), peribronchial cuffing, inter- and intralobular septal thickening, and new or increased pleural effusions. These features have reported sensitivities of 35%–65% for the diagnosis of acute rejection (10,11). Absence of ground-glass opacities almost excludes acute rejection in a postoperative lung transplant.



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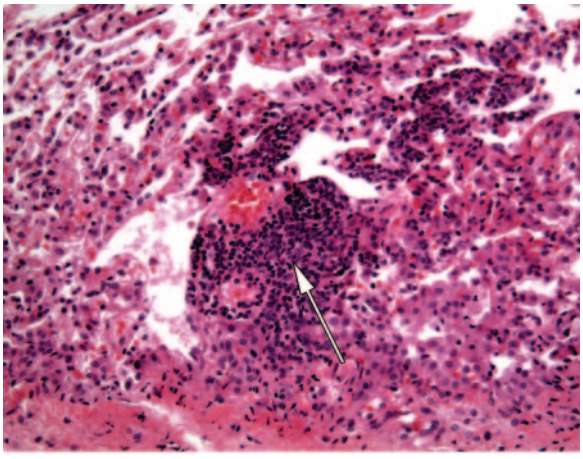


c.

Figure 3. Acute rejection in a patient with bilateral lung transplants for end-stage pulmonary fibrosis secondary to sarcoidosis. **(a)** Radiograph, obtained over 3 weeks after transplantation, shows pleural effusions, airspace opacities (arrow), and interlobular septal thickening. **(b)** Axial CT image shows patchy and multifocal bilateral ground-glass opacities, peribronchial and septal thickening (arrow), and pleural effusion due to acute cellular rejection. **(c)** High-power photomicrograph (original magnification, ×200; hematoxylin-eosin [H-E] stain) of a transbronchial biopsy specimen shows moderate (A3) acute rejection, with a marked perivascular inflammatory infiltrate of mononuclear cells (arrow) that extends into alveolar septa and without evident pneumocyte damage.

In contrast, the dramatic improvement of abnormal radiologic features within 48 hours after intravenous administration of methylprednisolone favors a diagnosis of acute rejection. Currently, transbronchial biopsy is the reference standard procedure for diagnosing acute rejection. Perivascular and parenchymal lymphocytic infiltrates are typical histologic findings (11,12).

Teaching Point

Bronchial Anastomotic Complications

Bronchial anastomotic complications that are common after lung transplantation include stenosis, tissue degeneration, infection, and dehiscence. The overall prevalence of such complications is approximately 15% (13). Donor bronchus ischemia caused by disruption of the native bronchial circulation is a key factor underlying airway-related complications. Other risk factors include recurrent infection and rejection.

Teaching Point

Bronchial dehiscence usually occurs within the 1st month after lung transplantation. The presence of a bronchial wall defect, fixed or dynamic bronchial narrowing, bronchial wall irregularity, extraluminal air, or a combination of these features at CT is indicative of anastomotic dehiscence (Fig 4). Indirect findings that are suggestive

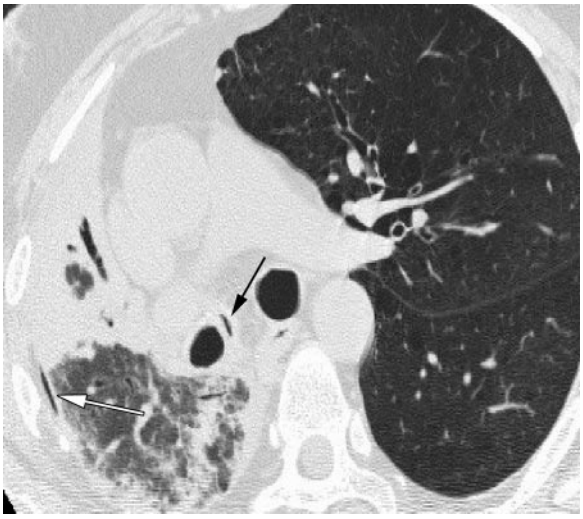


Figure 4. Bronchial dehiscence in a patient with a right lung transplant for α_1-antitrypsin deficiency. Axial chest CT image, obtained more than 4 weeks after lung transplantation, shows a crescent of air outside the airway (black arrow), medial to the right main bronchus. This finding was due to an anastomotic leak. A small pneumothorax (white arrow) represents a bronchopleural fistula.

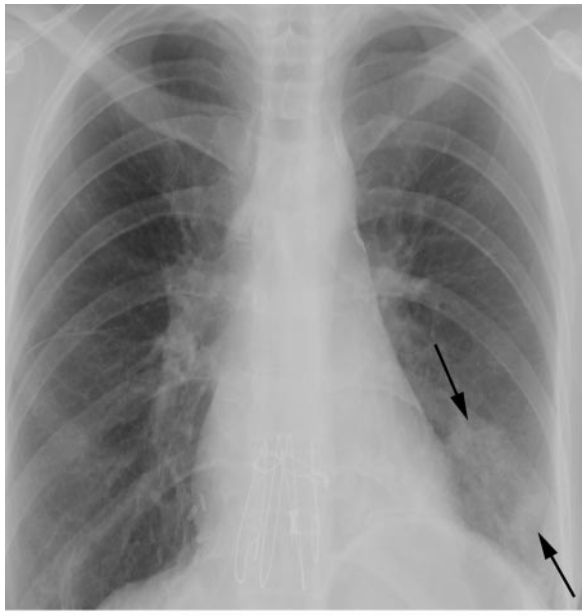
of an air leak or poor allograft aeration include pneumothorax, pneumomediastinum, and ipsilateral lung volume loss (14). Bronchial dehiscence may resolve without sequelae, may result in a stricture that requires stent placement, or may be fatal. Small soft-tissue irregularities and linear air pockets with a diameter of less than 4 mm anterior to the site of anastomosis are normally seen in lung transplants in which the telescoping technique of anastomosis was used (the donor bronchus is intussuscepted into the recipient bronchus or vice versa) (14). Unfortunately, CT does not reliably depict mucosal necrosis, which is the earliest sign and a useful predictor of dehiscence. If CT findings are negative, direct bronchoscopy should be performed to identify mucosal necrosis.

Infections

Pulmonary infections are a leading cause of morbidity and mortality and may occur at any time after transplantation. Certain organisms are more common than others or occur most frequently in a particular postoperative period. Factors that predispose transplant recipients to infection include aspiration, colonization of an atelectatic lobe, impaired mucociliary function due to allograft denervation, altered phagocytosis, communication of the donor lung with the atmosphere, absence of a cough reflex, interruption of the lymphatic flow, and administration of immunosuppressive drug therapy (15).

Risk factors for early postoperative infection include an excessive duration of donor organ ischemia (>76 hours), insufficient donor arterial oxygen tension (<350 mm Hg) before organ harvest, recipient age of more than 40 years, positive donor sputum culture, prolonged ventilatory support, and excessive tracheobronchial secretions. CT is useful for confirming and quantifying infiltrates, selecting appropriate regions of the lung for bronchoscopy, and determining the response to specific antimicrobial treatment. However, imaging features are relatively nonspecific to the causative organism (15).

Bacteria are the most common cause of infection in postoperative lung transplant recipients, particularly Gram-negative bacteria such as *Pseudomonas aeruginosa* and *Klebsiella* species. Pneumonia is the most frequent manifestation of such bacterial infections; it occurs in as many as 75% of lung transplant recipients within 3 months after transplantation (16). The risk of bacterial infection is greatest within the 1st month after lung transplantation (16). Features that may be observed on chest radiographs and CT images



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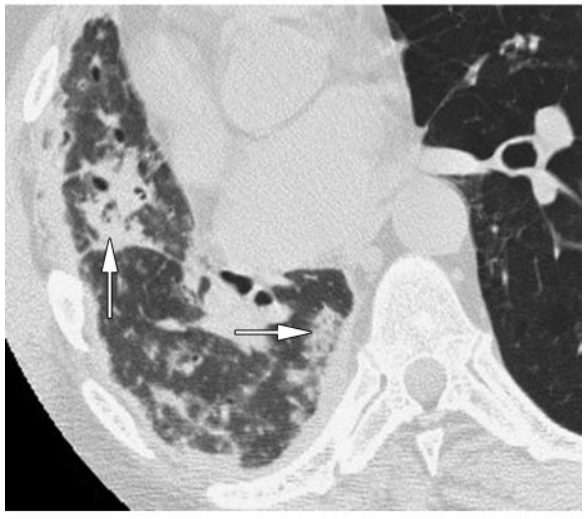

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Figure 5. Bacterial infection. **(a)** Chest radiograph obtained in a patient with bilateral lung transplants for pulmonary fibrosis shows patchy and confluent airspace consolidation with air bronchograms (arrows) within the lingula. Transbronchial biopsy cultures revealed the presence of *P aeruginosa*. **(b)** Chest CT image obtained in another patient, who received a right lung transplant for chronic obstructive pulmonary disease (COPD), demonstrates foci of consolidation (arrows) within the right middle and lower lobes of the allograft lung, findings indicative of bacterial pneumonia.

