Three of the articles in this issue of AJR Integrative Imaging offer SAM and CME credits.

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These CME articles consist of two parts: one, the text and related images appearing in this supplement; and two, the self-evaluation quiz, which is available online at www.arrs.org. You should read the articles, review the accompanying images and refer to the articles referenced in this supplement, then complete the self-evaluation quiz. To obtain CME credit you must complete the self-evaluation quiz online. Visit www.arrs.org and go to the left-hand menu bar under Publications/Journals/SAM Articles. There is no charge for ARRS members to participate in this program. Non-members pay a fee to access CME and SAM material.

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In compliance with the Essentials and Standards of the ACCME, authors of the CME activities in this publication are required to disclose all relevant financial relationships with any commercial interest to the ARRS. The ACCME defines “relevant financial relationships” as financial relationships in any amount occurring within the past 12 months that create a conflict of interest.

Drs. Agarwal, Attili, Chasen, Day, Dillon, Donnelly, Epstein, Holloway, Jan, Mueller, Ng, Parker, Patsios, Paul, Strother, Thomas, and Worrell, have all indicated that they have no commercial interests to disclose.

SAM and CME Credit

Imaging of Lung Transplantation: Self-Assessment Module. To obtain 1 SAM credit and 1.5 CME credits, you must follow the instructions on page SXX.

CT Virtual Endoscopy in the Evaluation of Large Airway Disease: Self-Assessment Module. To obtain 1 SAM credit and 1.5 CME credits, you must follow the instructions on page SXX.

Radiologic Signs in Thoracic Imaging: Case-Based Review and Self-Assessment Module. To obtain 1 SAM credit and 1.5 CME credits, you must follow the instructions on page SXX.

Imaging of Lung Transplantation: Self-Assessment Module, CT Virtual Endoscopy in the Evaluation of Large Airway Disease: Self-Assessment Module, and Radiologic Signs in Thoracic Imaging: Case-Based Review and Self-Assessment Module are qualified by the American Board of Radiology (ABR) in meeting the criteria for self-assessment toward the purpose of fulfilling requirements in the ABR Maintenance of Certification. To obtain SAM credit, visit www.arrs.org and go to the left-hand menu bar under Publications/Journals/SAM Articles.
Instructions for Authors

A complete set of AJR Instructions for Authors, including information about figure processing and electronic submission requirements, can be found at www.arrs.org.

AJR Integrative Imaging submissions should follow the formats outlined below.

1. Reviews and Self-Assessment Modules

Although these articles may have a variety of formats (see specific types below), common elements include educational objectives, multiple-choice self-assessment questions that refer directly to the educational objectives, explanation of the correct and incorrect responses, and references. It is expected that some multiple-choice questions may be case-based. Each illustration should have a detailed description, either in the legend or in the text, and include the age, sex, and condition of the patient, as well as a description of the technology used to produce the image (e.g., endoluminal 3D CTC image of 32-year-old man with...).

Author instructions: The review portion of the manuscript should have 5,000–10,000 words of text, 10–25 figure parts, and as many references as needed. The self-assessment portion should have a least 10 four-option multiple-choice questions with complete solutions. The multiple-choice questions should have a single best response, and should be acceptable to the American Board of Radiology (ABR). The multiple-choice questions may be used to introduce the case discussions, to assess comprehension, or both. The solution to each multiple-choice question should explicitly state why each of the answer options is or is not the best response, and should have at least one reference. Redundancy of information presented in the solutions with that presented in the article text is to be expected.

Type 1. Case-based: This format consists of a set of educational case scenarios related by a theme. The case presentations consist of the clinical presentation, the rationale for imaging, a description of the images, four-option multiple-choice questions, explanations of the best and incorrect responses, and concluding commentary. The exact format depends on the particular case. The theme that relates the cases may be any combination of anatomy, clinical presentation, pathophysiology, technique, demographics, etc. These articles should have a minimum of six case scenarios. The following is an example of a case-based review and SAM (Editor’s note: Fewer case scenarios were required at the time this SAM was qualified by the ABR):


Type 2. Evidence-based: This format consists of discussions of one or more clinical management issues. The scientific evidence for different courses of management is presented in the context of illustrative case scenarios. These articles should have a minimum of six case scenarios. The following is an example of an evidence-based review and accompanying self-assessment module (Editor’s note: Fewer multiple choice questions were required at the time this SAM was qualified by the ABR):

• Momeni AK, Roberts CC, Chew FS. Imaging of Chronic and Exotic Sinonasal Disease: Self-Assessment Module. AJR 2007; 189[suppl]:S46–S48

2. Radiological Reasoning

These are case presentations that step the reader through an expert’s analysis of a difficult case. The case is presented progres-
sively, with the expert’s thought process described in detail. Con-
cluding comments tie up loose ends and provide references and
additional relevant factual material. Clinical reasoning presenta-
tions should fit on approximately five journal pages. The title of
the article should reflect the clinical or imaging presentation, not
the specific pathologic diagnosis. The abstract should include the
diagnosis and the take-home message of the article.

Author instructions: 2,000–4,000 words, NOT including the
multiple choice questions and solutions, 5–10 figure parts. Three
voices: case presenter, expert discussant, and expert commenta-
tor. Do not include a review of the literature because these may be
found elsewhere (e.g., textbooks and actual review articles). Each
article should be followed by five four-option multiple-choice
questions that will be used to assess comprehension. Each of the
best and non-best responses should be explicitly explained in the
solutions, and each solution should have at least one reference.

Radiological reasoning articles are often used as required read-
ing for self-assessment modules (see SAM Type 5, above), there-
fore, authors of radiological reasoning manuscripts are strongly
encouraged to submit a companion self-assessment module
manuscript at the same time. The following is an example of a ra-
diological reasoning article and accompanying self-assessment
module (Editor’s note: Fewer multiple choice questions were re-
quired at the time this SAM was qualified by the ABR):
• Liu PT. Radiological Reasoning: Acutely Painful Swollen
  Finger. AJR 2007; 188:[suppl]S13–S17
• Roberts CC, Liu PT, Chew FS. Imaging Evaluation of Ten-
don Sheath Disease: Self-Assessment Module. AJR 2007;
  188:S10–S12

3. Teaching File

Teaching file cases are standard cases that are well il-
lustrated, typically with an interesting twist. Unlike case reports,
which seek to extend the frontiers of knowledge, teaching file
cases are intended as exemplars of known appearances and pre-
sentations of disease, with the goal of educating the reader. The
standard presentation includes clinical history, clinical images,
radiologic description, focused differential diagnosis, final diag-
nosis, and commentary. An abstract should be prepared that
provides an educational objective and a conclusion. The title of
the article should reflect the clinical or imaging presentation
rather than the specific pathologic diagnosis. Authors should
provide two four-option multiple-choice questions with com-
plete solutions. Each of the best and non-best responses should
be explicitly explained in the solutions, and each solution
should have at least one reference. Authors will need to provide
indexing terms and coding.

Teaching file cases should be 1,000–2,000 words, NOT in-
cluding the multiple-choice questions and solutions, and typi-
cally no more than eight figure parts. Some teaching file
manuscripts may be selected for publication as Web exclusives.
Teaching File cases are often used as required reading for self-
assessment modules (see SAM Type 5, above), therefore, teaching
file manuscripts that are amenable to such use or are
accompanied by a companion self-assessment module manu-
script are much more likely to receive serious consideration.
The following is an example of a teaching file article and ac-
companying self-assessment module (Editor’s note: Fewer mul-
tiple choice questions were required at the time this SAM was
qualified by the ABR):
• Sutcliffe JB III, Bui-Mansfield LT. AJR Teaching File: In-
termittent Claudication of the Lower Extremity in a Y oung
  Patient. AJR 2007; 189[suppl]:S17–S20
• Chew FS, Bui-Mansfield LT. Imaging Popliteal Artery Dis-
case in Young Adults with Claudication: Self-Assessment
  Module. AJR 2007; 189[suppl]:S13–S16
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Imaging of Lung Transplantation: Review

Yuen Li Ng1, 2, Narinder Paul3, Demetris Patsios3, Anna Walsham4, Tae-Bong Chung3, Shaf Keshavjee5, Gordon Weisbrod3

OBJECTIVE

Lung transplantation is an established treatment for end-stage pulmonary disease. Complications of lung transplantation include airway stenosis and dehiscence, reimplantation response, acute rejection, infection, postransplantation lymphoproliferative disorder, and bronchiolitis obliterans syndrome. The incidence of graft rejection and airway anastomosis experienced in the early years of lung transplantation have been significantly reduced by advances in immunosuppression and surgical techniques. Infection is currently the most common cause of mortality during the first 6 months after transplantation, whereas chronic rejection or obliterative bronchiolitis is the most common cause of mortality thereafter. This article reviews the radiologic findings of different surgical techniques as well as the common early and late complications of lung transplantation.

CONCLUSION

Radiology plays a pivotal role in the diagnosis and management of complications of lung transplantation. Advancements in surgical technique and medical therapy influence the spectrum of expected radiologic findings. Familiarity with the radiologic appearances of common surgical techniques and complications of lung transplantation is important.

Introduction

The first successful isolated single-lung transplantation procedure was performed by the Toronto General Hospital group at the University of Toronto in 1983 [1]. Lung transplantation has since become an established treatment for end-stage pulmonary disease [2]. The registry of the International Society for Heart and Lung Transplantation (ISHLT) recorded an all-time high of 2,169 lung transplantations in 2005 [3]. The main indications for lung transplantation in the 18 months before this writing were chronic obstructive pulmonary disease (COPD, 38%), idiopathic pulmonary fibrosis (IPF, 19%), cystic fibrosis (16%), and α,1-antitrypsin deficiency emphysema (8%) (Table 1). The reported survival rates from January 1994 to June 2005 were 87% at 3 months, 78% at 1 year, 62% at 3 years, 50% at 5 years, and 26% at 10 years [3]. Overall, sepsis was the predominant cause of death in the first 6 months after transplantation, whereas chronic graft failure was the main cause of death after 6 months [2].

Surgical Techniques

Single-lung transplantation is usually performed through a posterolateral thoracotomy. On the other hand, bilateral lung transplantation is generally performed through a transverse thoracosternotomy involving bilateral sequential single-lung transplantation [2]. The technique of en bloc double-lung transplantation with tracheal anastomosis is now rarely performed because of the increased rate of anastomotic dehiscence.

Bilateral lung transplantation accounted for 63% of lung transplantation procedures in 2005 [3]. Bilateral lung transplantation is usually performed for chronic pulmonary sepsis such as cystic fibrosis and bronchiectasis (Table 1). It is also the dominant procedure for primary pulmonary hypertension. Bilateral lung transplantation for both COPD and IPF has increased in recent years. This trend may be explained by the higher overall survival rate after bilateral transplantation, by the increased lung function to buffer complications, and by institutional preferences and practices. The lung transplantation program at our institution prefers the use of bilateral lung transplants [2, 3].

Airway anastomotic dehiscence was one of the major obstacles to success in the early years of lung transplantation [4]. The early surgical techniques aimed to reduce the incidence of bronchial dehiscence by improved healing of the anastomoses using intercostal muscle, pericardium, or omentum to wrap the end-to-end bronchial anastomoses [5, 6]. However, the development of significant complications such as diaphragmatic hernias associated with the omental...
**TABLE 1: Distribution of Diagnoses and Procedures Among Adult Lung Transplant Recipients (January 1995 to June 2006) [3]**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Single Lung Transplants</th>
<th>Double Lung Transplants</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic obstructive pulmonary disease or emphysema</td>
<td>4,305 (52)</td>
<td>2,225 (24)</td>
<td>6,530 (38)</td>
</tr>
<tr>
<td>Idiopathic pulmonary fibrosis</td>
<td>2,193 (26)</td>
<td>1,217 (13)</td>
<td>2,410 (19)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>167 (2.0)</td>
<td>2,722 (29)</td>
<td>2,889 (16)</td>
</tr>
<tr>
<td>Alpha-1-antitrypsin deficiency emphysema</td>
<td>626 (7.5)</td>
<td>795 (8.5)</td>
<td>1,421 (8.1)</td>
</tr>
<tr>
<td>Primary pulmonary hypertension</td>
<td>65 (0.8)</td>
<td>575 (6.2)</td>
<td>640 (3.6)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>178 (2.1)</td>
<td>260 (2.8)</td>
<td>438 (2.5)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>30 (0.4)</td>
<td>473 (5.1)</td>
<td>503 (2.6)</td>
</tr>
<tr>
<td>Lymphangioleiomyomatosis</td>
<td>59 (0.7)</td>
<td>116 (1.2)</td>
<td>175 (1)</td>
</tr>
<tr>
<td>Cancer</td>
<td>7 (0.1)</td>
<td>12 (0.1)</td>
<td>19 (0.1)</td>
</tr>
</tbody>
</table>

Note—Data are numbers (%) of patients. Reprinted with permission from [3].

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**Fig. 1—Bronchial anastomosis.**

A. Schematic diagram shows end-to-end and “telescope” anastomoses.

B. 41-year-old woman who underwent bilateral lung transplantation in 1980s. CT scan shows area of fat attenuation (asterisk) in thorax, representing omentum used to wrap bronchial end-to-end anastomoses.

C and D. Axial (C) and coronal (D) CT reformations show normal posttransplantation appearance of telescope anastomoses. Note bronchial overlap; smaller bronchus is “telescoped” into larger bronchus. Internal margin of anastomosis is not sutured and may result in endoluminal flap (arrowhead, D).
Lung Transplantation

Bronchial dehiscence is the most common airway complication in the early postoperative period, affecting 2–3% of cases [2, 6, 12] and typically occurring 2–4 weeks after transplantation [6, 9, 10]. CT typically shows the presence of extraluminal gas and, occasionally, the focal bronchial wall defect that is pathognomonic of this condition [14] (Fig. 2). Indirect signs of bronchial dehiscence include the presence of a new or persistent air leak, pneumothorax, and pneumomediastinum.

Bronchial stricture formation is seen in approximately 10% of cases; it occurs later in the postoperative period, an average of 3 months after surgery [6, 9, 10]. There is thought to be an increased incidence of stricture formation with the use of the telescope anastomosis technique [8]. CT with multiplanar reconstructions is helpful in depicting strictures and webs and is

Airway Complications

The incidence of airway complications has decreased with improved surgical and donor preservation techniques, immunosuppression, and posttransplantation surveillance [4, 8, 10]. Airway complications have been estimated to occur in approximately 5–15% of lung transplants [4, 6, 9, 10]. The healing of bronchial anastomoses relies on healthy retrograde collateral perfusion from the pulmonary arterial circulation in the initial postoperative period because bronchial arteries are not reanastomosed during transplantation [6, 11]. A suboptimal vascular supply predisposes to ischemia and subsequent ulceration, leading to bronchial dehiscence, stricture formation, and bronchomalacia [6, 12]. Infection and rejection may also play a role.

Airway complications such as bronchial dehiscence and stricture are usually diagnosed by bronchoscopy. However, CT is valuable and is more sensitive than chest radiography in the diagnosis of airway complications [13].

Fig. 2—Bronchial dehiscence in 28-year-old woman 11 days after bilateral lung transplantation. Patient developed persistent bilateral pneumothoraces (curved arrows) despite bilateral thoracostomy drains (arrowheads). Cause was revealed on CT, which shows focal defect at right bronchial anastomosis and extraluminal air (straight arrow). Note also left lower lobe pneumonia causing consolidation and atelectasis.

Fig. 3—Bronchial stricture in 36-year-old man 6 weeks after bilateral lung transplantation.

A and B, Low-dose (50-mA) axial CT scan (A) and coronal reconstruction (B) show focal tight stenosis at left bronchial anastomosis (arrows).
particularly useful in assessing the extent of bronchial stenoses in order to plan bronchoscopic stent insertion [15] (Fig. 3).