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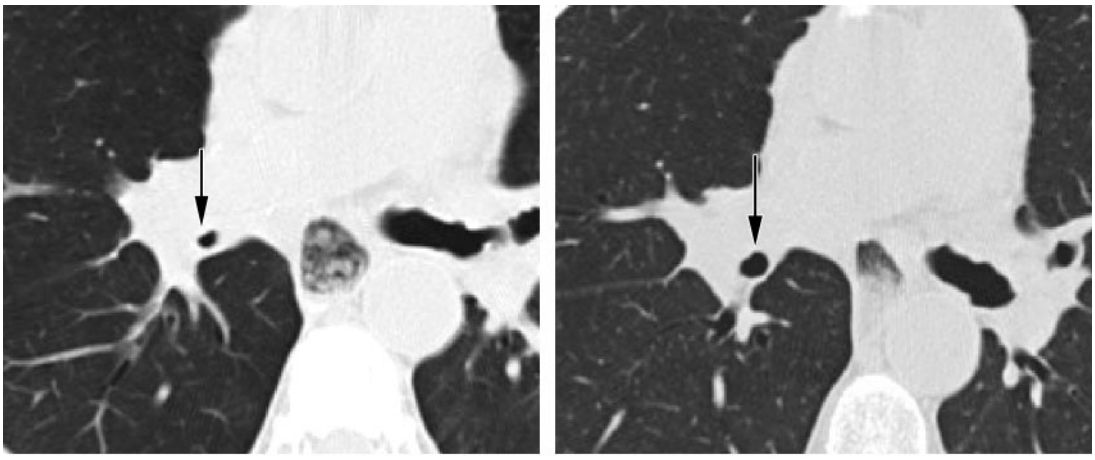

a. b.

Figure 7. Bronchial stenosis in a patient with bilateral lung transplants for pulmonary fibrosis due to systemic sclerosis. **(a)** Axial chest CT image, obtained more than 12 weeks after transplantation, shows stenosis of the bronchus intermedius (arrow). Esophageal food residue from dilatation caused by scleroderma also is visible. **(b)** Axial chest CT image, obtained after balloon dilation of the intermediate bronchus, shows mild residual stenosis (arrow).

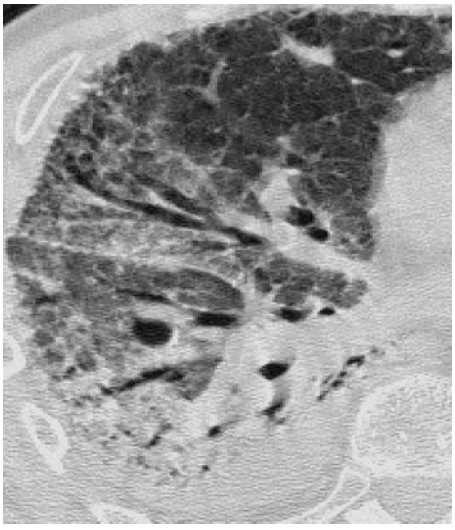

Figure 6. Pneumonia in a patient with a right lung transplant for end-stage emphysema. High-resolution axial CT image, obtained more than 8 weeks after transplantation, shows extensive multifocal ground-glass and airspace opacities within the middle and lower lobes of the right lung. Sputum cultures later revealed the presence of *Candida*.

include atelectasis; bronchocentric opacities; subsegmental, segmental, or lobar airspace consolidation (Fig 5); branching nodular and linear opacities (a "tree-in-bud" appearance); interlobular septal thickening; and pleural effusions (16).

Candida infections typically occur within the first 3 months after lung transplantation (17). Many imaging manifestations have been observed in such cases of candidiasis, specifically pneumonia, mediastinitis, bronchial anastomotic inflammation, and catheter-associated esophagitis (17). Radiologic findings include patchy and confluent regions of infiltration, nodules (occasionally miliary), masslike foci of consolidation or airspace consolidation, and interstitial lung patterns (Fig 6) (17).

Primary Late Complications (2–4 Months)

Bronchial Stenosis and Bronchomalacia

Bronchial anastomotic stenosis and bronchomalacia are usually seen within 4 months of lung transplantation, although the overall incidence of airway-related complications is decreasing with improvements in preservation methods, surgical techniques, and immunosuppressive therapy. Fixed bronchial narrowing because of stricture, with a significant stenosis defined as a reduction of more than 50% in bronchial diameter (18,19), may be demonstrated at CT (Fig 7). With regard to bronchomalacia, airway collapse or transient narrowing of the anastomosis or other airway segments may be detected with expiratory CT or with dynamic CT during respiration (19). Bronchomalacia also may be detected at bronchoscopy during spontaneous breathing (19).

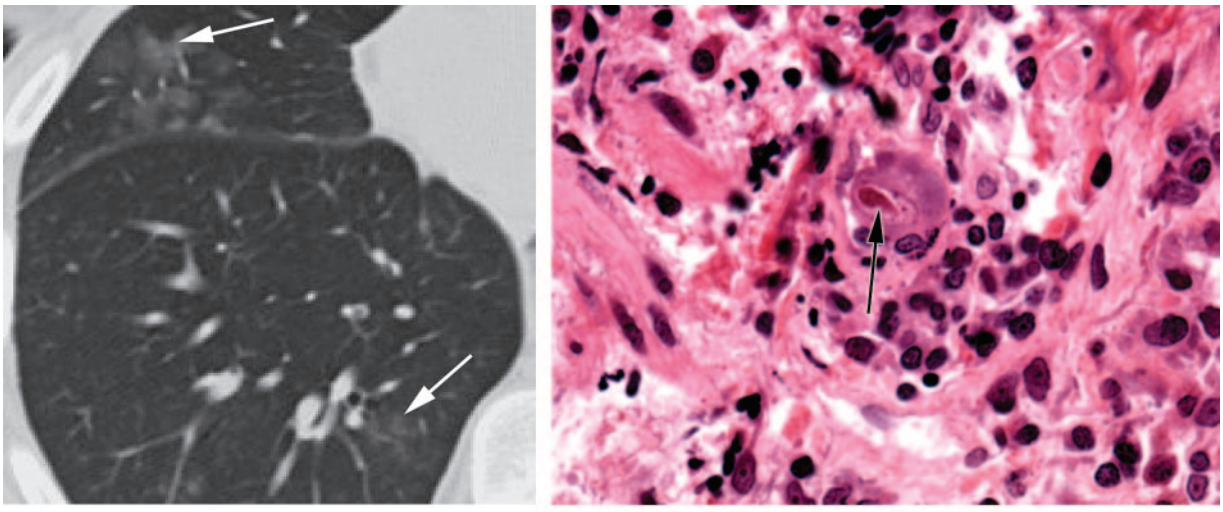

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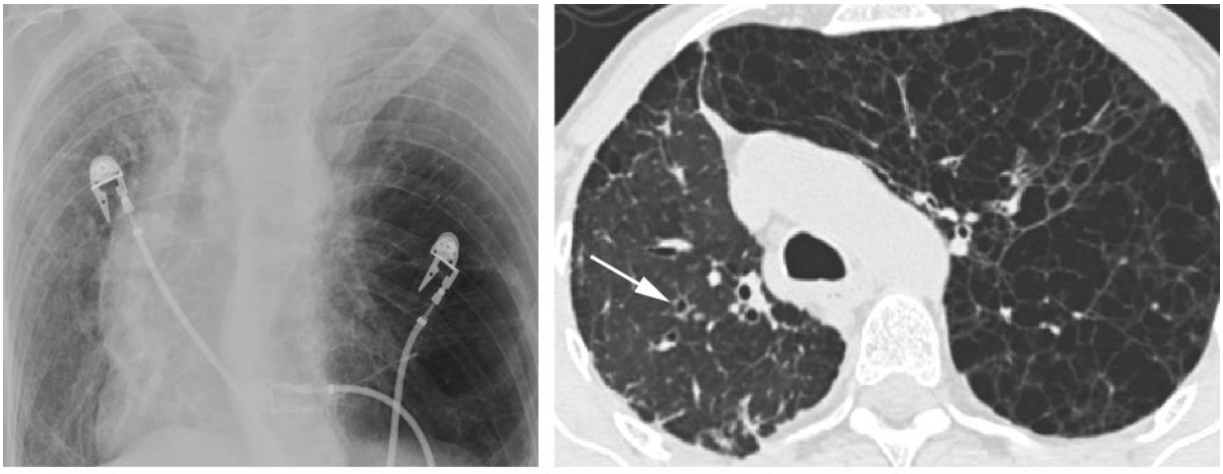
Figure 8. Pneumonia due to CMV infection in a patient with bilateral lung transplants for end-stage pulmonary fibrosis. **(a)** Axial chest CT image, obtained more than 8 weeks after lung transplantation, shows patchy and confluent ground-glass nodularity (arrows) within the middle and lower lobes of the allograft right lung. A transbronchial biopsy specimen from the right middle lobe later demonstrated inclusion bodies, a finding suggestive of viral infection. **(b)** High-power photomicrograph (original magnification, ×400; H-E stain) reveals a markedly enlarged endothelial cell with an intranuclear eosinophilic inclusion surrounded by a clear halo (arrow). Perivascular mononuclear cell inflammatory infiltration also is evident.



a. b.

Figure 9. Respiratory viral infection in a patient with a right lung transplant for lymphangioleiomyomatosis and a 2-week history of increasing cough and shortness of breath. **(a)** Chest radiograph, obtained 12 weeks after lung transplantation, shows diffuse ground-glass opacification with bronchial wall thickening in the allograft lung. **(b)** Axial chest CT image helps confirm diffuse ground-glass opacification and bronchial wall thickening (arrow) in the allograft lung. The native left lung shows diffuse disease with multiple thin-walled cysts, findings characteristic of lymphangioleiomyomatosis. Respiratory cultures were positive for RSV antigen.

Viral Infection

Cytomegalovirus.—Cytomegalovirus (CMV) is the most common cause of opportunistic infection. The rate of CMV infection in lung transplant recipients has been reported to be at least 50% (7). Seronegative recipients who receive seropositive donor lungs are at the highest risk for primary infection after transplantation (7). CMV

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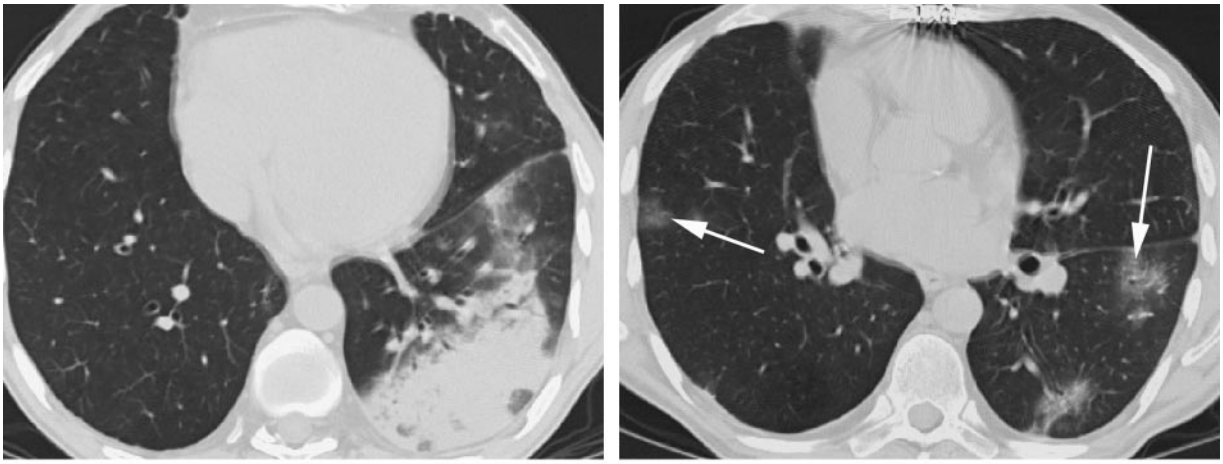


a. b.

Figure 10. *Aspergillus* infection in a patient with bilateral lung transplants for cystic fibrosis. Axial high-resolution CT images, obtained more than 8 weeks after lung transplantation, demonstrate dense airspace consolidation of the left lower lobe **(a)** and bilateral ground-glass nodules (arrows in **b**) with surrounding halos of decreased attenuation (halo sign). A bronchoalveolar lavage culture was positive for *Aspergillus*.

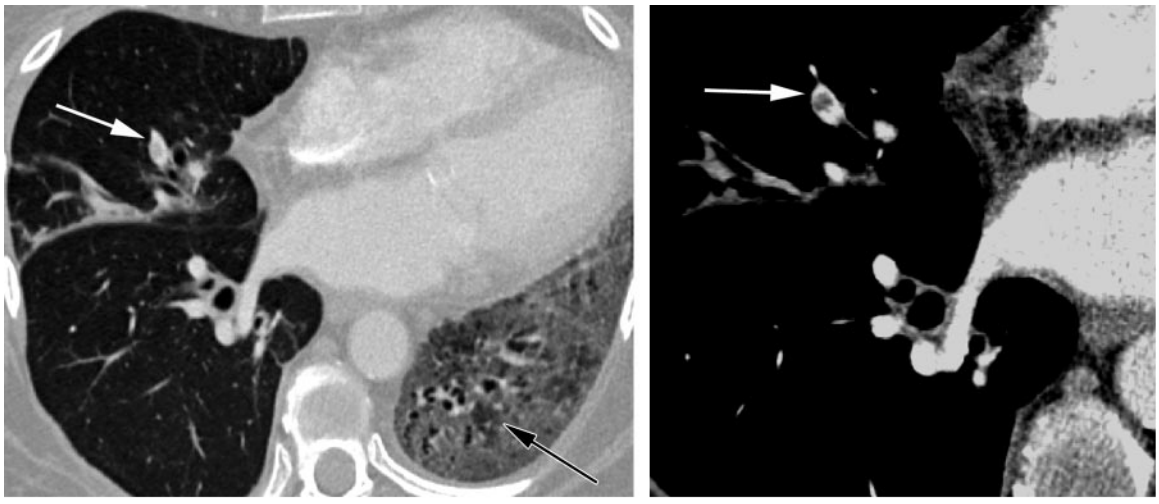
infection typically occurs between 1 and 6 months and is rarely seen earlier than 2 weeks after lung transplantation. Pneumonia is the most common manifestation of CMV infection (7). Frequently seen radiographic patterns include focal or diffuse parenchymal haziness, lobar consolidation, and small pleural effusions. CT better depicts the radiologic manifestations of CMV infection, which affect the allograft almost exclusively. The most common CT manifestations include ground-glass opacities, tree-in-bud opacities, airspace consolidation, nodules, interlobular septal thickening, pleural effusions, thickened and enhancing pleura, and bronchiectasis (Fig 8) (16,20).

Other Respiratory Viruses.—In addition to CMV, a number of community-acquired viruses—particularly respiratory syncytial virus (RSV), parainfluenza virus, adenovirus, and influenza viruses—may infect lung transplant recipients. Most such infections occur from 2 weeks to 2 years after transplantation, relatively late in the postoperative temporal continuum (21,22). The rate of occurrence of community-acquired viral infection varies between 8% and 14%. Such infection is considered a significant risk factor for development of bronchiolitis obliterans. CT and chest radiographic findings (21,22) include perihilar and heterogeneous ground-glass opacities (parainfluenza virus and RSV infections) (Fig 9); bronchial wall thickening (adenovirus, influenza virus, and RSV infections); bronchial dilatation (RSV infection); peribronchial, peribronchiolar, and centrilobular opacities (parainfluenza virus infection); airspace opacities (adenovirus and RSV infections); masslike foci of consolidation (adenovirus infection); and pleural effusions (adenovirus infection). RSV infection should be considered, particularly during the winter and spring, in the presence of these imaging features in association with acute bronchiectasis and tree-in-bud opacities.