**Vascular Complications**

Vascular anastomotic stenoses, which are more common at the arterial anastomoses, are rare, occurring in fewer than 4% of cases [16]. The risk of pulmonary infarction is greatest in the immediate postoperative period because the transplanted lung does not have an alternative bronchial blood supply. Perfusion scintigraphy may aid in making the diagnosis. The prognosis is usually dismal, but successful outcomes have recently been reported with angioplasty and stent insertion [8].

**Mechanical Complications**

Size mismatch between donor lung and recipient thoracic cavity may cause mechanical complications. Most centers will accept size differences of within 25% [17, 18]. If the donor lung is too large for the recipient, distortion of airways and atelectasis may occur, with retained secretions and secondary infections. This may lead to scarring. The oversized lung graft may be intraoperatively reduced to match the capacity of the recipient. If the donor lung is too small for the recipient, graft hyperexpansion may lead to hemodynamic compromise, limited exercise tolerance, or frank pulmonary hypertension, all because of an inadequate vascular bed [17]. In patients with emphysema who undergo single-lung transplantation, the small graft may be compressed by the emphysematous native lung, resulting in restrictive pulmonary function [18]. Lung volume reduction surgery may be performed during the transplantation procedure.

Pulmonary torsion is a rare but serious complication that may occur in the immediate postoperative period. Imaging features of pulmonary torsion are related to the torquing of the hilar structures, the airway, and the vasculature, and include a collapsed lobe (due to airway compromise) or an expansile consolidated lobe (due to hemorrhagic infarction) in an atypical location [19]. Other features that may be present are bronchial cutoff, inappropriate hilar displacement associated with an atelectatic lobe, abnormal position of pulmonary vasculature and bronchi, rapid opacification of a lobe or

**Fig. 4**—Pneumothorax after transbronchial biopsy in 45-year-old man. This patient experienced right pleuritic pain after surveillance bronchoscopy and transbronchial biopsy.

A, Immediate chest radiograph shows localized right basal pneumothorax (asterisk).

B, Subsequent CT scan confirms localized right basal hydropneumothorax associated with right lower lobe atelectasis and bronchiectasis.

**Fig. 5**—Pleural empyema and hematoma in 49-year-old man whose condition deteriorated clinically 8 days after bilateral lung transplantation. CT scan reveals focal fluid collection (single asterisk) in left anterior hemithorax containing gas, suggestive of empyema. Note also large focal collection in right basal hemithorax with higher-attenuation hematoma (double asterisks). Findings were confirmed at thoracotomy.
Lung Transplantation

Lung, and change in position of an opacified lobe on sequential radiographs. Once pulmonary torsion is suspected, immediate surgery is indicated to avoid death from lobar infarction.

**Pleural Complications**

Pleural complications are seen in 22–34% of patients after transplantation [20, 21]. Bilateral-lung and heart–lung transplantsations frequently result in a single communicating pleural space. Therefore, fluid and gas collections are often bilateral [8].

Pneumothorax is the most common pleural complication; it usually resolves with the insertion of thoracostomy drains [8, 21]. New, persistent, or enlarging pneumothoraces should prompt further investigations to elucidate the cause of the air leak (Fig. 2). Pneumothorax may also occur after transbronchial biopsy (Fig. 4).

Pleural effusions develop in almost all patients because of increased capillary permeability and impaired lymphatic clearance of the transplanted lung [12, 20]. They are usually self-limiting and resolve within 2 weeks. Persistent or delayed effusions suggest complicated effusions such as empyema, organized hematoma, rejection, and posttransplantation lymphoproliferative disorder (PTLD). Empyema occurs in approximately 4% of patients and may affect both hemithoraces, with potential disastrous consequences [8, 20] because it is the only pleural complication associated with an increased mortality rate [21]. Therefore, empyema should be excluded in the presence of a new or enlarging pleural effusion (Fig. 5).

**Pulmonary Parenchymal Complications**

Many pulmonary parenchymal complications after lung transplantation have nonspecific radiologic findings. Correlation with the time interval from transplantation is helpful to narrow the differential diagnoses (Fig. 6). Clinical correlation and bronchoscopy with transbronchial biopsy are also often required.

**Reimplantation Response**

Reimplantation response, also known as reperfusion edema, is a form of noncardiogenic pulmonary edema that occurs in more than 95% of patients [22] (Fig. 7). It frequently begins by postoperative day 1, is always present by day 3, peaks by day 4 or 5, and resolves by day 10 [8, 11]. Persistence beyond the first week suggests infection or acute rejection. Reimplantation response is usually diagnosed after

![Diagram showing typical time course for onset of pulmonary parenchymal complications after lung transplantation. PTLD = posttransplantation lymphoproliferative disorder.](image)

![Reimplantation response in 33-year-old woman 2 days after bilateral lung transplantation. A, Chest radiograph shows typical features of reimplantation response: bilateral perihilar and basal consolidation. B, CT scan shows bilateral patchy ground-glass opacities and septal thickening in addition to consolidation.](image)
exclusion of left ventricular failure, fluid overload, transplant rejection, and infection [22, 23].

Chest radiography and CT typically show bilateral perihilar and basal air-space consolidation [22]. The pathogenesis is probably multifactorial: increased vascular permeability due to ischemia and subsequent reperfusion, lymphatic interruption, lung denervation, decreased surfactant production, and surgical trauma [12].

**Acute Rejection**

Acute rejection usually occurs within the first 3 weeks, typically between postoperative days 5 and 10 [8] (Fig. 8). Most patients experience two or three significant rejection episodes in the first 3 months after transplantation [12]. Repeated episodes of acute rejection are associated with an increased risk of chronic rejection (i.e., bronchiolitis obliterans syndrome) [24].

The radiographic features may be similar to those of reimplantation response and infection. The presence of new, persisting, or progressive perihilar and basal opacities or pleural effusions with septal lines 5–10 days after transplantation without other signs of left ventricular failure is suggestive of acute rejection [8, 25]. CT findings include ground-glass opacities, interlobular septal thickening, nodules, consolidation, and volume loss. Ground-glass opacities are often patchy and localized in mild rejection but widespread in severe rejection [26]. However, CT has limited accuracy in the diagnosis or grading of severity of acute rejection [24].

Patients may be asymptomatic or may present with dyspnea, fever, leukocytosis, and decreased exercise tolerance. Investigations reveal a decrease in arterial oxygenation and forced expiratory volume in 1 second (FEV₁). The most useful feature is the dramatic clinical and radiographic response to corticosteroids and increased immunosuppression [8, 23]. Transbronchial biopsy is often performed to confirm the diagnosis and to exclude infection [8].
Infection is the most common complication after transplantation and is a major cause of morbidity and mortality [2]. Patients have increased susceptibility to infection because of immunosuppression, lung denervation and loss of the cough reflex, impaired mucociliary function, and lymphatic drainage [8, 27].

Bacterial infections predominate in the first 4 weeks after transplantation; viral infections are generally not seen until the following month. Fungal infections can occur at any period after transplantation. Pneumocystis pneumonia is now uncommon because of the routine use of trimethoprim-sulfamethoxazole prophylaxis [12].

**Bacterial Infection**

Bacterial infections account for at least 50% of all infections [11]. The incidence is highest in the first month, but remains a significant complication throughout the patient’s life.
Death is unusual in the immediate postoperative period because of the wide use of broad-spectrum antibiotics.

The most common causative organisms are gram-negative bacilli such as *Klebsiella* organisms, *Pseudomonas aeruginosa*, and *Enterobacter cloacae*. Gram-positive organisms such as *Staphylococcus aureus* are also observed [8, 11]. In patients with cystic fibrosis, the presence of *Burkholderia cepacia* is associated with severe postoperative infections and reduced survival rates [2].

Radiologic features are similar to those of nontransplant patients: lobar or multifocal consolidation, ground glass opacity, cavitation, and lung nodules [8, 27].

**Fungal Infection**

Fungal infections, most commonly *Candida* and *Aspergillus* organisms, usually occur between 10 and 60 days after transplantation [27]. They are less common but are associated with a higher mortality rate than viral infections [8]. *Candida* species frequently colonize the airways, but invasive pulmonary infection is uncommon.

Aspergillosis is more prevalent in lung transplantation patients than in other immunocompromised patients. Locally invasive or disseminated infection with *Aspergillus* organisms accounts for 2–33% of infections after lung transplantation and 4–7% of all lung transplantation deaths [27]. *Aspergillus* organisms can cause indolent pneumonia or fulminant angioinvasive infection with systemic dissemination (Fig. 9). CT commonly reveals a combination of ill-defined nodules, cavitary opacities, consolidation, and ground-glass opacity [27]. Symptoms are nonspecific and include fever, cough, pleuritic chest pain, and hemoptysis [8].

*Aspergillus* infections in the airway are seen in 5% of patients, mostly in the first 6 months. They are usually asymptomatic and are detected on surveillance bronchoscopy. Such an infection may cause ulcerative tracheobronchitis that is usually radiologically occult and can lead to bronchial dehiscence, stenosis, or bronchomalacia [8].

**Viral Infection**

Cytomegalovirus (CMV) is the second most common cause of pneumonia in lung transplantation patients and is the most common opportunistic infection [8] (Fig. 10). CMV pneumonia most commonly occurs between 1 and 12 months, with a peak incidence at 1–4 months [27].

Chest radiographs may be normal or may show diffuse parenchymal haziness or reticulonodular interstitial opacities. CT findings include areas of ground-glass attenuation, micronodules, consolidation, reticulation, and small pleural effusions [8, 27].

Patients may be asymptomatic or develop fulminant pneumonia. Clinical manifestations include dyspnea, fever, cough, and malaise [12]. CMV pneumonia is associated with an increased risk of superadded bacterial and fungal infections as well as the development of bronchiolitis obliterans syndrome. Diagnosis can be made by bronchoalveolar lavage and transbronchial biopsy.

Primary infection occurs in CMV-seronegative recipients who receive a graft from a seropositive donor. Infection develops in more than 90% and is serious in 50–60% of cases [27]. Thus, CMV matching between donor and recipient is performed whenever possible. Secondary infection develops from reactivation of a latent virus after immunosuppres-
sion or from infection with a different CMV strain and is usually less serious than the primary infection [8].

Other viral agents include herpes simplex virus, adenovirus, and respiratory syncytial virus.

**Posttransplantation Lymphoproliferative Disorder**

PTLD is a spectrum of diseases that vary from a histologically benign polyclonal lymphoid proliferation to aggressive high-grade lymphoma [28]. It may manifest from 1 month to several years after transplantation but tends to occur within the first year, peaking at 3–4 months [23] (Fig. 11). The incidence is approximately 5% (range, 1.8–20%), and it is more common with lung transplantation than with other solid organ transplantations [11, 28]. The variability in the incidence probably reflects differences in immunosuppression, ages of the study population, rates of Epstein-Barr viral (EBV) infections, and CMV prophylaxis.

Radiographically, PTLD usually manifests as solitary or multiple pulmonary nodules or masses [28]. Extrapulmonary involvement—hilar or mediastinal adenopathy, thymic enlargement, pleural effusions, and pericardial mass-

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**Fig. 12—Obliterative bronchiolitis in two patients.**

A and B, Chest radiograph (A) in 35-year-old woman 9 months after bilateral lung transplantation shows decreased vascular markings and increased lung volumes. CT scan (B) shows minor bronchial dilatation and mosaic attenuation. Transbronchial biopsy revealed obliterative bronchiolitis.

C and D, Inspiratory (C, 50 mAs) and expiratory (D, 20 mAs) CT scans show bronchial dilatation and air trapping in right lower lobe in 45-year-old man with known obliterative bronchiolitis.
es—is less common [11]. Clinical manifestations include low-grade fever, lethargy, and weight loss. Patients may also be asymptomatic.

PTLD is thought to be secondary to B-lymphocyte proliferation in response to EBV infection [11]. It is more commonly seen in EBV-seronegative recipients who receive an EBV-seropositive donor lung. Aggressive immunosuppression regimens are also thought to be a cause [28]. Most cases respond to antiviral agents (e.g., acyclovir) and a reduction or cessation of immunosuppressive therapy.

Fig. 13—Recurrent disease in three patients. A, Recurrent disease in 52-year-old woman 2 years after bilateral lung transplantation for sarcoidosis. CT scan shows nonspecific opacities in right lower lobe; transbronchial biopsy revealed noncaseating granulomas. B, 47-year-old woman with lymphangioleiomyomatosis (LAM) underwent bilateral lung transplantation. She developed chylothorax (arrow indicates fat–fluid level) and retroperitoneal lymphadenopathy, which proved at histology to be recurrent LAM. C, 58-year-old woman underwent bilateral lung transplantation 18 months earlier for multifocal bronchioloalveolar carcinoma. CT scan shows multiple nodules. Transbronchial biopsy confirmed recurrent disease.
Obliterative Bronchiolitis

Obliterative bronchiolitis is thought to be a manifestation of chronic rejection, affecting up to 50% of patients (Fig. 12). It is a major source of morbidity and mortality and is now the greatest limitation to long-term survival after lung transplantation [2, 8, 11]. It usually develops within 6–18 months after transplantation but may occur as early as the second month. Significant association with previous multiple episodes of acute rejection and CMV pneumonia has been reported. Other potential risk factors include other lung infections, gastroesophageal reflux, and human leukocyte antigen mismatching [29].

Obliterative bronchiolitis is a histologic diagnosis; changes affect the small airways in a patchy distribution. Transbronchial biopsy may not be diagnostic, particularly in the early stages [30]. Therefore, the disorder is frequently diagnosed clinically, using the term “bronchiolitis obliterans syndrome,” on the basis of an otherwise unexplained decline in lung function [29]. Patients generally present with a cough and worsening dyspnea [11].

The chest radiograph may be normal or may show attenuated pulmonary vessels, bronchial cuffing, subsegmental atelectasis, and irregular linear opacities [13, 31]. Lung volumes can be normal or mildly increased. CT typically shows bronchial dilatation, bronchial wall thickening, and mosaic attenuation that are most marked in the lower lobes [31]. Air trapping is frequently depicted on expiratory CT in patients with obliterative bronchiolitis and can also be seen on inspiratory CT in areas of lower attenuation with attenuated pulmonary vessels. However, the presence of air trapping is of limited sensitivity for the early diagnosis of obliterative bronchiolitis [32].

Recurrence Disease

Recurrence disease in the transplanted lung is uncommon, affecting approximately 1% of recipients. Sarcoidosis, lymphangioleiomyomatosis, bronchioalveolar carcinoma, and Langerhans cell histiocytosis have been reported to recur in the transplanted lung [8, 33]. The radiologic features of recurrent disease in the donor lung are similar to those of the original disease, but they may mimic other posttransplantation complications such as infection, rejection, and PTLD.

Sarcoidosis is the most commonly reported disease to recur, with a frequency of 35% [34] (Fig. 13A). Recurrence of sarcoidosis has been reported as early as 2 weeks and as late as 2 years after transplantation. It is an incidental finding at transbronchial lung biopsy in most cases. Transbronchial biopsy shows multiple noncaseating giant cell epithelioid granulomas. Because granulomas can also be seen with mycobacterial or fungal infection, it is important to exclude these diagnoses. A negative transbronchial lung biopsy does not exclude recurrent sarcoidosis because of the patchy nature of the disease.

Patients who have undergone lung transplantation for lymphangioleiomyomatosis have increased morbidity and mortality due to complications related to their underlying disease—for example, native lung pneumothorax, chylothorax, chylous ascites, hemorrhagic renal angiomyolipomas, and recurrence of disease—from 1 to 5 years after transplantation [34] (Fig. 13B).