Aspergillus Infection

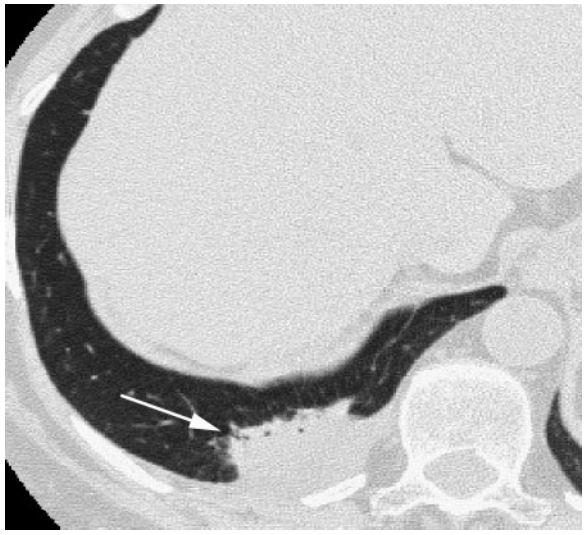
With prevalence rates ranging up to 40%, infection due to *Aspergillus* occurs 1–6 months after lung transplantation, with the peak incidence within the first 3 postoperative months (17). *Aspergillus* infections may manifest as ulcerative tracheobronchitis, bronchial anastomotic infection, aspergilloma, necrotizing pneumonia, invasive pulmonary disease, disseminated infection, or empyema (23). Typical features on chest radiographs and CT images include focal nodular and masslike regions of consolidation; cavitation; nodules (solitary or multiple) with a surrounding rim of ground-glass opacity, referred to as the "halo" sign; and pleural thickening (Fig 10).

Figure 11. Acute pulmonary embolism in a patient with a right lung transplant for usual interstitial pneumonitis. **(a)** Axial chest CT image, obtained more than 12 weeks after lung transplantation, shows fibrosis in the native left lung (black arrow) and acute pulmonary emboli in arteries within the allograft (white arrow). **(b)** Magnified view of an axial chest CT image demonstrates a central filling defect (arrow) and local distention of a middle-lobe segment of the right pulmonary artery.



a. b.

Figure 12. Pneumonia of the native lung in a patient with a left lung transplant for COPD. Axial chest CT image, obtained more than 12 weeks after transplantation, depicts masslike consolidation (arrow) in the posterior basal segment of the lower lobe of the native right lung. Fluid from bronchoalveolar lavage was positive for *Scedosporium apiospermum*.



Pulmonary Embolism and Infarction

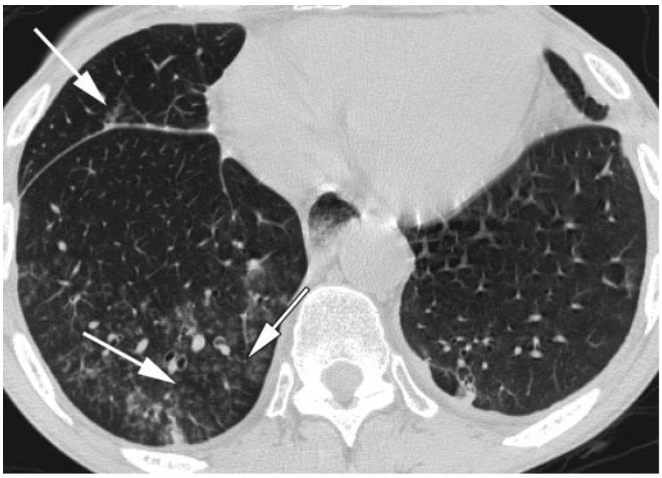
Pulmonary thromboembolic events tend to occur within 4 months after transplantation, and most occur within the allograft (24). An incidence of 27% has been reported (24). Prolonged (>48 hours) mechanical ventilation in the early posttransplantation period has been cited as a risk factor, and the postulated mechanism is increased perfusion within the allograft and the arterial anastomosis, which acts as a thrombogenic surface. Radiographic findings are relatively nonspecific and indirect, including regional vascular attenuation and parenchymal hyperlucency, peripheral wedge-shaped consolidation, pleural effusion, dilated central pulmonary arteries, and cardiomegaly. CT pulmonary arteriography offers a superior method of diagnosis of suspected pulmonary thromboembolic disease. Vascular findings of acute pulmonary embolism include central arterial filling defects, localized arterial distention, and abrupt arterial occlusion (Fig 11). Nonvascular findings include wedge-shaped consolidation, "mosaic hypoperfusion" or oligemia, atelectasis, and pleural effusion (25).

Complications That Affect the Native Lung

Native lung complications may occur at any time after a single-lung transplantation and may include infection (Fig 12), pneumothorax, primary lung malignancy, and, less commonly, pulmonary

RadioGraphics

Figure 13. *Mycobacterium* infection in a patient with bilateral lung transplants for end-stage pulmonary fibrosis. **(a, b)** Axial chest CT images, obtained more than 12 weeks after lung transplantation, demonstrate tree-in-bud nodularity and multiple ground-glass opacities (arrows in **a**) in the middle and lower lobes of the right lung and consolidation (arrow in **b**) in the lower lobe. Subsequent bronchoalveolar lavage cultures from the right middle and lower lobes were positive for nontuberculous *Mycobacterium*. **(c)** Medium-power photomicrograph (original magnification, ×100; H-E stain) shows granulomatous inflammation with giant cells obliterating a bronchiole (arrow). Note the presence of organizing pneumonia with intraalveolar fibrous plugs (*).



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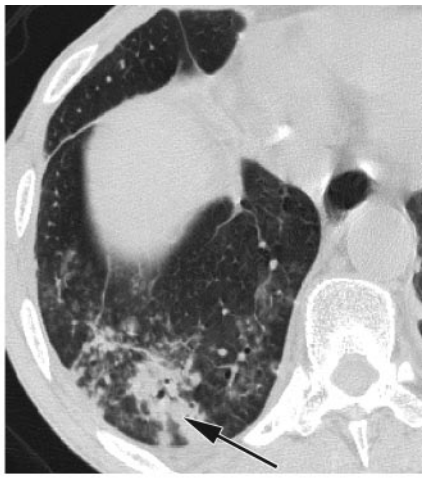

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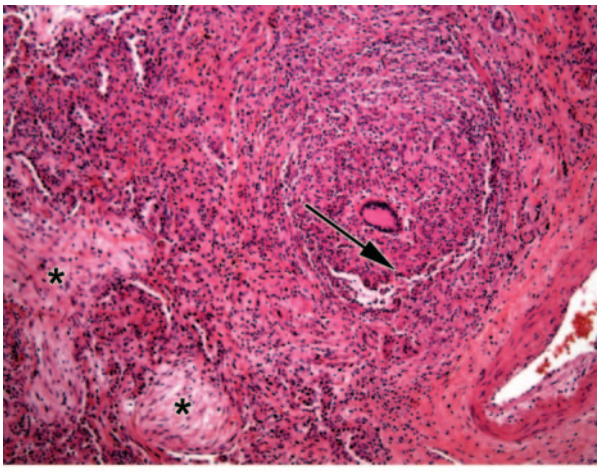


c.

embolism and pulmonary infarction (26). Within the context of single-lung transplantation for end-stage emphysema, hyperinflation of the native lung is a common finding.

Secondary Late Complications (≥4 Months)

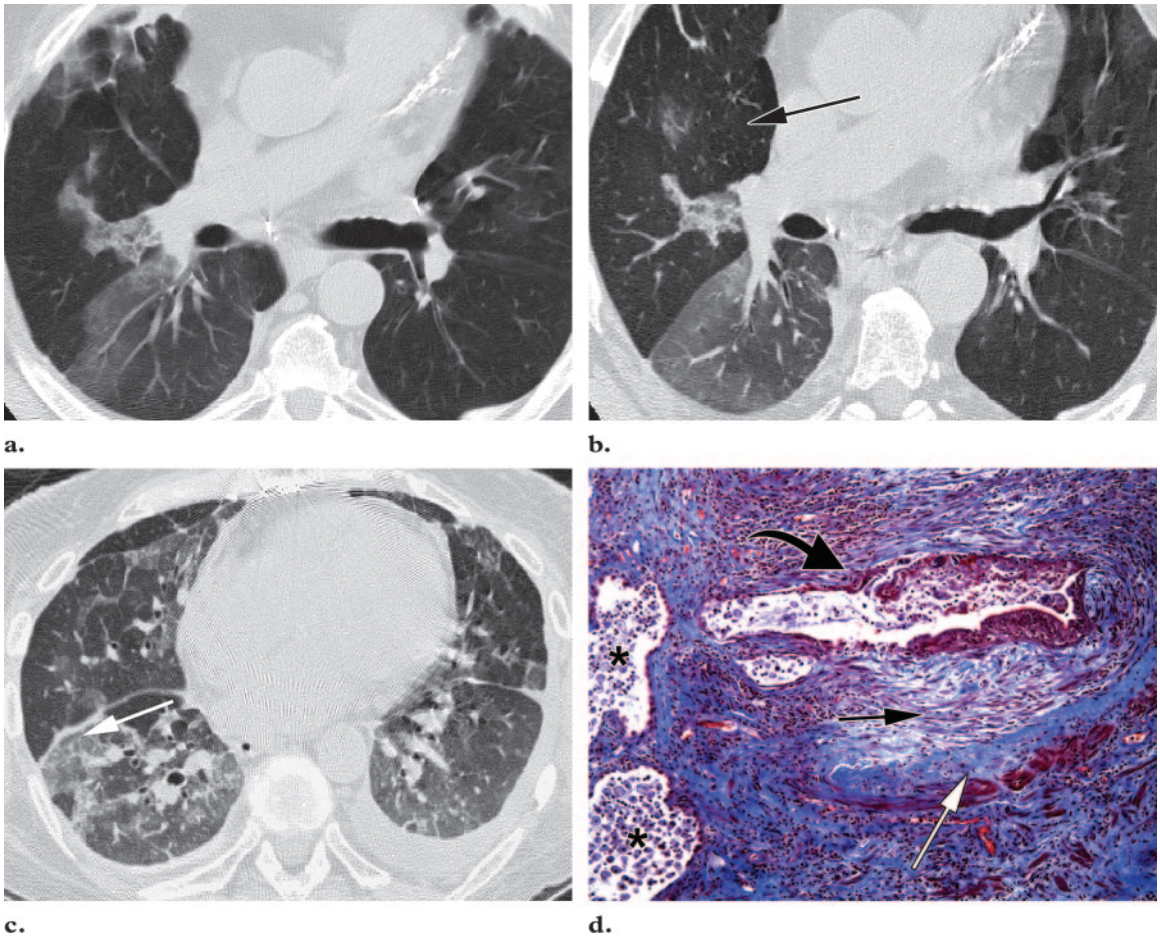
Mycobacterial Infection

Mycobacterial infections caused by typical or atypical species are relatively uncommon and generally occur late in the postoperative time continuum, 4 months or more after surgery (17,27). In this regard, both primary and postprimary tuberculosis have been reported. Radiologic findings include clusters of multiple small nodules, nodular ground-glass opacities or infiltrates, consolidation, cavitation, interlobular septal thickening, pleural thickening, unilateral or bilateral pleural effusions, and low-density mediastinal lymphadenopathy (17,27) (Fig 13).

Chronic Rejection

Chronic rejection of a lung transplant is a clinicopathologic syndrome characterized by bronchiolitis obliterans, a dense development of eosinophilic fibrous scarring of the small airways. The term *bronchiolitis obliterans syndrome* is used to describe the less specific graft dysfunction with a physiologic airflow obstruction and a decline in forced expiratory volume in 1 second from the posttransplantation baseline. Chronic allograft rejection remains the major late complication of lung transplantation; it affects at least 50% of recipients at 5 years, irrespective of specific risk factors. Nevertheless, a number of conditions are

Figure 14. Chronic rejection in a patient with bilateral lung transplants for COPD. **(a)** Inspiratory axial chest CT image shows mosaic attenuation (regions of mixed hypo- and hyperattenuation). **(b)** Expiratory high-resolution CT image shows a hypoattenuating region (arrow) produced by air trapping, a hallmark of chronic rejection due to bronchiolitis obliterans. **(c)** Inspiratory high-resolution CT image demonstrates bilateral hypoattenuating regions, nodularity, interlobular septal thickening (arrow), bronchial wall thickening, and patchy regions of ground-glass opacity. **(d)** Medium-power photomicrograph (original magnification, ×100; Masson trichrome stain) of a specimen from a right lung biopsy reveals active bronchiolitis obliterans with fibroblastic proliferation (straight black arrow), mononuclear cell inflammatory infiltration (curved black arrow), and dense fibrous scarring (white arrow) of the lamina propria. The presence of intraalveolar foamy macrophages (*), which in this case are due to obstructive pneumonitis, is nonspecific but usually indicative of small-airway obstruction.



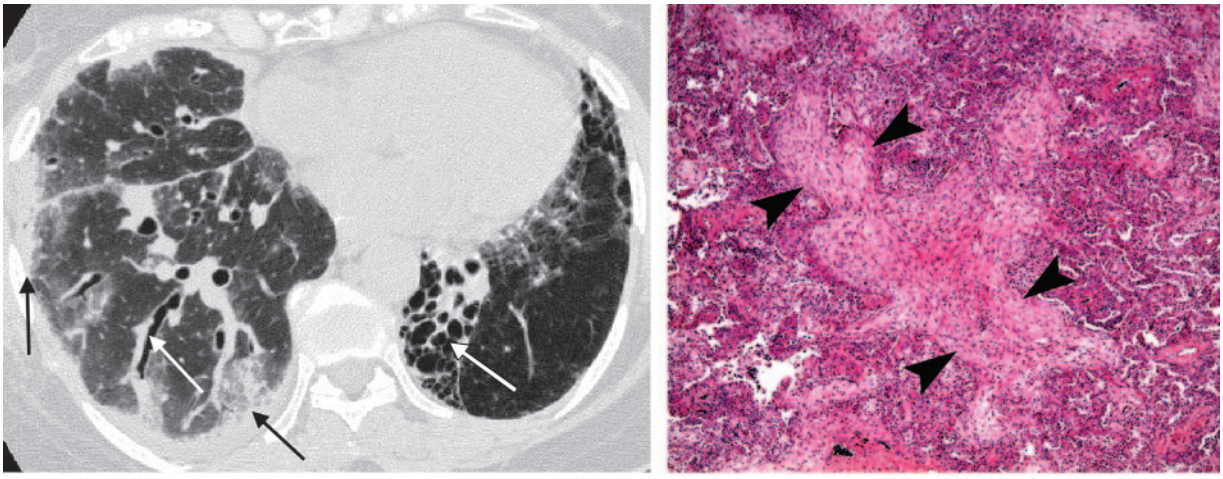
considered risk factors for rejection. These include acute cellular rejection, lymphocytic bronchitis, pulmonary infections with CMV and other viruses, and HLA mismatch (28). Chronic rejection usually occurs at approximately 6 months after lung transplantation (29) but has been reported to occur at 3 months.

Chest radiographic findings may include hyperinflation, decreased peripheral vascularity, regional volume contraction, subsegmental atelectasis, increased linear opacities, and bronchiectasis (30); however, radiographs often may appear normal. CT findings of chronic rejection include bronchiectasis, bronchial wall thickening, nodular and linear branching opacities, air trapping, regional volume expansion or contraction, mosaic lung attenuation, decreased or distorted peripheral arteries, interlobular septal thickening, and peribronchovascular infiltrates (Fig 14) (30,31). It has been suggested that bronchiectasis, bronchial wall thickening, and air trapping with resultant mosaic lung attenuation are predictive of the development of bronchiolitis obliterans or bron-

Teaching Point

RadioGraphics

Figure 15. Cryptogenic organizing pneumonia in a patient with a right lung transplant for end-stage pulmonary fibrosis secondary to sarcoidosis. **(a)** Axial chest CT image, obtained more than 16 weeks after lung transplantation, shows patchy ground-glass and airspace opacities predominantly in subpleural regions (black arrows) and bronchiectasis (white arrow) of the right lung. In the native left lung, fibrosis with cicatricial bronchiectasis (arrow) is evident. **(b)** Low-power photomicrograph (original magnification, ×40; H-E stain) shows arborizing polypoid plugs of fibroblastic tissue within the distal airways (arrowheads). The fibroblastic tissue consists of plump spindle cells within a collagen-poor, slightly basophilic extracellular matrix.



a. b.

chiolitis obliterans syndrome (31). However, air trapping at expiratory high-resolution CT is most indicative of chronic rejection.