Recurrence of bronchioalveolar carcinoma has occurred in approximately 50% of patients who survive the trans-
plantation [33] (Fig. 13C). Recurrence is usually limited to a transplant graft and is slow-growing despite immunosuppression. Lung transplantation for the treatment of multifocal bronchioloalveolar carcinoma is not widely established, and represents only approximately 0.1% of transplantations recorded by the ISHLT [3] (Table 1). Lung transplantation is unlikely to be curative but can achieve a 5-year survival rate of 39%, which is similar to that for other end-stage pulmonary diseases [33].

Upper Lobe Fibrosis

Upper lobe fibrosis is uncommon, reported to occur 18–72 months (average, 42 months) after lung transplantation [35] (Fig. 14). The exact pathogenesis is unknown but is hypothesized to be a rare manifestation of chronic rejection. Pathologic assessment may show nonspecific inflammation and fibrosis.

High-resolution CT findings include interlobular septal thickening, gradual development of coarse reticular opacities, and mild peripheral ground-glass opacities. The progression of established fibrosis may occur with traction bronchiectasis, honeycombing, architectural distortion, and volume loss. The upper lobes are initially involved, with the subsequent development of smaller volumes of fibrosis in the superior segments of the lower lobes [35]. The basal segments are minimally involved.

Patients develop progressive dyspnea. Pulmonary function tests may show a mixed obstructive and restrictive pattern.

Complications After Transbronchial Biopsy

Solid and cavitary nodules (2–15 mm) with surrounding ground-glass attenuation may be identified on CT up to 1 month after transbronchial biopsy [36] (Fig. 15). The ground-glass attenuation represents hemorrhage secondary to biopsy. The nodules may not be immediately evident on chest radiographs. The temporal relationship to the biopsy and the location at known biopsy sites should prevent confusion with infection or rejection.

Summary

Radiology plays a pivotal role in the diagnosis and management of complications of lung transplantation. Radiologists should be familiar with the radiologic appearances of common surgical techniques as well as those of complications of lung transplantation. Because the radiologic pattern of disease may be nonspecific, it is critical to know the time course from lung transplantation and relevant postoperative history in order to generate a clinically useful and relevant radiologic opinion.

References

Imaging of Lung Transplantation: Self-Assessment Module

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ABSTRACT

Objective

The educational objectives of this continuing medical education activity are for the reader to exercise, self-assess, and improve skills in diagnostic radiology with regard to imaging of lung transplantation and to improve familiarity with the complications of lung transplantation.

Conclusion

The articles in this activity review the imaging and complications of lung transplantation and discuss the role of imaging in the assessment of complications from lung transplantation.

INTRODUCTION

This self-assessment module on imaging of lung transplantation has an educational component and a self-assessment component. The educational component consists of one required article that the participant should read. The self-assessment component consists of 10 multiple-choice questions with solutions. All of these materials are available on the ARRS Website (www.arrs.org). To claim CME and SAM credit, each participant must first order the CME activity, then enter his or her responses to the questions online.

EDUCATIONAL OBJECTIVES

By completing this educational activity, the participant will:
A. Exercise, self-assess, and improve his or her understanding of the imaging of lung transplantation.
B. Exercise, self-assess, and improve his or her understanding of the complications of lung transplantation.

REQUIRED READING


INSTRUCTIONS

1. Complete the educational and self-assessment components included in this issue.
3. Select Publications/Journals/SAM Articles from the left-hand menu bar.
4. Order the online SAM as directed. (The SAM must be ordered to be accessed even though the activity is free to ARRS members.)
5. The SAM can be accessed at www.arrs.org/My Education/My Online Products, but you must be logged in to access this personalized page.
6. Answer the questions online to obtain SAM credit.

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QUESTION 1
Concerning early complications of lung transplantation, which of the following is TRUE?

A. Bronchial dehiscence is usually diagnosed on chest radiography.
B. Reimplantation response is a form of noncardiogenic pulmonary edema and occurs in more than 95% of lung transplantation patients.
C. CT features of acute rejection, such as ground-glass opacities, interlobular septal thickening, nodules, and consolidation, are accurate in the diagnosis and assessment of severity of acute rejection.
D. Acute rejection responds poorly to corticosteroids.

QUESTION 2
Concerning late complications of lung transplantation, which of the following statements is FALSE?

A. Obliterative bronchiolitis usually develops 6–18 months after transplantation and is associated with previous multiple episodes of acute rejection and cytomegalovirus (CMV) pneumonia.
B. Obliterative bronchiolitis is a histologic diagnosis affecting the small airways and is reliably excluded by negative transbronchial biopsy.
C. Upper lobe fibrosis is hypothesized to be a rare manifestation of chronic rejection in lung transplantation patients.
D. Posttransplantation lymphoproliferative disorder occurs more commonly in patients with lung transplants than in patients with other solid organ transplants.

QUESTION 3
Which of the following statements regarding infection after lung transplantation is FALSE?

A. Bacterial infections usually occur in the first month after transplantation.
B. Most common bacterial infections are due to gram-negative bacilli such as Klebsiella organisms and Pseudomonas aeruginosa.
C. Aspergillosis is more prevalent in lung transplantation patients than in other immunocompromised patients.
D. Pulmonary nodules on CT with a surrounding halo of ground glass are specific for invasive aspergillosis in lung transplantation patients.

QUESTION 4
Which of the following statements is TRUE regarding CMV infection after lung transplantation?

A. CMV infection is the most common cause of pneumonia.
B. CMV infection is the most common opportunistic infection.
C. Primary CMV infection occurs in seropositive recipients who receive a graft from a seropositive donor.
D. Secondary CMV infection develops from reactivation of a latent virus or from infection with a different CMV strain and is usually more serious than primary infection.
E. Posttransplantation lymphoproliferative disorder is thought to be secondary to B-lymphocyte proliferation in response to CMV infection.

QUESTION 5
Which of the following features is LEAST commonly seen on CT in obliterative bronchiolitis after lung transplantation?

A. Bronchial wall thickening and dilatation.
B. Nodules.
C. Pleural effusion.
D. Mosaic attenuation.
E. Air trapping.

QUESTION 6
Concerning pulmonary parenchymal complications after lung transplantation, which of the following is LEAST LIKELY to manifest as pulmonary nodules?

A. Invasive pulmonary aspergillosis.
B. Reimplantation response.
C. Bronchial carcinoma.
D. Hematoma after transbronchial biopsy.
E. Posttransplantation lymphoproliferative disorder.
Question 7
Which of the following statements concerning patients after lung transplantation is FALSE?
A. Acute rejection is the most common cause of mortality during the first 6 months after lung transplantation.
B. Obliterative bronchiolitis is the most common cause of mortality in lung transplantation patients beyond 6 months after transplantation.
C. Empyema is the only pleural complication associated with increased mortality and should be excluded in a new or enlarging pleural effusion after lung transplantation.
D. The overall reported 5-year survival rate for lung transplantation patients is approximately 50%.

Question 8
Which of the following statements concerning airway complications after lung transplantation is FALSE?
A. Airway anastomotic complications was one of the major obstacles to success in the early years of lung transplantation but is now rarely encountered (< 1% of lung transplantation patients).
B. Bronchial dehiscence is the most common airway complication in the early postoperative period, typically occurring 2–4 weeks after transplantation.
C. CT occasionally shows a focal bronchial wall defect that is pathognomonic of bronchial dehiscence.
D. Bronchial stricture formation occurs later in the postoperative period, an average of 3 months after transplantation.

Solution to Question 1
Option B is the best response. Reimplantation response occurs in more than 95% of lung transplantation patients [1]. The pathogenesis is probably multifactorial: increased vascular permeability due to ischemia and subsequent reperfusion, lymphatic interruption, lung denervation, decreased surfactant production, and surgical trauma [2]. Option A is not the best response. Airway complications are usually diagnosed at bronchoscopy. Chest radiographs are unreliable in the diagnosis of airway complications [3]. CT is useful in the diagnosis of bronchial dehiscence, showing extraluminal gas and focal bronchial wall defects [4]. CT can also show bronchial stenoses and is particularly valuable in assessing the length of stenoses to plan for stent insertion and assessing position of stents [5]. Option C is not the best response. CT features of acute rejection are non-specific (i.e., ground-glass opacities, interlobular septal thickening, nodules, and consolidation), and CT is of limited accuracy in the diagnosis or grading of severity of acute rejection [6]. Transbronchial biopsy is often performed to confirm the diagnosis and to exclude infection [7]. Pathology showed perivascular lymphocytic infiltrates, which may progress to extend into the alveolar septa and alveoli. Acute rejection is histologically graded on a scale of 0–4 on the basis of the severity of the reaction. Option D is not the best response. The most useful diagnostic feature of acute rejection is the dramatic clinical and radiographic response to corticosteroids and increased immunosuppression [7, 8].
Solution to Question 2

Option B, which is not true, is the best response. Obliterative bronchiolitis is a histologic diagnosis affecting the small airways in a patchy distribution; transbronchial biopsy may not be diagnostic, particularly in the early stages [9]. Therefore, this disorder is frequently diagnosed clinically, using the term “bronchiolitis obliterans syndrome,” on the basis of an otherwise unexplained decline in lung function [10]. Option A is a true statement and therefore is not the best response [7]. Option C is not the best response. Upper lobe fibrosis is uncommon, reported to occur 18–72 months after lung transplantation [11]. The exact pathogenesis is unknown but is hypothesized to be a rare manifestation of chronic rejection. Pathology may show nonspecific inflammation and fibrosis. Option D is not the best response. Post-transplantation lymphoproliferative disorder (PTLD) is a spectrum of diseases that vary from a histologically benign polyclonal lymphoid proliferation to aggressive high-grade lymphoma [12]. The incidence is approximately 5% (range, 1.8–20%), which is more common than in patients with other solid organ transplants [12, 13]. In contrast to other solid organ transplantation patients, PTLD in lung transplantation patients usually manifests as pulmonary nodules or masses [12], and extrapulmonary involvement is less common (e.g., hilar or mediastinal adenopathy, thymic enlargement, pleural effusions, and pericardial masses) [13].

Solution to Question 3

Option D is the best response. Pulmonary nodules with a surrounding halo of ground glass (i.e., the CT halo sign) were originally described in patients with angioinvasive pulmonary aspergillosis [14]. Since then, however, this appearance has been recognized in other infections (e.g., candidiasis, cytomegalovirus [CMV]), neoplastic disorders (e.g., PTLD, bronchioalveolar carcinoma), and inflammatory conditions (e.g., hematoma after transbronchial biopsy) [15]. Options A and B are not the best responses. Bacterial infections account for at least 50% of all infections [13]. The incidence is highest in the first month, but the possibility of bacterial infection remains throughout the patient’s life. Most common causative organisms are gram-negative bacilli such as Klebsiella organisms, Pseudomonas aeruginosa, and Enterobacter cloacae. Gram-positive organisms such as Staphylococcus aureus are also observed [7, 13]. Option C is not the best response. Aspergillosis is more prevalent in lung transplantation patients than in other immunocompromised patients. Locally invasive or disseminated aspergillosis infection accounts for 2–33% of infections after lung transplantation and 4–7% of all lung transplantation deaths [16]. Aspergillosis can cause indolent pneumonia or fulminant angioinvasive infection with systemic dissemination.

Solution to Question 4

Option B is the best response. CMV is the most common opportunistic infection after lung transplantation [16]. Option A is not the best response. CMV is the second most common cause of pneumonia (after bacterial infection) in lung transplantation patients [16]. Options C and D are not the best responses. Primary infection occurs in CMV-seronegative recipients who receive a graft from a seropositive donor. Infection develops in more than 90% and is serious in 50–60% of cases [16]. Thus, CMV matching between donor and recipient is performed whenever possible. Secondary infection develops from reactivation of a latent virus after immunosuppression or from infection with a different CMV strain. It is usually less serious than a primary infection [7]. Option E is not the best response. PTLD is thought to be secondary to B-lymphocyte proliferation in response to Epstein-Barr virus (EBV) infection [13]. It is more commonly seen in EBV-seronegative recipients who receive an EBV-seropositive donor lung.

Solution to Question 5

Option C is the best response. Pleural effusion is the least likely of the listed findings to be seen in obliterative bronchiolitis. CT findings of obliterative bronchiolitis include bronchial dilatation, bronchial wall thickening, nodular and linear opacities, air trapping, mosaic attenuation, and peribronchovascular infiltrates that are most marked in the lower lobes [17]. Air trapping is the most frequent feature. However, its presence may be intermittent in patients with obliterative bronchiolitis and is of limited sensitivity for the early diagnosis of obliterative bronchiolitis [18]. Options A, B, D, and E, which are likely findings, are not the best responses.

Solution to Question 6

Option B is the best response. Reimplantation response (or reperfusion edema) is a form of noncardiogenic pulmonary edema. Chest radiography and CT typically show bilateral perihilar and basal air-space opacification [1]. Options A, C, D, and E are not the best responses. Pulmonary nodules after lung transplantation are largely due to infection, PTLD, and malignancy [19]. Chest radiography is a useful screening tool, but CT is more sensitive in detecting and characterizing nodules. Bronchoscopy with bronchioalveolar lavage and transbronchial biopsy, as well as CT-guided and video-assisted thoracic surgery biopsy, should also be considered. Solid and cavitary nodules with surrounding ground-glass attenuation may be identified on CT up to 1 month after transbronchial biopsy. The ground-glass attenuation represents hemorrhage secondary to biopsy. The temporal relationship to the biopsy and the location at known biopsy sites should prevent confusion with infection [20].

Solution to Question 7

Option A is the best response. Infection is the most common cause of mortality during the first 6 months after lung transplantation [21]. Patients have an increased susceptibility to infection because of immunosuppression, lung
denervation with loss of the cough reflex, impaired mucociliary function, and lymphatic drainage [7, 16]. Option B is not the best response. Chronic rejection or obliterative bronchiolitis is the most common cause of mortality more than 6 months after lung transplantation [21]. Option C is not the best response. Pleural effusions occur in almost all patients but are usually self-limiting and resolve within 2 weeks [2, 22]. Persistent or new effusions suggest a complication such as empyema. A single communicating pleural space commonly develops after bilateral lung and heart–lung transplantations. Therefore, empyema may affect both hemithoraces with potentially disastrous consequences [7, 22–24]. Option D is not the best response as it is a true statement. The reported survival rates from January 1994 to June 2005 were 87% at 3 months, 78% at 1 year, 62% at 3 years, 50% at 5 years, and 26% at 10 years.

**Solution to Question 8**

**Option A, which is not true, is the best response.** Although the incidence of airway complications has decreased with improved surgical and donated-organ preservation techniques, immunosuppression, and posttransplantation surveillance [7, 25, 26], airway complications still cause significant morbidity and have been estimated to occur in approximately 5–15% of lung transplantation patients [24–28]. Options B and C are not the best responses. Bronchial dehiscence is the most common airway complication in the early postoperative period, affecting 2–3% of cases [2, 21, 27]. CT typically shows the presence of extraluminal gas and, occasionally, the focal bronchial wall defect that is pathognomonic of this condition [4]. Indirect signs of bronchial dehiscence include the presence of a new or persistent air leak, pneumothorax, and pneumomediastinum. Option D is not the best response because it is a true statement. Bronchial stricturing formation is seen in approximately 10% of patients [26–28].