Cryptogenic Organizing Pneumonia

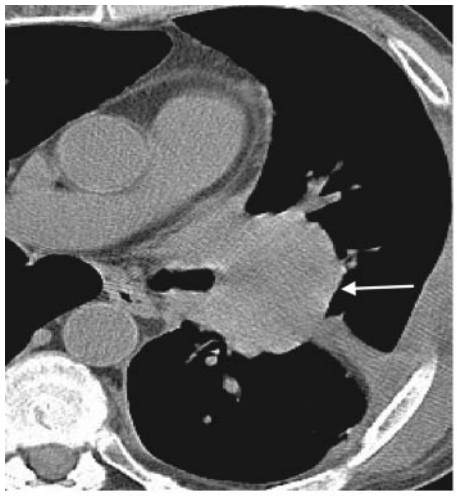
Cryptogenic organizing pneumonia occurs in 10%–28% of patients after lung transplantation and is characterized by the presence of inflammation and fibromyxomatous granulation tissue within the alveoli, alveolar ducts, and small airways (32). Although bronchiolitis obliterans with organizing pneumonia has been reported to occur in conjunction with chronic rejection and with bacterial and CMV infections, the condition is most commonly associated with acute rejection, and it responds rapidly to high-dose corticosteroid therapy.

High-resolution CT often shows evidence of airspace consolidation, ground-glass opacities, nodular or masslike consolidation, and linear or reticular opacities. Additional findings include bronchiectasis, bronchiolectasis, fibrosis, lung volume loss, and air trapping (Fig 15) (32,33).

Posttransplantation Lymphoproliferative Disorder

Posttransplantation lymphoproliferative disorder typically manifests within the 1st year and has been reported to occur as early as 1 month after transplantation. It is represented by a spectrum of lymphoid neoplasms that are primarily of B-cell origin (34). Epstein-Barr virus is found in approximately 90% of patients with this disorder; seronegative status for Epstein-Barr virus prior to transplantation is thought to be a major risk factor for the development of posttransplantation lymphoproliferative disorder (34). The incidence of the disorder varies between 2.8% and 6.1% at 1 year after transplantation (34,35). When the disorder occurs early in the postoperative period, it tends to follow a benign course and responds favorably to antiviral therapy and a reduction of immunosuppression. Its manifestations include multiple pulmonary nodules (with or without the "halo" sign), consolidation, interlobular septal thickening, pleural effusion, and mediastinal lymphadenopathy (Fig 16). Late disease, which is treated primarily with chemotherapy and irradiation, may develop more than 1 year after transplantation and is predominantly associated with extrathoracic involvement.

Figure 16. Posttransplantation lymphoproliferative disorder in a patient with a left lung transplant for COPD. **(a, b)** Axial chest CT images, obtained more than 12 months after lung transplantation, demonstrate a large left hilar mass (arrow in **a**) and two nodules in the lingula and left lower lobe (arrows in **b**). **(c)** High-power photomicrograph (original magnification, ×200; H-E stain) of a biopsy specimen shows marked infiltration of the bronchiolar wall with destruction of the smooth-muscle layer by large atypical lymphocytes (arrows).



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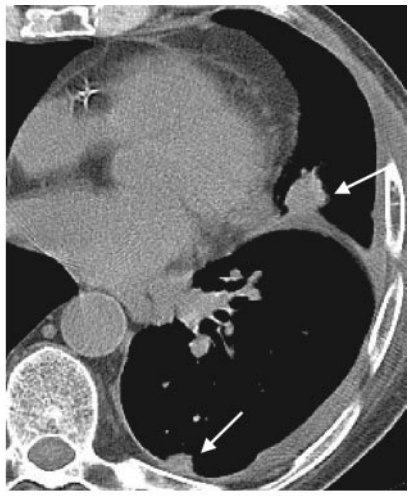

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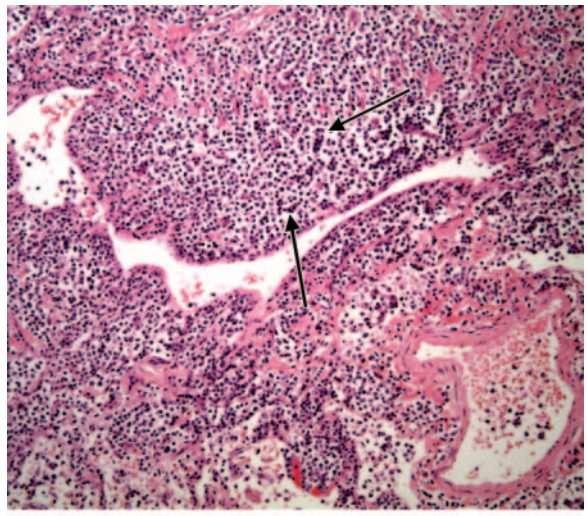
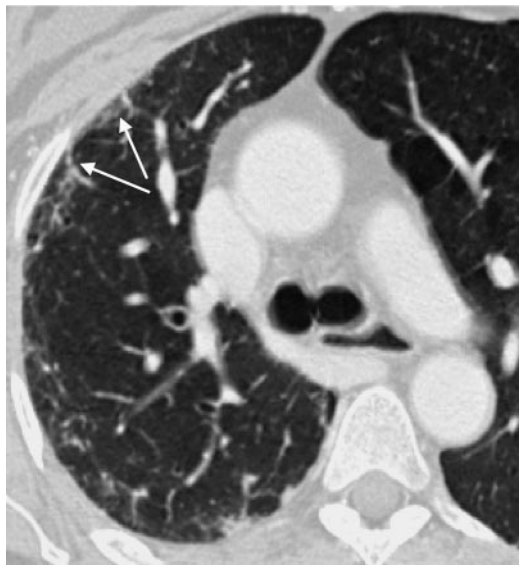
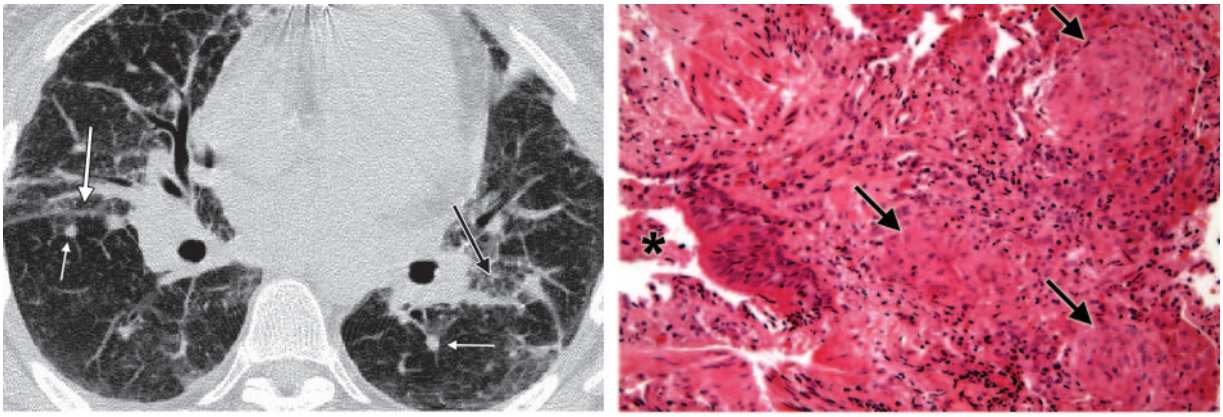


c.

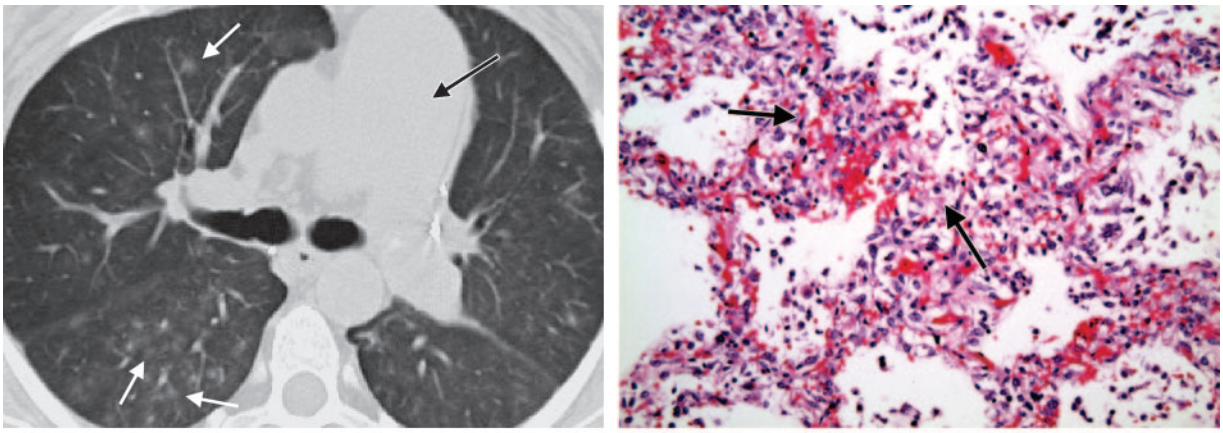
Figure 17. Fibrosis in a patient with a right lung transplant for severe centrilobular emphysema related to cigarette smoking. High-resolution CT image, obtained more than 24 months after lung transplantation, demonstrates regions of fibrosis (arrows) in the upper lobe of the allograft.





a. b.