**Solution to Question 9**

**Option B is the best response.** Pneumothorax usually resolves with the insertion of thoracostomy drains [7, 23]. New, persistent, or enlarging pneumothoraces should prompt further investigation to elucidate the cause of the air leak. Option A is not the best response. Pneumothorax is the most common pleural complication after lung transplantation [7, 23]. Bilateral lung and heart–lung transplantations frequently result in a single communicating pleural space. Therefore, pneumothoraces are often bilateral [7]. Options C and D are not the best responses. Pleural effusions develop in almost all transplantation patients because of increased capillary permeability and impaired lymphatic clearance of the transplanted lung [2, 22]. They are usually self-limiting and resolve within 2 weeks. Persistent or delayed effusions suggest complicated effusions such as empyema, organized hematoma, rejection, and PTLD.

**Solution to Question 10**

**Option D is the best response.** The CT image shows bilateral ground-glass opacities, air-space consolidation, and interlobular septal thickening. At day 2 after lung transplantation, reimplantation response is the most likely diagnosis. Reimplantation response frequently begins by day 1, is always present by day 3, peaks by day 4 or 5, and resolves by day 10 [7, 13]. In clinical practice, it is usually diagnosed after exclusion of left ventricular failure, fluid overload, transplant rejection, and infection [1, 8]. Options A, B, and C are not the best responses. The radiologic features of acute rejection and pneumonia may be similar to those of reimplantation response [16, 29]. However, acute rejection and pneumonia tend to occur later than reimplantation response after lung transplantation. Acute rejection usually occurs within the first 3 weeks, typically between days 5 and 10 [7]. Bacterial pneumonia tends to predominate in the first month after lung transplantation, and fungal pneumonia usually occurs between 10 and 60 days after transplantation [16].

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Objective

The purpose of this article is to illustrate the usefulness and limitations of CT virtual endoscopy in the evaluation of large airway disease.

Conclusion

CT virtual endoscopy is a postprocessing tool that is easy to perform and that can aid in depicting disorders of the large airways without additional radiation or cost other than added time in postprocessing. The benefits of this technique include noninvasive diagnostic surveillance and preoperative planning.

Introduction

CT virtual endoscopy has been used to evaluate pathologic processes of the nasopharynx, larynx, and tracheobronchial tree [1–5]. Findings are generally made first on the CT source images. The stunning CT virtual endoscopic images subsequently generated allow pulmonologists and otolaryngologists the anatomic perspectives of the large airway that they are clinically accustomed to viewing. Effective clinical consultation requires the practicing radiologist to be familiar with the technique of generating these images, as well as the anatomy and pathologic conditions shown.

CT Virtual Endoscopy Technique

Unlike virtual colonoscopy, no preprocedural patient preparation is needed to evaluate the large airways. CT virtual endoscopy applications are performed retrospectively to aid in the depiction of data detected on routine image interpretation that may be useful to referring physicians. The high contrast of an air-filled lumen renders 3D and 4D imaging that closely resembles the conventional endoscopic correlate. All CT virtual endoscopy review was performed after approval of the institutional review board, using diagnostic neck and chest CT scans at our institution. All CT examinations were performed on either the 64-MDCT Brilliance CT scanner or the 16-MDCT MX8000iDCT CT scanner (both Philips Healthcare) using routine departmental protocols (Table 1). With the 64-MDCT scanner, isotropic data are acquired routinely on all chest and neck CT scans. Because dose efficiency is quite high with the 64-MDCT scanner, there is no significant radiation cost to the patient for isotropy. Some additional radiation dose occurs when acquiring isotropic data with the 16-MDCT scanner. At our institution, isotropic data are routinely acquired on neck CT examinations to allow high-quality multiplanar reformations. Although no preprocedure preparation is required, imaging of the proximal airways can be optimized for lumen distention with maximum aeration using either the modified Valsalva or the phonation technique [6].

Postprocessing was performed with the virtual endoscopy application. Using CT virtual endoscopy application software, preset tissue algorithms (e.g., trachea) change the color scheme and set thresholds that define the tissue–air interface. Once the data are loaded into the endoscopy application, the cursor can be moved into the airway lumen, and the observer’s view is directed as desired using the swivel tool to provide the best images of the desired region. It is helpful to orient the image to correspond with a conventional endoscopic view. For example, nasal endoscopy is performed in a face-to-face doctor–patient orientation. This is in contrast to bronchoscopy, in which the bronchoscopist is usually positioned behind the patient, having the same right–left orientation. Labeling the CT virtual endoscopic images may be necessary for clarification. Postprocessing requires approximately 10 additional minutes per examination.

Virtual Nasopharyngoscopy and Laryngoscopy

Choanal Atresia

CT virtual endoscopy of the normal nasopharynx from a posterior viewpoint provides a look at the eustachian tube openings in reference to the choanae and nasopharyngeal walls, an area difficult to appreciate with conventional CT
This is compared to a 4-year-old girl in whom the right posterior nasal cavity is blocked, consistent with choanal atresia (Figs. 1B and 1C). Note the abnormally thickened vomer in choanal atresia, a finding important in diagnosis and preoperative planning [7].

**TABLE 1: Protocols Used in CT Virtual Endoscopy Examples**

<table>
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<tr>
<th>Scanner</th>
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<th>mAs</th>
<th>Collimation (mm)</th>
<th>Pitch</th>
<th>Rotation Time (s)</th>
<th>Matrix</th>
<th>Field of View (mm)</th>
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<td>Neck</td>
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<td>300</td>
<td>64 × 0.625</td>
<td>0.891</td>
<td>0.75</td>
<td>512</td>
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<tr>
<td>Chest</td>
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<td>0.906</td>
<td>0.75</td>
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Note—Both scanners are by Philips Healthcare.

[1] (Fig. 1A). This is compared to a 4-year-old girl in whom the right posterior nasal cavity is blocked, consistent with choanal atresia (Figs. 1B and 1C). Note the abnormally thickened vomer in choanal atresia, a finding important in diagnosis and preoperative planning [7].

**Epiglottitis**

Compare the normal epiglottis (Fig. 2A) with that of an immunocompromised patient who presented to the emergency department with a markedly thickened epiglottis and symptoms consistent with acute epiglottitis (Figs. 2B
and 2C). CT virtual endoscopy can provide a familiar view to the endoscopist for planning subsequent intervention, which is usually required when the airway is compromised by more than 50% [8].

Vocal Cord Lesions

When imaging the glottis, evaluation of submucosal extent of disease is the mainstay of the CT examination. However, CT virtual endoscopy can direct biopsy planning of cord lesions. With CT virtual endoscopy, the 3D location of polypoid lesions is easier to appreciate. True polyps most often occur along the anterior third of the vocal cord, whereas polypoid corditis, a form of Reinke’s edema, is usually more diffuse. Reinke’s edema is a chronic laryngeal disease found almost exclusively in smokers that is difficult to diagnose with imaging alone. Imaging of a 46-year-old woman with a long history of smoking and hoarseness who presented with increasingly labored breathing is shown (Fig. 3). CT virtual endoscopy depicts diffuse vocal cord edema with a superimposed polypoid area of swelling (Fig. 3A). Both true polyps and Reinke’s edema can cause acoustic dysfunction, but the latter is much more likely to cause airway compromise [9]. When glottic obstruction is present, we have found it difficult to delineate laryngeal structures with CT virtual endoscopy (Figs. 2B and 3A). However, laryngeal airway distension techniques may help when evaluating known laryngeal disease [6].
Radiologists should be able to recognize the normal tracheal architecture and anatomic variants. In particular, normal structures such as the transverse aorta can indent the large airways and need not be confused with extrinsic lesions when viewed endoscopically. Note how CT virtual endoscopy nicely shows the posterolateral location of a tracheal bronchus from an endoluminal perspective (Fig. 4). CT virtual endoscopy of the trachea is a useful postprocessing tool because views of disorders can closely resemble those of conventional endoscopy, making this a much appreciated extra step from the endoscopist’s perspective.

**Virtual Tracheoscopy**

Biopsy planning in the workup of a lung mass hinges on lesion location and size. A decision must be made whether to perform percutaneous, open, or transbronchial biopsy. Virtual tracheobronchoscopy can guide this decision-making algorithm by assessing extrinsic mass effect. If a peribronchial lesion is exerting mass effect, transbronchial biopsy may be performed successfully. In this example, we studied a 64-year-old man with vocal cord paralysis due to mediastinal invasion of non–small cell lung cancer. In conjunction with the axial CT appearance, virtual tracheoscopy can further evaluate true vocal cord paralysis (Figs. 5A and 5B) second-

**Non–Small Cell Lung Cancer**
ary to recurrent laryngeal nerve involvement by a stage T4 mediastinal mass (Figs. 5C and 5D). Note the obscuring of the right bronchial orifice as compared with a more normal-caliber distal trachea (Fig. 4). Virtual tracheobronchoscopy has promise for transluminal biopsy planning [5].

Postintubation Tracheal Stenosis
Endotracheal intubation is the most common cause of acquired tracheal stenosis, which may follow prolonged tracheal balloon inflation. With the implementation of low-pressure cuffs, the incidence has been reduced to less than 1% [10]. Presented here is one such example in a 14-year-old boy who sustained burns and underwent intubation for less than a week, 1 month before this CT examination (Fig. 6). Focal stenoses, usually less than 2 cm in length, can be difficult to appreciate on conventional radiographs [10]. Likewise, focal stenoses may be overlooked on routine axial CT images because the orientation of the stenosis is in the plane of image acquisition. Tracheal stenoses are much better appreciated with coronal reformations and CT virtual endoscopy, which is a view that is helpful to the surgeon [5].

Recurrent Respiratory Papillomatosis
Juvenile-onset recurrent respiratory papillomatosis usually begins in the larynx, specifically along the anterior third of the vocal cords [11], but can spread anywhere in the tracheobronchial tree. Involvement of the lower airways and lungs occurs in 5–28.8% of patients and carries a more serious prognosis [11]. Managing this disease may require countless bronchoscopies and laser treatment of dominant papillomas in effort to prevent airway compromise and malignant degeneration [10]. Between treatments, CT virtual endoscopy can provide surveillance, particularly in the evaluation of larger lesions. Although abundant information regarding texture of the mucosa and lesions can be obtained with fiberoptic imaging (Figs. 7B and 7D), the relative size of the lesions is nicely depicted on the CT vir-
tual endoscopic images (Figs. 7A and 7C). This noninvasive examination can be of value to patients who often undergo countless endoscopic procedures for surveillance, as in the example of this 23-year-old woman, who was diagnosed at age 2 with this unrelenting disease that has now progressed to involve the lung parenchyma (Fig. 7E).

**Tracheobronchial Amyloidosis**

Tracheobronchial amyloidosis is the most common subtype of pulmonary amyloidosis. The interstitial and nodular parenchymal patterns occur less frequently [11]. Irregular narrowing and thickening of the tracheobronchial wall are seen routinely on cross-sectional imaging. Here, in a

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**Fig. 5 (continued)—64-year-old man with non–small cell lung cancer.**

C, Virtual tracheoscopy image with abnormal extrinsic compression of distal right trachea caused by mass lesion (asterisk). D, Axial PET/CT fusion image of chest shows primary tumor.

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**Fig. 6—14-year-old male burn patient with tracheal stenosis.**

A–C, Virtual tracheoscopy image just above stenosis (arrow, A), correlative conventional endoscopic image (B), and contrast-enhanced coronal CT image (C) show short segment stenosis and dystrophic calcification in submucosa (arrows, C).

(Fig. 6 continues on next page)
54-year-old woman who presented initially with shortness of breath and who was treated with bronchoscopically directed debulking. CT virtual endoscopy shows the airway lumen and extent of obstruction, which correlate well with the conventional endoscopic view (Figs. 8A–8C). This can be differentiated on axial CT from tracheobronchopathia osteoplastica, which contains calcification in the diseased tracheal wall and characteristically spares the posterior membrane. Wegener’s granulomatosis is another infiltrative disease of the trachea that often involves the subglottic airway, causing stenosis [10, 12]. CT virtual endoscopy has been shown to increase sensitivity for diagnosing subglottic stenoses in these patients [12].

Treatment of tracheobronchial amyloidosis is difficult and historically has been limited to bronchoscopically directed debulking by forceps resection and laser therapy [9]. More recently, external beam radiation therapy (EBRT) has been described as a viable alternative [13]. Volume-rendering techniques can provide an overview of the infiltrated tracheal wall, which can potentially help direct EBRT planning (Fig. 8D).

Technical Limitations

Asymmetry is a guide to pathology on endoscopy, but asymmetries on CT, particularly in the larynx, are most often caused by poor aeration [6]. Because of this, virtual laryngoscopy has low specificity in evaluating mucosal lesions of the valleculae, pyriform sinuses, and larynx [2]. Therefore, findings on virtual laryngoscopy should always be evaluated in the context of the original CT data set [2].

The extent of airway compromise may be overestimated on CT virtual endoscopy when the airway is significantly stenosed. The apparent degree of stenosis may vary with different tissue–air threshold values. Lower threshold values increase the apparent stenosis, and higher thresholds can produce mucosal gaps [3]. This phenomenon is exemplified in the case of polypoid corditis, with different threshold values yielding different appearances of the pathology (Fig. 9). The degree of glottic narrowing must be approximated with the source CT images. In this case, actual luminal compromise was estimated to be 85% by conventional endoscopy. Therefore, threshold values should be tailored to reflect relative lumen size. This can be performed easily at the workstation by using the mouse to appropriately “window” the threshold value of the 3D image or by manually entering different values into the display options. This also applies to endoluminal lesions. Note that mass lesion size is generally underestimated using CT virtual endoscopy, and measurements should instead be made from 2D source CT data [4].

To reiterate, the CT virtual endoscopic images shown in this article were created retrospectively with no changes in routine departmental scanning protocols (Table 1). However, in the evaluation of distal airway disease, advanced protocols such as cardiac gating and submillimeter collimation should be considered [14]. Finally, we found no significant qualitative differences in CT virtual endoscopy images created from the 16-MDCT scanner (Figs. 2 and 8) versus those generated from the 64-MDCT scanner (Figs. 3 and 6).

Conclusion

CT virtual endoscopy can be a useful adjunct in the evaluation of large airway disease. It often elicits a favorable
Figure 7—23-year-old woman with recurrent respiratory papillomatosis that was diagnosed when she was 2 years old. A–D, Virtual tracheoscopy from subglottic and distal tracheal images (A and C) show innumerable plaquelike and exophytic lesions. Compare these with correlative fiberoptic endoscopic images (B and D).

(Fig. 7 continues on next page)
Fig. 7 (continued)—23-year-old woman with recurrent respiratory papillomatosi-
sis that was diagnosed when she was 2 years old. E, Coronal oblique CT image using lung window setting shows irregularity of airway and associated pulmonary parenchymal cavities.

Fig. 8—54-year-old woman with tracheobronchial amyloidosis. A and B, CT virtual endoscopic view (A) and correlatve conventional endoscopic view (B) show tracheal narrowing and featureless mucosal surface (asterisk, A). (Fig. 8 continues on next page)
Fig. 8 (continued)—54-year-old woman with tracheobronchial amyloidosis.
C, Contrast-enhanced axial CT image through region of maximal luminal narrowing shows infiltrative thickening of tracheal wall (arrow).
D, Three-dimensional volume-rendered image of trachea shows significant eccentric luminal narrowing (arrow).

Fig. 9—Effect of varying tissue–air interface values in CT virtual endoscopy.
A, Preset threshold value of –682 HU exaggerates polypoid lesion and shows artifactual obstruction of glottic opening (arrow).
B, Threshold value of –427 HU better depicts the true lumen size (arrow) as compared with axial CT source image.

(Fig. 9 continues on next page)
CT Virtual Endoscopy of Airway Disease

Fig. 9 (continued)—Effect of varying tissue–air interface values in CT virtual endoscopy.

C. Threshold value of –100 HU underestimates glottic narrowing (arrow) and produces artificial gaps in tissue surfaces.

response from referring physicians. Recognizing its limitations is important, however, to interpret it correctly. In this article, we provide examples to illustrate the usefulness of CT virtual endoscopy. We also present some technical parameters necessary for the success of virtual endoscopy. CT virtual endoscopy provides information to clinicians in a format they are most familiar with: endoscopy. Like conventional endoscopy, CT virtual endoscopy can be used for surgical planning, disease monitoring, or patient education.

References

CT Virtual Endoscopy in the Evaluation of Large Airway Disease: Self-Assessment Module

Bradley P. Thomas¹, Megan K. Strother, Edwin F. Donnelly, John A. Worrell

ABSTRACT

Objective

The educational objectives of this continuing medical education activity are for the reader to exercise, self-assess, and improve skills in diagnostic radiology with regard to the imaging evaluation of large airway disease and understanding the basics of CT virtual endoscopy techniques as well as their limitations.

Conclusion

The articles in this activity review the imaging evaluation of large airway disease and the basics and limitations of CT virtual endoscopy.

INTRODUCTION

This self-assessment module on imaging evaluation of large airway disease has an educational component and a self-assessment component. The educational component consists of three required articles that the participant should read. The self-assessment component consists of 10 multiple-choice questions with solutions. All of these materials are available on the ARRS Website (www.arrs.org). To claim CME and SAM credit, each participant must first order the CME activity, then enter his or her responses to the questions online.

EDUCATIONAL OBJECTIVES

By completing this educational activity, the participant will:

A. Exercise, self-assess, and improve his or her understanding of the evaluation of large airway disease.
B. Understand the basics of CT virtual endoscopy techniques and how the images are produced.
C. Be able to name some disease entities of the large airways that may be further evaluated with CT virtual endoscopy.
D. Learn some limitations of CT virtual endoscopy.

REQUIRED READING

1. Thomas BP, Strother MK, Donnelly EF, Worrell JA. CT virtual endoscopy in the evaluation of large airway disease: review. AJR 2009; 192[suppl]:500–500

INSTRUCTIONS

1. Complete the educational and self-assessment components included in this issue.
3. Select Publications/Journals/SAM Articles from the left-hand menu bar.
4. Order the online SAM as directed. (The SAM must be ordered to be accessed even though the activity is free to ARRS members.)
5. The SAM can be accessed at www.arrs.org/My Education/My Online Products, but you must be logged in to access this personalized page.
6. Answer the questions online to obtain SAM credit.

Keywords: airway disease, choanal atresia, CT virtual endoscopy, infiltrative airway disease, transbronchial biopsy

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**Solution to Question 1**

**Option B is the best response.** The threshold values in CT virtual endoscopy refer to definition of tissue–air interface [1]. IV contrast administration has no bearing on CT virtual endoscopy. Option A is not the best response. Endoscopic field of view is a variable that can be chosen by the user at the CT workstation. Option C is not the best response. Postprocessing takes approximately 10 minutes per examination. Option D is not the best response.

**Solution to Question 2**

CT virtual endoscopy of the posterior nasopharynx can further depict hypertrophy of the adenoid tonsils and the re-
relationship to the eustachian tubes, an area that is difficult to appreciate with conventional CT [2]. Option C is the best response. The eustachian tube itself cannot be evaluated because it is not normally an air-filled structure. Option B is not the best response. Although some mass effect may be seen with a paratonsillar abscess, it would not be further differentiated from paratonsillar phlegmon or other cause of mass effect with CT virtual endoscopy alone. Option A is not the best response. CT virtual endoscopy is usually postprocessed from static CT images and therefore is unable to evaluate dynamic airway collapse. Option D is not the best response.

Solution to Question 3
Airway distension maneuvers such as a modified Valsalva maneuver may help to improve symmetry of the upper airways [3]. Option C is the best response. Having the patient swallow or breathe rapidly would introduce motion artifact; Options A and D are not the best responses. Administration of IV contrast material has not been shown to be useful in CT virtual endoscopy. Option B is not the best response.

Solution to Question 4
CT virtual endoscopy is not well-suited for the evaluation of mucosal lesions [4]. Option B is the best response. CT virtual endoscopy can help to display complex 3D anatomy and provide useful images from unconventional endoscopic views. Options C and D are not the best responses. There is no added cost or radiation with CT virtual endoscopy. Option A is not the best response.

Solution to Question 5
Measurements on CT virtual endoscopy do not correlate well with conventional axial CT images [5]. Option A is the best response. Lesion size will vary with different tissue–air threshold values, so option D is not the best response. Lesion texture cannot be readily assessed with CT virtual endoscopy; option B is not the best response. Furthermore, CT virtual endoscopy should not be interpreted without using the source images. Option C is not the best response.

Solution to Question 6
CT virtual endoscopy is useful in transluminal biopsy planning [6]. Option A is the best response. However, submucosal extent of disease cannot be assessed using standard surface-rendered virtual endoscopic images. Option D is not the best response. Lack of airway distension is a common cause of asymmetry and not a reliable indicator of supraglottic malignancy using CT virtual endoscopy. Option C is not the best response. Measurement of endoluminal mass lesions has been shown to be inaccurate with CT virtual endoscopy. Option B is not the best response.

Solution to Question 7
Reinke’s edema can have a diffuse, polypoid distribution that can cause airway compromise [7], which means option C is the best response. It usually has a chronic course and is not an acute surgical emergency. Option B is not the best response. It may not be seen with conventional CT or CT virtual endoscopy, depending on the degree of true cord edema. Option A is not the best response. Reinke’s edema is a laryngeal disease caused by chronic irritation and does not spread to other parts of the airway. Option D is not the best response.

Solution to Question 8
CT virtual endoscopy is useful for evaluating tracheal stenosis by further depicting the length of the stenosis and assessment of the distal airway [6]. Option C is the best response. Although iatrogenic causes are the reason for focal tracheal stenoses, the incidence after endotracheal intubation is less than 1% [8]. Option A is not the best response. Tracheal stenosis can easily be overlooked on routine axial CT images because the focal stenosis is in the imaging plane. Option B is not the best response. Fiberoptic endoscopy is invasive and carries the risk of airway compromise; CT virtual endoscopy is noninvasive. Option D is not the best response.

Solution to Question 9
Recurrent respiratory papillomatosis has a worse prognosis when it involves the distal airways [9]. Option A is the best response. Recurrent respiratory papillomatosis usually begins in the larynx, not the distal airways. Option C is not the best response. It is a disease of younger, not older patients. Option B is not the best response. This disease process can cause significant morbidity, including malignant degeneration of papillomas [8]. Option D is not the best response.

Solution to Question 10
Tracheobronchial amyloidosis is the most common of the three types of pulmonary amyloidosis [8]. Option D is the best response. The nodular and interstitial forms are less common. Options A and B are not the best responses. Pleural effusions are not specific for this disease. Option C is not the best response.

References
Radiologic Signs in Thoracic Imaging: Case-Based Review and Self-Assessment Module
Mark S. Parker1, Marvin H. Chasen2, Narinder Paul3

ABSTRACT

Objective
Chest imaging remains one of the most complicated sub-specialties of diagnostic radiology. The successful interpretation of thoracic imaging studies requires the recognition and understanding of the radiologic signs that are characteristic of many complex disease processes.

Conclusion
The educational objectives for this case-based self-assessment module are for the participant to exercise, self-assess, and improve his or her understanding of important thoracic radiologic signs that are useful in establishing the diagnosis of particular diseases of the chest.

INTRODUCTION
This self-assessment module on several radiologic signs used in thoracic imaging to assist radiologists in establishing a particular diagnosis of pathologic processes affecting the chest has a self-assessment component and an educational component. The self-assessment component consists of six previously unpublished case-based studies with accompanying clinical histories and radiologic images. These cases have been selected to illustrate specific radiologic imaging signs. A series of multiple-choice questions follows each case, with solutions and a discussion of that particular radiologic sign and its cause. The educational component consists of suggested readings or references that accompany each case that the participant should review. To claim CME and SAM credit, each participant must log on to the ARRS Website (www.arrs.org) and enter his or her responses to the questions online.

EDUCATIONAL OBJECTIVES
By completing this educational activity, the participant will:
A. Exercise, self assess, and improve his or her understanding of selected radiologic signs useful in establishing a particular diagnosis of pathologic processes affecting the chest.
B. Exercise, self assess, and improve his or her understanding of the underlying cause for these particular imaging signs.

REQUIRED ACTIVITIES
1. Six interactive case scenarios presented in this article.

RECOMMENDED READING

INSTRUCTIONS
1. Complete the educational and self-assessment components included in this issue.
3. Select Publications/Journals/SAM Articles from the left-hand menu bar.
4. Order the online SAM as directed. (The SAM must be ordered to be accessed even though the activity is free to ARRS members.)
5. The SAM can be accessed at www.arrs.org/My Education/My Online Products, but you must be logged in to access this personalized page.
6. Answer the questions online to obtain SAM credit.
**Scenario 1**

**Clinical History**
A 52-year-old woman presented to her primary care physician with a several-week history of nonproductive cough, mild dyspnea, chest tightness, and wheezing (Fig. 1).

**Description of Images**
Frontal chest radiography (Fig. 1A) shows an ill-defined left perihilar opacity partially silhouetting the left heart border.

**Diagnosis**
The diagnosis is luftsichel sign of left upper lobe collapse secondary to an obstructing endobronchial carcinoid tumor (Kulchitsky cell type I).

**Solution to Question 1**
The radiographic features of pulmonary edema may include an increased cardiothoracic ratio, widening of the vascular pedicle, vascular redistribution or engorgement, discrepant arterial-to-bronchial ratios, interstitial Kerley lines, and possibly pleural effusions [1, 2]. Option A is not the best response because none of these signs is present. Pure pneumonia is an air-space-replacing process characterized by an equal exchange of air in the alveoli for pus and thus preservation of lung volume [3, 4]. Therefore, Option B is not the best response. Option D is not the best response because the location and morphology of the perihilar opacity support a parenchyma-based, not a mediastinum-based, lesion.

**Option C, atelectasis, and left upper lobe atelectasis in particular, is the best response.** This case illustrates both direct and many indirect signs of volume loss. More important, the case shows the luftsichel sign. “Luftsichel,” which is German for “air crescent,” is an indirect sign of overinflation characterized by hyperexpansion of the superior segment of the left lower lobe and its insinuation between the collapsed upper lobe and the mediastinum. This particular imaging sign is seen in the setting of left upper lobe atelectasis and is a manifestation of compensatory overinflation in response to the upper lobe volume loss [5]. Because of the absence of a horizontal fissure in the left thorax, as the upper lobe loses volume, the oblique fissure becomes vertically oriented in a plane roughly parallel to the anterior chest wall. The oblique fissure continues to shift further anteriorly and medially, with progressive volume loss until the atelectatic upper lobe is contiguous with the left heart border and partially silhouetting its border (i.e., the silhouette sign) and creating an ill-defined parahilar haze (i.e., the “veil sign”) on the frontal examination [5–8].

As the apical segment of the collapsing upper lobe moves anteromedially, the superior segment of the left lower lobe overinflates and fills in the vacated apex with aerated lung that can mimic an apical pneumothorax; option E is not the best response. However, the observation of additional indirect signs of volume loss, such as the juxtaphrenic peak, diaphragmatic elevation, and the partial loss of definition of the left heart border, allow the appropriate differentiation. Additionally, a true pneumothorax can be confidently diagnosed by the recognition of a white visceral pleural line as opposed to a
black edge due to a Mach effect [9, 10]. Such a white visceral pleural reflection is not present in this patient. Furthermore, a true visceral pleural reflection will also follow the contour of the lung periphery and not simply fade imperceptibly with the lung parenchyma, as was also seen in our patient [9, 10]. However, radiologists should be cautioned about the uncommon relationship between lobar atelectasis and pneumothorax. A localized pneumothorax may occur adjacent to an atelectatic lobe and has been described as a sign of bronchial obstruction that is referred to as “pneumothorax ex vacuo.” In such cases, treatment should be directed to the underlying bronchus and not to the pleural space [11].

The overinflated superior segment of the lower lobe may insinuate itself between the collapsed upper lobe and the transverse aorta, creating a sharp crisp crescent or paraaortic radiolucency referred to as the luftsichel sign. The diagnosis of left upper lobe collapse on single anteroposterior or posteroanterior chest radiographs can sometimes be difficult. When a lateral chest radiograph is available (Fig. 1B), the diagnosis of left upper lobe collapse is more easily made by noting a retrosternal sigmoid-shaped band of increased opacity representing the anteriorly displaced oblique fissure secondary to complete collapse of left upper lobe.

The luftsichel sign is a classic and helpful imaging finding on frontal chest radiograph. Once lobar atelectasis has been identified, the cause (e.g., mucus plug, aspirated foreign body, primary or secondary obstructing endobronchial tumors, and so forth) must be determined either through bronchoscopy or CT evaluation.

Endobronchial carcinoids are rare neuroendocrine tumors, accounting for approximately 2% of all lung neoplasms and 12–15% of all carcinoid tumors [12, 13]. These tumors originate from bronchial mucosa neurosecretory cells and are classified as low-grade malignant neoplasms because of their potential for local invasion, local recurrence, and occasional metastasis [12, 13]. Endobronchial carcinoids have the potential to synthesize and secrete various peptide hormones and neuroamines (e.g., adrenocorticotropic hormone, serotonin, somatostatin, and bradykinin). These tumors are not associated with smoking [12–14]. Histologically, carcinoid tumors are categorized as either Kulchitsky cell carcinoma (KCC) type I (i.e., typical carcinoid) or KCC type II (i.e., atypical carcinoid). KCC type I is the classic endobronchial carcinoid and is the least aggressive [12, 13]. These lesions are usually well defined, are smaller than 2.5 cm in diameter, are located centrally in the mainstem bronchi, and affect relatively young patients, with a marked female predilection (10:1, females to males). Only 3% of typical carcinoid tumors metastasize to sites other than regional lymph nodes. The prognosis is excellent, with a 5-year survival rate of 92% [12–14]. KCC type II is the atypical carcinoid tumor and is responsible for 25% of pulmonary carcinoid tumors [12, 13]. These latter lesions tend to behave more aggressively, are larger, occur in peripheral locations, and usually affect older patients, with a male preponderance. Regional lymph node metastases are more common, occurring in up to 50% of patients. Distant metastases to the liver, bone, and CNS occur in one third of patients [12–14]. The prognosis is less favorable, with a 5-year survival rate of 69%. Surgical excision is the preferred treatment, typically lobectomy or pneumonectomy. Tracheobronchial sleeve resection may be used for central carcinoid lesions with normal distal lung parenchyma. CT can prospectively evaluate the likelihood of tumor resection and is valuable in monitoring patients postoperatively for potential recurrence [12–14].

**Treatment**

The treatment is left upper lobectomy. The patient has since relocated and is now being followed up at another institution. The current disease status is otherwise unknown.
Scenario 2

Clinical History

A 68-year-old asymptomatic nonsmoking woman underwent preoperative screening chest radiography in preparation for a total knee arthroplasty. The radiographic findings prompted subsequent chest CT (Fig. 2).

Description of Images

A frontal chest radiograph (Fig. 2A) reveals a vague opacity in the right midthorax overlying the fourth and fifth anterior ribs. The ribs appear intact. The inferior margin of this mass is well delineated; however, the superior margin is ill-defined or incomplete. On lateral chest radiography (Fig. 2B), the lesion appears better defined and is lentiform in morphology. The long axis of this mass parallels the long axis of the right oblique fissure. The anterior, superior, and inferior borders appear better defined than the posterior border. Chest CT using the mediastinal window setting (Fig. 2C) reveals a large, slightly lobulated homogeneous mass. Two subtle punctuate hypervascular foci are seen in the periphery of the lesion. Lung window settings (Figs. 2D and 2E) confirm the lesion is localized to the right oblique fissure.