Figure 18. Recurrence of sarcoidosis in a patient with bilateral lung transplants for end-stage pulmonary fibrosis secondary to sarcoidosis. **(a)** High-resolution CT image, obtained more than 16 weeks after lung transplantation, shows multiple pulmonary nodules (small white arrows), nodularity along the right major fissure (large white arrow), peribronchial thickening, ground-glass opacities, and patchy architectural distortion (black arrow). **(b)** High-power photomicrograph (original magnification, ×200; H-E stain) of a specimen from bronchoscopic biopsy reveals multiple discrete nonnecrotizing granulomas (arrows) in the wall of a bronchiole (*).



a. b.

Figure 19. Recurrence of pulmonary capillary hemangiomatosis in a patient with bilateral lung transplants for pulmonary hypertension associated with pulmonary capillary hemangiomatosis. **(a)** High-resolution CT image, obtained more than 16 weeks after transplantation, demonstrates multiple bilateral bronchocentric ground-glass opacities (white arrows) and an enlarged pulmonary trunk (black arrow). Enlargement of the main pulmonary artery to 42 mm is indicative of hypertension. **(b)** High-power photomicrograph (original magnification, ×200; H-E stain) of a bronchoscopic biopsy specimen reveals thickened alveolar septa with proliferating capillaries (arrows), findings indicative of recurrent pulmonary capillary hemangiomatosis.

Upper-Lobe Fibrosis

Progressive upper-lobe fibrosis occurs 1–4 years after transplantation (Fig 17). Radiographic features include interlobular septal thickening and reticular or ground-glass opacities, traction bronchiectasis, honeycombing, architectural distortion, and loss of lung volume. The relatively nonspecific high-resolution CT findings likely represent inflammatory and fibrotic changes found at histopathologic analysis that are believed to be associated with chronic rejection (36).

Recurrence of Primary Disease

Recurrence of primary disease in the allograft may appear as early as 2 weeks or as late as 2 years after transplantation. Sarcoidosis is the most commonly recurrent primary disease, with a reported recurrence rate of approximately 35% (Fig 18) (37,38). Other diseases that have been reported to recur in lung transplants include lymphangioleiomyomatosis, Langerhans cell histiocytosis, talc granulomatosis, giant cell pneumonitis, panbronchiolitis, pulmonary alveolar proteinosis, and pulmonary capillary hemangiomatosis (Fig 19). The radiologic features are specific to the recurrent disease, which often is discovered incidentally at CT or biopsy because the patient is asymptomatic.

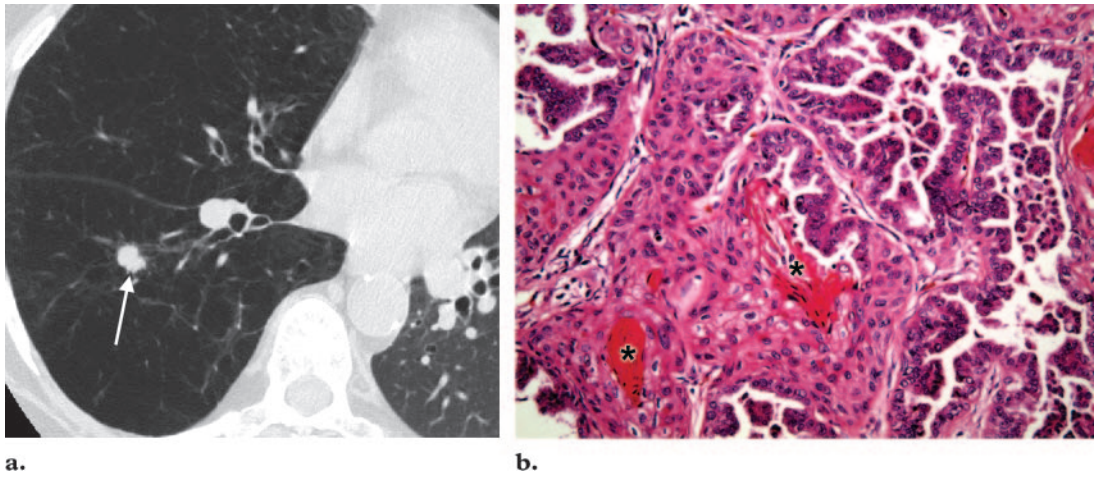


Figure 20. Bronchogenic carcinoma in a patient with a left lung transplant for COPD. **(a)** Axial chest CT image of the native right lung, obtained 4 years after transplantation, shows a new spiculated solid pulmonary nodule (arrow) that later was proved to be a non–small cell lung carcinoma. **(b)** High-power photomicrograph (original magnification, ×200; H-E stain) of a specimen from a needle biopsy reveals an admixture of keratinizing squamous cell carcinoma (*) and micropapillary adenocarcinoma.

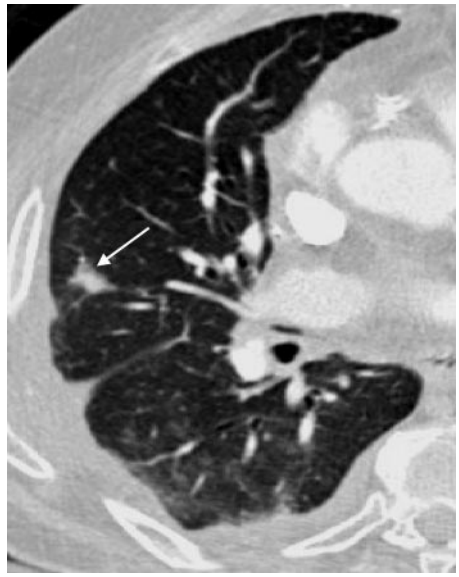


Figure 21. Focal hematoma after a transbronchial biopsy in a patient with a right lung transplant. High-resolution CT image, obtained 2 days after the biopsy, demonstrates a new solitary nodule (arrow). The nodule later spontaneously resolved.

Bronchogenic Carcinoma

Bronchogenic carcinoma typically occurs in the native lung at least 1 year after transplantation, with a frequency of less than 1% in the population of lung transplant recipients and of 2% and 4% in those who received a lung transplant for treatment of emphysema or pulmonary fibrosis, respectively (39,40). It usually manifests as a noncalcified solitary pulmonary nodule or mass with irregular margins (Fig 20), and the prognosis is generally poor. Risk factors are heavy tobacco use (most common), advanced age, impaired immunosuppression, and lung fibrosis or emphysema preexistent to transplantation.

Transbronchial Biopsy–associated Complications

Bronchoscopy with transbronchial biopsy may be performed at any time after lung transplantation to aid in the diagnosis of acute and chronic allograft rejection, infection, and recurrence of primary disease (16). Overall complication rates for this procedure range between 6% and 12%.

Complications such as alveolar hemorrhage, pulmonary hematoma, pulmonary laceration, intrapulmonary or air-filled cysts, pneumothoraces, and infection have been described (16,41). The radiologic appearances vary, depending on the complication. The most common features are small (<1.5-cm) focal nodular or nonspecific alveolar opacities that usually are located within 2 cm of the pleura and correspond to biopsy sites (Fig 21) (16,42). These nodules may be solid or cavitary, often are surrounded by a halo of ground-glass opacity, and may persist up to 1 month after biopsy.

Conclusion

By recognizing the relevant radiologic manifestations and identifying their temporal relationships to transplantation, radiologists can help clarify the wide spectrum of nonspecific, overlapping, and sometimes confusing clinical and imaging findings of complications after lung transplantation.