QUESTION 2
Where is this lesion MOST LIKELY located?
A. Lung parenchyma.
B. Mediastinum.
C. Pleura.
D. Chest wall.

QUESTION 3
What is the MOST LIKELY diagnosis?
A. Primary lung cancer.
B. Chest wall chondrosarcoma.
C. Pseudotumor or vanishing tumor of the pleura.
D. Localized fibrous tumor of the pleura.

Fig. 2—68-year-old asymptomatic nonsmoking woman who underwent preoperative screening chest radiography in preparation for total knee arthroplasty. Radiographic findings prompted subsequent chest CT.
A, Frontal chest radiograph reveals vague opacity in right midthorax overlying fourth and fifth anterior ribs. Ribs appear intact. Inferior margin of this mass is well delineated; however, superior margin is ill-defined or incomplete.
B, On lateral chest radiograph, lesion appears better defined and is lentiform in morphology. Long axis of this mass parallels long axis of right oblique fissure. Anterior, superior, and inferior borders appear better defined than posterior border.

(Fig. 2 continues on next page)
Diagnosis

The diagnosis in this patient is localized fibrous tumor of the pleura, as indicated by the incomplete border sign.

Solution to Question 2

Extrapulmonary masses, when projected en face to the x-ray beam, can simulate the presence of an intraparenchymal lesion [15]. The incomplete border sign illustrated in this patient is useful in distinguishing between extrapulmonary (options B, C, and D) and intrapulmonary (option A) lesions. Option A is not the best response. Appropriate localization is necessary before the proper differential diagnosis can be determined.

Extrapulmonary masses often exhibit tapered or ovoid superior and inferior borders and are convex toward the lung [15]. The overlying pleura of extrapulmonary lesions smooths out surface irregularities which, combined with the interface of the mass with lung air, give it a relatively sharply defined appearance [15]. However, this otherwise sharp border may be lost where the mass becomes continuous with the

Fig. 2 (continued)—68-year-old asymptomatic nonsmoking woman who underwent preoperative screening chest radiography in preparation for total knee arthroplasty. Radiographic findings prompted subsequent chest CT. C, Chest CT scan at mediastinal window setting reveals large, slightly lobulated homogeneous mass. Two subtle punctuate hypervascular foci are seen in periphery of lesion. D and E, CT images at lung window settings confirm lesion is localized to right oblique fissure.

Thoracic Imaging
pleura of the chest wall, thus forming an incompletely visualized border on radiography (Figs. 2A and 2B) and creating the so-called incomplete border sign [15–17].

Mediastinum- and chest wall–based masses may also show an incomplete border sign [15]. However, the location of this lesion on the frontal radiograph (Fig. 2A) would argue against a mediastinal or chest wall cause. Options B and D are not the best responses. Localization of the lesion to the oblique fissure on the lateral chest radiograph (Fig. 2B) supports a pleural cause, which is subsequently confirmed on CT (Figs. 2C–2E). Option C is the best response.

The most common extrapulmonary lesions include, but are not limited to, loculated pleural effusions, various rib lesions (e.g., fractures, primary and secondary tumors), mesenchymal tumors, neural tumors, hematomas, lipomas, and various cutaneous lesions (e.g., neurofibromas) [15].

Solution to Question 3

The incomplete border sign supports a conclusion that the lesion in question is extrapulmonary. Option A is not the best response.

Although chest wall metastases are the most common malignant chest wall neoplasm in adults, chondrosarcoma is the most common primary malignant tumor of the adult chest wall [18–20]. Chondrosarcomas are malignant neoplasms with cartilaginous differentiation. Option B is not the best response. This neoplasm typically arises in the anterior chest wall and involves the sternum or costochondral cartilages. Less frequently, chondrosarcomas arise in the ribs (17%) and scapulae [18–20]. Chondrosarcomas occur across a wide age range but typically affect patients between the ages of 30 and 60 years. Most tumors manifest as palpable chest wall masses that may grow rapidly and become painful [18–20]. Males are affected slightly more frequently than females, in a ratio of 1.3:1.0 [18–20]. On radiologic imaging, variable intratumoral calcifications (e.g., rings, arches, flocculent, or stippled) can be identified, and osseous destruction is often present [18–20]. Surgical resection is the treatment of choice. The 5-year survival rate is more than 60% and may approach 80% in patients without metastases. Poor prognosis is associated with incomplete tumor resection, metastases, local recurrence, and patient age older than 50 years [18–20].

Interlobar pleural fluid collections are typically ovoid or lentiform when viewed in tangent and may simulate a mass on conventional radiography [21]. The long axis of such fluid collections is usually oriented along the long axis of the interlobar fissure [21]. Fluid has a tendency to accumulate in the interlobar fissure in the setting of cardiac decompensation and to localize in the horizontal fissure in particular [21]. The fluid collections tend to be spontaneously absorbed when the heart failure has been relieved and are therefore referred to as either pseudotumors or vanishing tumors of the pleura [21]. Option C is not the best response. Invariably, concomitant radiographic evidence of cardiac decompensation is seen or an ipsilateral pleural effusion is present [21].

Localized or solitary fibrous tumor of the pleura is a rare pleural neoplasm but is the second most common primary pleural neoplasm after malignant mesothelioma [22–24]. Option D is the best response. Although most of these tumors are related to the pleura, they have also been described in other intra- and extrathoracic locations. These tumors typically occur in adult men and women in the fifth through eighth decades of life. Many patients are asymptomatic and are diagnosed incidentally because of abnormal chest radiographic findings, as in our patient (Figs. 2A and 2B). Symptoms typically relate to tumor size and include cough, chest pain, and dyspnea. Hypertrophic pulmonary osteoarthropathy is seen in 20–25% of patients. Symptomatic hypoglycemia occurs in less than 5% of patients [22–24]. Radiographically, localized fibrous tumors of the pleura present as well-defined, variably sized, lobular extrapulmonary nodules or masses (i.e., incomplete border sign) and typically abut the pleura [23, 24] (Figs. 2A and 2B). CT reveals a noninvasive lobular soft-tissue mass of variable size that abuts at least one pleural surface or may exhibit an interlobar fissure location (Figs. 2C–2E). Smaller lesions are more homogeneous in attenuation, whereas larger lesions may appear heterogeneous. Foci of calcification and enhancing vessels may be observed in the lesion [23, 24] (Fig. 2C). These tumors are not related to mesothelioma, asbestos exposure, or tobacco abuse. Benign and malignant variants have been described. Prognosis is related more to resectability than to histologic features [22–24].

Treatment

The tumor was successfully resected in its entirety at open thoracotomy. The patient remained disease-free at the time of the last follow-up CT examination 12 months before this writing.

Scenario 3

Clinical History

A 33-year-old man presented with a 3- to 4-day history of dyspnea and a nonproductive cough. A chest radiograph (not shown) revealed bilateral perihilar air-space opacities with intervening normal aerated lung. He was admitted to the general medicine ward with a presumptive diagnosis of community-acquired pneumonia and began taking levofloxacin. Over the next 3 days, he developed progressive hypoxia and was subsequently transferred to the intensive care unit for mechanical ventilation and nitric oxide therapy. Follow-up chest radiography (not shown) before intubation revealed progressive bilateral perihilar air-space disease. Subsequent chest CT pulmonary angiography on the same day did not show a pulmonary em-
bolus but did reveal an interesting pattern of air-space disease (Fig. 3).

**Description of Images**

The selected CT images (Fig. 3) through the upper, mid, and lower lung zones reveal a patchy pattern of variable attenuation characterized by a combination of ground-glass opacities, consolidations, reduced lung attenuation resulting from mosaic perfusion, and intervening normal lung. Note the “head cheese sign.”

**Diagnosis**

The diagnosis is *Mycoplasma* pneumonia with associated bronchiolitis, as indicated by the head cheese sign.

**Solution to Question 4**

The combination of mixed densities in the lung parenchyma created by ground-glass opacities, air-space consolidations, reduced lung attenuation from mosaic perfusion, and intervening normal lung give the lung a geographic appearance on CT [25, 26] (Fig. 3). This pattern of mixed parenchymal lung densities has been likened to the morphologic appearance of the mixture of boiled pork scraps and pigs’ feet.

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**Fig. 3**—33-year-old man with 3- to 4-day history of dyspnea and nonproductive cough. Chest radiograph (not shown) revealed bilateral perihilar air-space opacities with intervening normal aerated lung. Patient was admitted to general medicine ward with presumptive diagnosis of community-acquired pneumonia and began taking levofloxacin. Over next 3 days he developed progressive hypoxia and was subsequently transferred to intensive care unit for mechanical ventilation and nitric oxide therapy. Follow-up chest radiograph (not shown) before intubation revealed progressive bilateral perihilar air-space disease.

**A–C,** Selected chest CT pulmonary angiography images using lung window setting through upper (A), mid (B), and lower (C) lung zones reveal patchy pattern of variable attenuation characterized by combination of ground-glass opacities, consolidations, reduced lung attenuation resulting from mosaic perfusion, and intervening normal lung.
in a gelatinous background known and marketed as head cheese or hog’s head cheese and is therefore known as the “head cheese sign” or “hog’s head cheese sign” [25, 26]. How does this particular imaging sign help radiologists in their diagnostic interpretation? CT must clearly show areas of ground-glass opacity and consolidation with concomitant mosaic perfusion (rather than one or the other) (Fig. 3). When these findings are present, they indicate a mixed infiltrative disease characterized by ground-glass or consolidation and an obstructive disease (usually associated with bronchiolitis) characterized by mosaic perfusion, with a decrease in vessel caliber and side branches in the hypoattenuating regions of lung parenchyma. The latter will often reveal air trapping on expiratory images [25–27]. The most common clinical causes of this CT pattern of disease include hypersensitivity pneumonitis, sarcoidosis, atypical infections (e.g., those caused by *Mycoplasma pneumoniae*) with associated bronchiolitis, and acute interstitial pneumonia [25–27]. Options A, B, and C, which are likely diagnoses, are not the best responses. Additional clinical and laboratory data would be necessary to further narrow the differential diagnosis. In this particular case, the diagnosis was an atypical infection with associated bronchiolitis secondary to *Mycoplasma pneumoniae*.

The CT pattern of multiple septic pulmonary emboli is much different. The latter disease process may be characterized by unilateral or bilateral areas of juxtapleural and wedge-shaped consolidation; diffuse, often angiocentric, nodules ranging from 0.5 to 3.5 cm in diameter, many of which show various stages of cavitation; and a peripheral rimlike pattern of enhancement after the administration of IV contrast media. Pleural effusions may also be identified in two thirds of patients, and 27% have identifiable hilar or mediastinal lymphadenopathy [28]. On the basis of the clinical presentation and the CT findings, Option D, multiple septic pulmonary emboli, would be the least likely diagnosis; therefore, option D is the best response.

Mycoplasmas are bacteria that lack a cell wall, adhere to ciliated respiratory epithelium, and produce hydrogen peroxide, which damages epithelial cells and interferes with ciliary function. *M. pneumoniae* are one of three human pathogenic *Mycoplasma* species [29]. Bacteria are transmitted from person to person thorough aerosolized droplets. Infection may occur the year round but usually occurs during fall and winter [29, 30]. Patients may present with fever, chills, malaise, anorexia, sore throat, dry cough, and headache. As the disease progresses, nearly all patients develop an intractable hacking cough, but only 3% of such patients develop pneumonia. Extrapulmonary features are common and may include cervical lymphadenopathy, skin rash, aseptic meningitis, nausea, vomiting, and diarrhea. Rarely, patients present with or develop acute respiratory distress syndrome [29–31]. Such patients have higher morbidity and mortality rates. In these latter cases, supportive mechanical ventilation is necessary in addition to corticosteroids and antibiotic therapy (e.g., erythromycin, azithromycin, tetracycline, clarithromycin, and so forth) [29–31]. After infection, patients may fully recover; or interstitial fibrosis, bronchiectasis, Swyer-James syndrome, and impaired pulmonary function may develop as sequelae of the infection [29, 30].

**Treatment**

Treatment is support with a mechanical ventilator and nitric oxide therapy, corticosteroids, and clarithromycin. The patient was maintained on mechanical ventilation for 5 days and then was successfully extubated. Eight days later, he was discharged and was subsequently lost to follow-up.

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**Scenario 4**

**Clinical History**

A 35-year-old woman presented with fatigue, chest pain, and weight loss over the past several months (Fig. 4).

**Description of Images**

A posteroanterior (Fig. 4A) chest radiograph shows a massively enlarged cardiomedial silhouette. Lateral chest radiography (not shown) showed complete obliteration of the retrosternal clear space. On closer inspection, the normal right and left pulmonary arteries and their respective interlobar divisions can be identified well in what appears to be lateral or peripheral margin of cardiomedial silhouette.

Fig. 4—35-year-old woman with fatigue, chest pain, and weight loss over past several months.

A, Posteroanterior chest radiograph shows massively enlarged cardiomedial silhouette. Lateral chest radiograph (not shown) showed complete obliteration of retrosternal clear space. On closer inspection, normal right and left pulmonary arteries and their respective interlobar divisions can be identified well in what appears to be lateral or peripheral margin of cardiomedial silhouette.

(Fig. 4 continues on next page)
bar divisions can be identified well in what appears to be the lateral or peripheral margin of the cardiomediastinal silhouette. Contrast-enhanced CT images (mediastinal window setting) through the main pulmonary artery level (Fig. 4B) and the myocardium (Fig. 4C) show a large aggressive anterior mediastinal mass intimately related to the ascending aorta and main pulmonary artery with invasion of the myocardium proper. A small pericardial effusion is present.

**Diagnosis**

The diagnosis is malignant peripheral nerve sheath tumor of the vagus nerve with mediastinal invasion, the hilum overlay sign.

**Solution to Question 5**

The proximal segment of the visible left or right pulmonary artery lies laterally to the cardiac silhouette or just within its edge on normal frontal chest radiography. As the myocardium enlarges in the setting of a cardiomyopathy or cardiomegaly or as the pericardial sac distends with fluid from pericardial effusion, the pulmonary artery segments are simply displaced outward but continue this same relationship to the cardiac silhouette [32, 33]. Options A and B are not the best responses. Alternatively, if either the left or right pulmonary artery can be seen 1.0 cm or more within the lateral edge of an opacity that appears to represent the cardiac silhouette, that opacity does not represent the cardiac silhouette and therefore cannot be the result of cardiomyopathy, cardiomegaly, or pericardial effusion, but is related instead to the presence of an anterior mediastinal mass [32, 33]. **Option C is the best response.** This is referred to as the hilum overlay sign, which can be used to determine that a lesion is extracardiac and localized to the anterior mediastinal compart-

**QUESTION 6**

**All of the following are TRUE statements regarding the “hilum convergence sign” EXCEPT:**

A. It differentiates a potential hilar mass from an enlarged pulmonary artery.
B. If the pulmonary arteries converge into the lateral border of the apparent hilar mass, the mass represents an enlarged pulmonary artery.
C. If the pulmonary arteries converge behind the apparent hilar mass, the mass represents an enlarged pulmonary artery.
D. If the convergence of the pulmonary arteries arises from the cardiac silhouette, a mediastinal mass is likely present.

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Fig. 4 (continued)—35-year-old woman with fatigue, chest pain, and weight loss over past several months. B and C, Contrast-enhanced chest CT scans using mediastinal window setting through main pulmonary artery level (B) and myocardium proper (C) show large aggressive anterior mediastinal mass intimately related to ascending aorta and main pulmonary artery as well as invasion of myocardium proper. Small pericardial effusion is present. DA = descending thoracic aorta, LLPA = left lower lobe pulmonary artery, PA = pulmonary artery, PV = pulmonary vein, RLPA = right lower lobe pulmonary artery, RA = right atrium, RV = right ventricle.
ment, thus steering the differential diagnosis in the appropriate direction [32, 33]. Because the lesion of concern is mediastinum-based, option D, pleural effusion, is not the best response. It likewise would be quite unusual for pleural effusion to present as perihilar ground-glass opacity. Additionally, the costophrenic angles are preserved. The mediastinal mass in this particular patient proved to be a malignant peripheral nerve sheath tumor (MPNST) arising from the intrathoracic vagus nerve in the mediastinum. MPNSTs are rare but aggressive sarcomas that arise from the nerve sheath or show features of nerve sheath differentiation; they more often involve the extremities, the head, and the neck. Intrathoracic MPNST is uncommon [34]. Although such tumors may occur in patients with neurofibromatosis 1 (von Recklinghausen’s disease) with an incidence of 0.16%, these tumors may also occur in patients with no signs of such (incidence of 0.001%), as in our patient [34–36]. Successful treatment requires complete surgical excision of the MPNST. Radiotherapy may delay recurrence but has little impact on patient survival. Conventional advanced soft-tissue sarcoma single-agent chemotherapy with doxorubicin has a poor response rate [34].

**Solution to Question 6**

Felson’s hilum convergence sign should be differentiated from the hilum overlay sign discussed in the solution to question 5 [32]. The hilum convergence sign is useful in distinguishing between a large pulmonary artery and a hilar mass [32]. Because the pulmonary artery branches arise from the main pulmonary artery trunk, an enlarged pulmonary artery will have branches that arise from its lateral margin, and its vessels will appear to converge toward the main pulmonary artery [32]. **Option B is the best response.** A true hilar mass may have the appearance of an enlarged pulmonary artery, but the vessels will not arise from its lateral margin but rather seem to pass through the margin as they converge on the true pulmonary artery [32]. Therefore, if the convergence of the pulmonary arteries appears behind the apparent hilar mass or appears to arise from the heart, a mediastinal mass is more likely [32]. Options A, C, and D are not the best responses.

**Treatment**

The treatment, which was unsuccessful, was surgical debulking of the tumor and palliative radiotherapy. The patient died over the next several weeks.

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**Scenario 5**

**Clinical History**

A 47-year-old man presented with chronic renal failure and dyspnea (Fig. 5).

**Description of Images**

A posteroanterior chest radiograph (Fig. 5A) shows globular enlargement of the cardiomediatinal silhouette. There is an increase in transverse diameter of the cardiomediatinal silhouette but no increase in its height. The proximal segments of the visible left and right pulmonary artery lie laterally to the cardiac silhouette. A coned-down lateral chest radiograph (Fig. 5B) reveals separation of the black retrosternal fat stripe from the black epicardial fat stripe by an opaque interface. No pleural effusion or interstitial edema is present. A contrast-enhanced coronal maximum-intensity-projection chest CT scan (Fig. 5C) shows separation of the visceral and parietal pericardial layers by a large fluid collection surrounding the myocardium.

**Diagnosis**

The diagnosis is uremic pericardial effusion, the water bottle sign.

**Solution to Question 7**

A frontal chest radiograph (Fig. 5A) shows globular enlargement of the cardiomediatinal silhouette with an increase in its transverse diameter but no increase in its height. As a result, the superior mediastinal borders appear straightened, giving the cardiomediatinal silhouette a morphology that has been likened to that of a water bottle, hence the designation “water bottle sign” [37, 38]. Applying the hilum overlay sign discussed in scenario 4, the proximal segment of the visible left and right pulmonary artery continues to lie laterally to the enlarged cardiac silhouette (i.e., negative hilum overlay), thus eliminating anterior mediastinal mass from diagnostic consideration. Option D is not the best response.

The pericardium consists of two layers. The visceral pericardium is attached to the surface of the myocardium and the proximal great vessels. The parietal pericardium forms the free wall of the pericardial sac [37–40]. The pericardial

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**QUESTION 7**

**What is the MOST LIKELY diagnosis?**

A. Lobar pneumonia.
B. Primary lung cancer.
C. Acute heart failure.
D. Anterior mediastinal mass.
E. Pericardial effusion.
sac itself normally contains 20–50 mL of fluid [37]. An excess of pericardial fluid may accumulate in a number of settings. **Option E is the best response.** The most common cause is myocardial infarction with left ventricular failure [37]. Fifty percent of patients with chronic renal failure develop uremic pericardial effusions [37]. Other causes of pericardial effusion may include hypoalbuminemia, myxedema, infection, drug reactions, trauma, neoplasia, and autoimmune disease [37]. The chest radiograph may appear relatively normal until the volume of pericardial fluid exceeds 250 mL [37–39]. The cardi mediastinal silhouette may then show symmetric enlargement and preservation of the normal hilar relationships, resulting in the water bottle–shaped morphology [37–39] (Fig. 5A). A well-penetrating lateral chest radiograph is even more sensitive in the early detection of pericardial effusion and may reveal separation of the retrosternal and epicardial fat stripe by more than 2 mm, which is sometimes referred to as the “Oreo [Nabisco] cookie sign,” “sandwich sign,” or “bun sign” [37–39] (Fig. 5B). The black epicardial and retrosternal fat stripes consti-
tute the outer dark cookie layers or slices of bread in the sandwich or bun, and the opaque intervening pericardial fluid, the white fluff of the cookie or the meat in the sandwich or bun. Although the cardiac silhouette is enlarged, the pulmonary vasculature appears normal, and signs of heart failure (e.g., vascular redistribution, Kerley B lines, and so forth) are absent (Fig. 5A). Option C is not the best response. CT is more sensitive in the detection of small pericardial effusions. Small effusions first collect dorsally to the left ventricle and along the left atrium. Larger effusions collect ventrally and laterally to the right ventricle. Very large effusions may envelop the myocardium, forming the “halo sign” [37, 40] (Fig. 5C). Lobar pneumonia and primary lung cancer are both air-space disease processes and are not appropriate considerations in this patient. Options A and B are not the best responses.

Uremic pericardial effusion commonly improves with intensified or increased frequency of peritoneal or hemodialysis [41]. More aggressive management may be needed if the pericardial effusion is larger than 250 mL, if it continues to increase despite intensive dialysis for 10–14 days, or if the patient develops tamponade [41, 42]. In these latter instances, pericardiocentesis, pericardial window, subxiphoid pericardiectomy, or pericardiectomy may be necessary [41, 42].

**Treatment**

The patient was successfully treated with a combination of increased hemodialysis and subxiphoid pericardiotomy.

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**Scenario 6**

**Clinical History**

A 62-year-old woman presented with a long-standing history of chronic atrial fibrillation; she had undergone cardiac surgery 7 days earlier (Fig. 6).

**Description of Images**

A posteroanterior chest radiograph (Fig. 6A) shows an increased cardiothoracic ratio. The pulmonary artery segment is enlarged, suggesting precapillary pulmonary hypertension. The aorta appears small from decreased forward cardiac output. A convex bulge is present along the left heart border related to left atrial chamber enlargement. Midline median sternotomy wires can be delineated. A lateral chest radiograph (Fig. 6B) reveals a convex bulge in the superoposterior cardiac border below the carina, with posterior displacement of the left lower lobe bronchus and opacification of the retrocardiac clear space. Right ventricular enlargement encroaches on the retrosternal clear space. Foci of residual pneumomediastinum and a retained subxiphoid pacer lead can be seen in the retrosternum. A newly placed mitral valve prosthesis is present. Thin curvilinear calcifications can also be seen paralleling the posterior wall of enlarged left atrium. No radiographic evidence of acute cardiac decompensation is seen.

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Fig. 6—62-year-old woman with long-standing history of chronic atrial fibrillation. Patient had undergone cardiac surgery 7 days earlier. **A**, Posteroanterior chest radiograph shows increased cardiothoracic ratio. Pulmonary artery segment is enlarged, suggesting precapillary pulmonary hypertension. Aorta appears small from decreased forward cardiac output. Convex bulge is present along left heart border related to left atrial chamber enlargement. Midline median sternotomy wires can be delineated. **B**, Lateral chest radiograph shows relative posterior displacement of left upper and lower lobe bronchus relative to right (arrows), forming “walking man sign.” Right ventricular enlargement encroaches on retrosternal clear space. Foci of residual pneumomediastinum and retained subxiphoid pacer lead can be seen in retrosternum. Newly placed mitral valve prosthesis is present. Thin curvilinear calcifications can also be seen paralleling posterior wall of enlarged left atrium. No radiographic evidence of acute cardiac decompensation is seen.
QUESTION 8
What is the MOST LIKELY diagnosis?

A. Acute heart failure.
B. Ebstein anomaly.
C. Mitral stenosis.
D. Mitral valve prolapse.

QUESTION 9
Which imaging sign is demonstrated on the lateral chest radiograph (Fig. 6B)?

A. Coeur en sabot sign.
B. Walking man sign.
C. Double density sign.
D. Doughnut sign.

QUESTION 10
What is the principal cause of acquired mitral stenosis?

A. Rheumatic heart disease.
B. Left atrial myxoma.
C. Left atrial thrombus.
D. Maternal ingestion of lithium in the first trimester of pregnancy.

posterior wall of the enlarged left atrium. No radiographic evidence of acute cardiac decompensation is seen.

Diagnosis
The diagnosis is mitral stenosis and left atrial calcification, as indicated by the walking man sign.

Solution to Question 8
Although the cardiothoracic ratio is enlarged, the vascular pedicle is not widened and there is no radiographic evidence of vascular redistribution or septal lines to support a diagnosis of acute heart failure (Fig. 6). Option A is not the best response. Ebstein anomaly is a congenital heart malformation manifested by apical displacement of the septal and posterior tricuspid valve leaflets, leading to atrialization of the right ventricle and a variable degree of malformation and displacement of the anterior leaflet [43]. Although chest radiography may be normal in patients with Ebstein anomaly, characteristic radiologic features include right atrial enlargement, which may occasionally be quite severe; inferior vena cava and ayzygos dilatation secondary to tricuspid regurgitation; hypoplasia of the aorta and main pulmonary artery; and a normal-sized left atrium [44]. These radiographic features are not present in this patient (Fig. 6). Option B is not the best response. Although mitral valve prolapse may be associated with cardiac dysrhythmias, enlargement of the left atrium (Fig. 6) is uncommon except in cases of prolapse complicated by severe mitral regurgitation [45, 46]. Option D is not the best response.

Mitral stenosis is characterized by narrowing of the inlet valve orifice of the left ventricular chamber, which interferes with normal opening during diastole [37, 47–49]. Option C is the best response. Affected patients typically have thickened valve leaflets, fused commissures, or thickened and shortened chordae tendineae. The normal mitral valve orifice area is 4–6 cm² [47–49]. In early diastole, a small pressure gradient exists between the atrium and the ventricle, but during most of diastole the pressures in these two chambers are relatively similar. When the mitral valve area narrows to less than 2.5 cm², blood flow is impeded, which causes an increase in left atrial pressure. Critical mitral stenosis occurs when the area is reduced to 1 cm² [47–49]. When this occurs, a left atrial pressure of at least 25 mm Hg is necessary to maintain normal cardiac output [47–49]. The increase in left atrial pressure enlarges the left atrium and increases pulmonary venous and capillary pressures, resulting in pulmonary venous congestion and reduced cardiac output. This scenario can mimic left ventricular failure, but left ventricular contractility is usually normal. Chronic atrial fibrillation commonly ensues as the left atrium enlarges [50]. Chronic elevation of left atrial pressures leads to pulmonary artery hypertension, tricuspid and pulmonary valve incompetence, right ventricular hypertrophy (Fig. 6) and, eventually, right heart failure [37, 47–49]. In cases of long-standing mitral stenosis, the left atrial wall may rarely calcify (Fig. 6B). Such calcification is more common in patients with endocarditis resulting from rheumatic heart disease; most affected patients also have heart failure and chronic atrial fibrillation [51]. Calcification of the mitral valve itself occurs in approximately 10% of affected patients. This should not be confused with mitral annulus calcification. Calcification of the mitral valve annulus does not indicate underlying mitral stenosis and is often a finding of senescence [37, 49].

Solution to Question 9
The term “coeur en sabot” refers to a heart that has a boot-shaped morphology as a result of uplifting of the cardiac apex because of right ventricular hypertrophy and the absence of a normal main pulmonary artery segment [44]. This is a feature on frontal chest radiographs most often associated with tetralogy of Fallot. Additional radiologic features of this congenital cardiac malformation include decreased pulmonary vascularity; a normal-sized heart because of the lack of pulmonary blood flow and heart failure; right atrial enlargement; and, in approximately 20–25% of affected patients, a right-sided aortic arch [44]. Option A is not the best response. The “double density sign” is an early radiologic feature of left atrial enlargement seen on frontal, not lateral, chest radiographs [52]. Option C is not the best response. This imaging sign manifests as an interface projecting over the right retro-
cardiac region (Fig. 6A). The interface represents the inferior margin of the enlarged left atrium as it pushes into the adjacent lung [52]. On frontal radiographs of adult patients, a left atrial dimension—defined as the distance from the midpoint of the double density to the inner margin of the left mainstem bronchus—greater than 7 cm suggests left atrial enlargement is present [52]. However, this sign and these dimensions are not reliable in pediatric patients [52]. The double density sign is often associated with splaying of the normal carinal angle of 60–90° and divergence of the caudal mainstem bronchi, creating a somewhat “wishbone” morphology in severe cases [52]. These latter two signs are best appreciated on well-exposed or well-penetrating frontal examinations. The “doughnut sign” is an imaging sign seen on lateral chest radiography; however, it suggests the presence of mediastinal lymphadenopathy, not cardiac valvular disease [53, 54]. Option D is not the best response. On normal chest radiography, the aortic arch and the right and left pulmonary arteries create an inverted horseshoe appearance [53, 54]. Subcarinal lymphadenopathy obliterates the notch in the horseshoe, forming a rounded circle likened to the morphology of a bagel or doughnut [53, 54].

The normal trachea, right and left upper lobe bronchi, and lower lobe bronchi are vertically aligned on a normal lateral chest radiograph. The walking man sign is a lateral chest radiography sign that is seen with posterior displacement of the left upper or lower lobe bronchus relative to the right bronchi, so that the bronchial relationship resembles the legs of a man in midstride [55]. Option B is the best response. Posterior displacement of the left bronchi is typically the result of mass effect on the bronchi by a markedly enlarged left atrium but is not pathognomonic of an enlarged atrium [55]. The walking man sign may also occur in the setting of subcarinal lymphadenopathy, mediastinal masses, left lower lobe volume loss, large hiatal hernias, and thoracolumbar scoliosis.

Solution to Question 10

Although it is rare today, mitral stenosis is still most commonly caused by rheumatic fever [5–8]. Option A is the best response. Approximately 40% of patients with rheumatic heart disease have isolated mitral valve stenosis. However, rheumatic involvement is identified in 99% of stenotic mitral valves examined at the time of valve surgery [47–49]. Other, less frequent, causes of mitral stenosis include congenital stenosis, an obstructing lesion such as a left atrial myxoma, atrial thrombus, systemic lupus erythematosus, rheumatoid arthritis, malignant carcinoid, various mucopolysaccharidoses, Fabry’s disease, Whipple’s disease, and methysergide therapy [37, 47–49]. Options B and C are not the best responses. Although it is somewhat controversial, maternal ingestion of lithium, ingestion of benzodiazepines, and exposure to various varnishing agents in the first trimester of pregnancy have been reported to be associated risk factors for Ebstein anomaly [56, 57]. Option D is not the best response.