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References

1. Unilateral lung transplantation for pulmonary fibrosis. Toronto Lung Transplant Group. N Engl J Med 1986;314:1140–1145.
2. Hadjiliadis D, Chaparro C, Gutierrez C, et al. Impact of lung transplant operation on bronchiolitis obliterans syndrome in patients with chronic obstructive pulmonary disease. Am J Transplant 2006;6:183–189.
3. de Perrot M, Chaparro C, McRae K, et al. Twenty-year experience of lung transplantation at a single center: influence of recipient diagnosis on long-term survival. J Thorac Cardiovasc Surg 2004;127:1493–1501.
4. Trulock EP, Edwards LB, Taylor DO, et al. The Registry of the International Society for Heart and Lung Transplantation: twentieth official adult lung and heart-lung transplant report—2003. J Heart Lung Transplant 2003;22:625–635.
5. Frost AE. Donor criteria and evaluation. Clin Chest Med 1997;18:231–237.
6. Frost AE, Jammal CT, Cagle PT. Hyperacute rejection following lung transplantation. Chest 1996; 110:559–562.
7. Collins J. Imaging of the chest after lung transplantation. J Thorac Imaging 2002;17:102–112.
8. Kundu S, Herman SJ, Winton TL. Reperfusion edema after lung transplantation: radiographic manifestations. Radiology 1998;206:75–80.
9. Ferrer J, Roldan J, Roman A, et al. Acute and chronic pleural complications in lung transplantation. J Heart Lung Transplant 2003;22:1217–1225.
10. King-Biggs MB. Acute pulmonary allograft rejection: mechanisms, diagnosis, and management. Clin Chest Med 1997;18:301–310.
11. Loubeyre P, Revel D, Delignette A, Loire R, Mornex JF. High-resolution computed tomographic findings associated with histologically diagnosed acute lung rejection in heart-lung transplant recipients. Chest 1995;107:132–138.
12. Gotway MB, Dawn SK, Sellami D, et al. Acute rejection following lung transplantation: limitations in accuracy of thin-section CT for diagnosis. Radiology 2001;221:207–212.
13. Alvarez A, Algar J, Santos F, et al. Airway complications after lung transplantation: a review of 151 anastomoses. Eur J Cardiothorac Surg 2001;19: 381–387.
14. Semenkovich JW, Glazer HS, Anderson DC, Arcidi JM Jr, Cooper JD, Patterson GA. Bronchial dehiscence in lung transplantation: CT evaluation. Radiology 1995;194:205–208.
15. Fishman JA, Rubin RH. Infection in organ-transplant recipients. N Engl J Med 1998;338:1741–1751.
16. Collins J, Muller NL, Kazerooni EA, Paciocco G. CT findings of pneumonia after lung transplantation. AJR Am J Roentgenol 2000;175:811–818.
17. Kanj SS, Welty-Wolf K, Madden J, et al. Fungal infections in lung and heart-lung transplant recipients: report of 9 cases and review of the literature. Medicine (Baltimore) 1996;75:142–156.
18. Boiselle PM, Feller-Kopman D, Ashiku S, Weeks D, Ernst A. Tracheobronchomalacia: evolving role of dynamic multislice helical CT. Radiol Clin North Am 2003;41:627–636.
19. Kshettry VR, Kroshus TJ, Hertz MI, Hunter DW, Shumway SJ, Bolman RM 3rd. Early and late airway complications: incidence and management. Ann Thorac Surg 1997;63:1576–1583.
20. Soyer P, Devine N, Frachon I, et al. Computed tomography of complications of lung transplantation. Eur Radiol 1997;7:847–853.
21. Matar LD, McAdams HP, Palmer SM, et al. Respiratory viral infections in lung transplant recipients: radiologic findings with clinical correlation. Radiology 1999;213:735–742.
22. Ko JP, Shepard JA, Sproule MW, et al. CT manifestations of respiratory syncytial virus infection in lung transplant recipients. J Comput Assist Tomogr 2000;24:235–241.
23. Franquet T, Muller NL, Oikonomou A, Flint JD. Aspergillus infection of the airways: computed tomography and pathologic findings. J Comput Assist Tomogr 2004;28:10–16.
24. Burns KE, Iacono AT. Pulmonary embolism on postmortem examination: an under-recognized complication in lung-transplant recipients? Transplantation 2004;77:692–698.
25. Coche E, Verschuren F, Hainaut P, Goncette L. Pulmonary embolism findings on chest radiographs and multislice spiral CT. Eur Radiol 2004; 14:1241–1248.
26. McAdams HP, Erasmus JJ, Palmer SM. Complications involving the native lung after single-lung transplantation: incidence, radiologic features, and clinical importance. Radiology 2001;218:233–241.
27. Kesten S, Chaparro C. Mycobacterial infections in lung transplant recipients. Chest 1999;115:741–745.
28. Sharples LD, McNeil K, Stewart S, Wallwork J. Risk factors for bronchiolitis obliterans: a systematic review of recent publications. J Heart Lung Transplant 2002;21:271–281.
29. Ikonen T, Kivisaari L, Taskinen E, Piilonen A, Harjula AL. High-resolution CT in long-term follow-up after lung transplantation. Chest 1997; 111:370–376.

30. Lee ES, Gotway MB, Reddy GP, Golden JA, Keith FM, Webb WR. Early bronchiolitis obliterans following lung transplantation: accuracy of expiratory thin-section CT for diagnosis. Radiology 2000;216:472–477.
31. Morrish WF, Herman SJ, Weisbrod GL, Chamberlain DW. Bronchiolitis obliterans after lung transplantation: findings at chest radiography and high-resolution CT. The Toronto Lung Transplant Group. Radiology 1991;179:487–490.
32. Chaparro C, Chamberlain D, Maurer J, Winton T, Dehoyos A, Kesten S. Bronchiolitis obliterans organizing pneumonia (BOOP) in lung transplant recipients. Chest 1996;110:1150–1154.
33. Arakawa H, Kurihara Y, Niimi H, Nakajima Y, Johkoh T, Nakamura H. Bronchiolitis obliterans with organizing pneumonia versus chronic eosinophilic pneumonia: high-resolution CT findings in 81 patients. AJR Am J Roentgenol 2001;176:1053–1058.
34. Scarsbrook AF, Warakaulle DR, Dattani M, Traill Z. Post-transplantation lymphoproliferative disorder: the spectrum of imaging appearances. Clin Radiol 2005;60:47–55.
35. Rappaport DC, Chamberlain DW, Shepherd FA, Hutcheon MA. Lymphoproliferative disorders after lung transplantation: imaging features. Radiology 1998;206:519–524.
36. Konen E, Weisbrod GL, Pakhale S, Chung T, Paul NS, Hutcheon MA. Fibrosis of the upper lobes: a newly identified late-onset complication after lung transplantation? AJR Am J Roentgenol 2003;181:1539–1543.
37. Collins J, Hartman MJ, Warner TF, et al. Frequency and CT findings of recurrent disease after lung transplantation. Radiology 2001;219:503–509.
38. Kazerooni EA, Jackson C, Cascade PN. Sarcoidosis: recurrence of primary disease in transplanted lungs. Radiology 1994;192:461–464.
39. de Perrot M, Wigle DA, Pierre AF, et al. Bronchogenic carcinoma after solid organ transplantation. Ann Thorac Surg 2003;75:367–371.
40. Choi YH, Leung AN, Miro S, Poirier C, Hunt S, Theodore J. Primary bronchogenic carcinoma after heart or lung transplantation: radiologic and clinical findings. J Thorac Imaging 2000;15:36–40.
41. Boehler A, Vogt P, Zollinger A, Weder W, Speich R. Prospective study of the value of transbronchial lung biopsy after lung transplantation. Eur Respir J 1996;9:658–662.
42. Kazerooni EA, Cascade PN, Gross BH. Transplanted lungs: nodules following transbronchial biopsy. Radiology 1995;194:209–212.

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RadioGraphics

Postoperative Complications of Lung Transplantation: Radiologic Findings along a Time Continuum

Mayil S. Krishnam, MD et al

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Page 958
The reported 1-, 5-, 10-, and 15-year survival rates are 75%, 50%, 35%, and 25%, respectively.

Page 959
Ischemia-reperfusion injury is a noncardiogenic pulmonary edema that typically occurs more than 24 hours after transplantation, peaks in severity on postoperative day 4, and generally improves by the end of the 1st week.

Page 961
The dramatic improvement of abnormal radiologic features within 48 hours after the intravenous administration of methylprednisolone favors a diagnosis of acute rejection.

Page 961
Bronchial anastomotic complications that are common after lung transplantation include stenosis, tissue degeneration, infection, and dehiscence. The overall prevalence of such complications is approximately 15%.

Page 968
CT findings of chronic rejection include bronchiectasis, bronchial wall thickening, nodular and linear branching opacities, air trapping, regional volume expansion or contraction, mosaic lung attenuation, decreased or distorted peripheral arteries, interlobular septal thickening, and peribronchovascular infiltrates.