Balloon valvotomy is usually the initial procedure of choice for symptomatic patients with moderate to severe mitral stenosis. Valvotomy can double the mean valve area, with a 50–60% decrease in the transmitral gradient, which provides symptomatic improvement. Surgical commissurotomy has a similar efficacy to that of balloon valvotomy but is usually reserved for patients with left atrial thrombus despite anticoagulation or a nonpliable or calcified valve. Mitral valve replacement is reserved for patients who are not candidates for either percutaneous balloon mitral valvotomy or surgical commissurotomy [58, 59]. Lifelong endocarditis antibiotic prophylaxis is recommended for procedures that may be associated with transient bacteremia (e.g., dental procedures, bronchoscopy, colonoscopy, cystoscopy, and so forth) [58–60].

Treatment

The treatment is mitral valve replacement. The patient was discharged on postoperative day 7. We have no additional information on her current clinical status.

Conclusion

This case-based self-assessment module describes several important radiologic signs that are useful in diagnosing various diseases affecting the chest, including the luftsichel sign of left upper lobe collapse; the incomplete border sign of pleural and chest wall-based lesions; the head cheese sign or hog’s head cheese sign of atypical infection with associated bronchiolitis, sarcoidosis, acute interstitial pneumonitis, and hypersensitivity pneumonitis; the hilum overlay sign, which is useful in localizing lesions to the anterior mediastinum; the hilum convergence sign that distinguishes an enlarged pulmonary artery from a true hilar mass; the water bottle sign and the Oreo cookie sign of pericardial effusion; and the walking man sign of left atrial enlargement. Future articles will continue this discussion of additional useful signs in thoracic imaging that can be applied to assist the radiologist in establishing the correct diagnosis or differential diagnosis in applicable cases.

References

Case History
A 50-year-old woman presents with nonspecific chest pain, a syncopal episode, and increasing dyspnea on exertion without edema, orthopnea, or paroxysmal nocturnal dyspnea. CT pulmonary angiography is performed to evaluate for pulmonary embolism. This is followed by cardiac MRI to further evaluate abnormal cardiac findings identified on CT pulmonary angiography. CT of the abdomen that was performed 7 months previously to investigate upper abdominal pain is also reviewed and found to include the area of abnormality.

Radiologic Description
Initial contrast-enhanced abdominal CT shows subtle thickening of the inferior right atrial wall near the diaphragm that was only appreciated in retrospect (Fig. 1A). Subsequent CT pulmonary angiography performed 7 months later using 120 kVp, 150 mA, and 1.25-mm slice thickness after the administration of 125 mL of the non-ionic IV contrast material iopromide (Ultravist 300, Bayer HealthCare) at 4 mL/s, reveals the dramatic rapid growth of a large soft-tissue mass centered on the right atrial free wall along with a right pleural effusion. The right lower lobe lung nodule was one of several similar lesions in the lungs (Fig. 1B). On cardiac MRI, the cine balanced steady-state free precession (balanced SSFP) sequence (TR/TE, 2.9/0.99) in four-chamber orientation shows a lobulated mass extending into and nearly obliterating the right atrial cavity but without involvement of the interatrial septum (Fig. 1C and video, Fig. S1C, in supplemental data at www.ajronline.org). The mass is predominantly isointense on axial ECG-gated breath-hold T1-weighted double inversion recovery fast spin-echo sequence (667/41) with a few areas of scattered hyperintensity compatible with hemorrhage (Fig. 1D) and has a heterogeneous hyperintense appearance on T2-weighted images (1,364/101) (Fig. 1E). The mass extends into the atrioventricular groove and encases the right coronary artery. On first-pass perfusion imaging with a gadolinium-based contrast agent (0.1 mmol kg of gadopentetate dimeglumine), marked peripheral linear and nodular tumor enhancement is evident (Fig. 1F and video, Fig. S1F, in supplemental data).

Differential Diagnosis
The differential diagnosis of a right atrial mass includes benign entities such as myxoma and thrombus and malignant causes such as metastatic involvement of the heart, primary cardiac angiosarcoma and other sarcomas, pericardial mesothelioma, and primary cardiac lymphoma.

Diagnosis
The diagnosis, based on biopsy of one of the lung metastases showing spindle cells, is primary cardiac angiosarcoma.

Commentary
Metastases are by far the most common cardiac neoplasms, 40 times more prevalent than primary cardiac tumors [1]. Primary cardiac tumors are rare lesions and include both benign and malignant histologic types, with myxomas being the most common [2]. Primary malignant cardiac tumors include angiosarcoma, undifferentiated sarcoma, rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, and primary cardiac lymphoma [1].

Angiosarcomas, although rare, are the most common primary malignant neoplasms of the heart, making up more than a third of cardiac sarcomas [1, 3]. Cardiac angiosarcomas present in adults around middle age, with cases in children and infants being rare. Males are more commonly affected. The clinical signs and symptoms are often nonspecific. Because of the propensity of the tumor to involve the right atrium and pericardium, patients may present with right-sided heart failure and tamponade [3, 4]. There is frequently metastatic spread at presentation, most commonly to the lungs, but also occasionally to lymph nodes, bone, liver, brain, bowel, spleen, adrenal glands, pleura, diaphragm, kidneys, thyroid, and skin [5]. The prognosis is universally poor; patients rarely survive beyond a year despite treatment [6]. In most cases, angiosarcomas involve the right atrial free wall [7] as a well-defined mass protruding into the right atrium and usually sparing the interatrial septum. CT and MRI can both show tumor infiltrat-
tion of the myocardium and direct extension into the pericardium [4]. The second, rarer subtype, is a diffusely infiltrative mass extending along the pericardium [4].

Initial evaluation is usually performed using echocardiography, which may be limited by factors such as operator dependence, restricted field of view, and unfavorable body habitus. Cardiac MRI enables the most comprehensive imaging assessment of cardiac neoplasms. In contrast to transthoracic echocardiography, cardiac MRI provides improved soft-tissue contrast, tissue characterization, and assessment of mediastinal and lung involvement by the tumor. The addition of imaging with a gadolinium-based contrast agent allows an assessment of the extent of tumor vascularity and further improves the differentiation from surrounding structures.

Angiosarcomas appear as irregular lobulated low-attenuation masses on CT that frequently extend to involve the adjacent pericardium and vessels. On MRI, they exhibit heterogeneous signal on T1- and T2-weighted sequences, which is

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**Fig. 1**—50-year-old woman with shortness of breath and chest pain.

**A**, Axial contrast-enhanced CT scan of abdomen shows subtle thickening of inferior right atrial wall. *d* = dome of diaphragm.

**B**, Subsequent CT pulmonary angiography image 7 months later reveals dramatic growth of large lobulated mass centered on right atrial wall, new subpleural right lower lobe lung nodule (arrow) that is one of many, and right pleural effusion. *d* = dome of diaphragm.

**C**, Four-chamber balanced steady-state free precession image shows lobulated mass extending into and nearly obliterating right atrial cavity but without involvement of interatrial septum. (See also supplemental video, Fig. S1C, at www.ajronline.org.)

**D**, Axial ECG-gated breath-hold T1-weighted double inversion recovery fast spin-echo image shows predominantly isointense mass with a few areas of scattered hyperintensity compatible with hemorrhage.

(Fig. 1 continues on next page)
Right Atrial Mass

thought to relate to hemorrhage, necrosis, and flow voids in
the tumor. These areas of high signal intensity interspersed
with areas of intermediate signal have been described as a
cauliflower appearance [8]. After administration of the gad-
olinium-based contrast agent, the tumor enhances heteroge-
neously and shows marked surface enhancement [1]. A sun-
ray appearance has also been described in cases with diffuse
pericardial enhancement as multiple lines emanating from
the epicardium to pericardium [9].

In our patient, a benign neoplasm—the most common
being a myxoma—or a nonneoplastic lesion such as throm-
bus are unlikely in view of the infiltrative nature of the
mass and the development of multiple new lung nodules,
which are consistent with metastases. Also, the marked pe-
ripheral enhancement on the first-pass imaging is in keep-
ing with a highly vascularized tumor. Although heteroge-
neous signal characteristics are common to both myxomas
and angiosarcomas, the former are generally more well-de-
fined, often with a stalk; tend to involve the interatrial se-
p tum; and are more common in the left atrium [10].

The most common malignant cardiac tumor is cardiac me-
tastasis, which can result from direct extension, hematoge-
 nous or venous extension, or retrograde flow by lymphatic
vessels. However, these manifest in patients with known non-
cardiac primary malignancy and widespread systemic dis-
ease. The most common malignancies metastatic to the heart
are lung and breast cancers, lymphoma, and leukemia, with
the pericardium rather than the myocardium being the most
common site of involvement. Only about 5% of metastases
are estimated to be endocardial or intracavitary lesions [5].

Differentiating angiosarcoma from other primary malig-
nant cardiac neoplasms can be challenging. Angiosarcoma is
statistically the most common primary malignant tumor and
arises most commonly in the right atrial free wall. Most other
cardiac sarcomas, such as undifferentiated sarcoma, leiomyo-
sarcoma, and fibrosarcoma, have a propensity to involve the
left atrium, an important differentiating feature [5]. Rhab-
domyosarcoma, the most common primary cardiac tumor in
children, does not have any chamber predilection [4].

Cardiac lymphoma is far more commonly seen as secondary
myocardial involvement related to extensive systemic disease.
Primary cardiac lymphoma—the absence of extracardiac dis-
ease at the time of diagnosis—is rare [5]. The primary form
usually occurs in immunocompromised individuals and favors
the right heart, as does angiosarcoma. However, lymphoma is
less likely to involve cardiac valves, show necrosis, or extend
into the cardiac chamber than angiosarcoma [11].

Pericardial mesothelioma is thought to be a distinct entity
and not an extension of pleural mesotheliomas into the
pericardium [5]. Pericardial mesothelioma encases the heart
and resembles metastatic involvement of the pericardium
[5]. Frank invasion of the epicardium is rarely seen [1].

Objective

The educational objective of this article is to describe the
MRI features of cardiac angiosarcoma and to highlight the
features differentiating it from other cardiac masses.

Conclusion

Cardiac angiosarcomas, although rare, are the most com-
mon primary malignant cardiac tumors. The location of
the tumor on the right atrial wall, its heterogeneous infiltr-
ative appearance, and its enhancement are important diag-
nostic features. The tumor is aggressive, and metastases to
the lungs are frequently discovered at presentation. The
long-term prognosis is universally poor.

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**FOR YOUR INFORMATION**

A data supplement for this article can be viewed in the online version of the article at: www.ajronline.org.
Case History
A 48-year-old woman with a history of hypertension who had undergone dilatation and curettage for vaginal bleeding related to uterine fibroids presents with palpitations and chest pain. A heart murmur is detected on physical examination. Echocardiography performed elsewhere depicted a possible right atrial myxoma with inferior vena caval involvement. She was then referred to our institution for further evaluation and treatment.

Radiologic Description
CT of the abdomen and pelvis was requested to assess the degree of inferior vena caval obstruction produced by the right atrial mass detected on the echocardiogram. Images were obtained before and after the administration of intravenous contrast material. Axial and coronal reformatted images were produced. The unenhanced images depicted no visible abnormality in the right atrium or inferior vena cava. The contrast-enhanced images depicted a continuous tubular filling defect projecting within the lumen of the right atrium and within the lumen of the inferior vena cava and extending inferiorly to the level of the confluence of the iliac veins (Figs. 1A–1C). No definite iliac vein involvement was depicted. The tubular filling defect had a visualized length of 20.8 cm and a transverse diameter of 0.5 cm. It appeared to have a small central focus of enhancement. Images of the pelvis showed the uterus to be markedly enlarged and extending superiorly to the level of the L4 vertebral body (Figs. 1D and 1E). Multiple focal heterogeneous myometrial lesions were identified with an appearance consistent with uterine leiomyomas.

MRI of the heart was performed to provide further assessment of the right atrial mass seen on the echocardiogram. Images were obtained in multiple planes both with and without gadolinium. These images confirm the presence of a tubular filling defect extending into the right atrium from the inferior vena cava (Figs. 1F and 1G). The abnormality was best visualized on the cine MR images using a white blood steady-state free precession (SSFP) pulse sequence (FIESTA [GE Healthcare]; fast imaging employing steady-state acquisition sequence on a GE Healthcare Sigma 1.5-T MRI scanner) without gadolinium. These cine images revealed that the filling defect was not attached to the wall of the right atrium or inferior vena cava. Instead, it was shown to move freely within the lumen of the right atrium and within the lumen of the inferior vena cava on images obtained during different phases of the cardiac cycle. During diastole, the mass appeared to prolapse across the tricuspid valve (Figs. 1H and 1I). MRI confirmed the central focus of flow in the center of the tubular structure (Fig. 1F).

An inferior vena cavagram was obtained using a right common iliac vein injection followed by a left common iliac vein injection. These images showed a long mobile filling defect extending from the left internal iliac vein into the left common iliac vein and up the length of the inferior vena cava (Fig. 1J).

Differential Diagnosis
An apparent filling defect in the inferior vena cava extending into the right atrium may be artifactual or actual [1, 2]. The most common artifactual filling defect is pseudothrombosis produced by an admixture of opacified and unopacified blood. Actual filling defects include bland thrombus and tumor thrombus. Bland thrombus may be idiopathic or may result from a hypercoagulable state. Tumor thrombus is most commonly seen with malignant tumors, including renal and hepatic tumors, that extend into the inferior vena cava but may also be seen with benign tumors, including intravenous leiomyomatosis, renal angiomylipoma, and adrenal pheochromocytoma.

Diagnosis
The diagnosis is tumor thrombus due to intravenous leiomyomatosis with angiodys features extending from uterine leiomyomata. This patient first underwent an open resection of the intracardiac and intravascular portions of the tumor through a right atrial approach. The pathology specimen from that surgery revealed intravenous leiomyomatosis. Subsequently, the patient underwent a supracervical hysterectomy and bilateral salpingo-oophorectomy. The pathology specimen from that surgery revealed extensive uterine leiomyomatosis as well as intravenous leiomyomatosis with focal vascular thrombosis. The cut surfaces of the myometrium...
revealed branching vascular spaces filled with gelatinous material and wormlike structures. Immunohistochemical stains showed strong diffuse labeling in tumor cell nuclei for progesterone receptor and smooth muscle actin, whereas staining for estrogen receptor was weak and focal.

**Commentary**

Intravenous leiomyomatosis is a rare benign tumor characterized by proliferation of smooth muscle cells in the veins [3, 4]. The tumor may arise directly from the wall of the vein but more commonly occurs as a result of growth of uterine leiomyomata into the myometrial veins [5]. From the myometrial veins, intravenous leiomyomatosis may spread to the pelvic veins, inferior vena cava, right atrium, right ventricle, and pulmonary artery [4–6]. Involvement of the adrenal and renal veins has also been reported [5].

Intravenous leiomyomatosis is one of the unusual growth patterns of histologically benign uterine leiomyomata [4]. Other unusual growth patterns of uterine leiomyomata include parasitic leiomyoma, disseminated peritoneal leiomyomatosis, diffuse leiomyomatosis, and benign metastasizing leiomyoma. Although they are histologically benign, these aggressive growth patterns resemble the behavior of malignant tumors.

Intravenous leiomyomatosis is seen almost exclusively in white women in the age range of 28–80 years (median age,
Fig. 1 (continued)—48-year-old woman with palpitations, chest pain, heart murmur, and right atrial mass seen on echocardiography.

D and E, Axial (D) and coronal (E) contrast-enhanced CT scans of mid pelvis show uterus to be markedly enlarged, lobulated, and heterogeneous, an appearance that likely represents presence of multiple uterine leiomyomas.

F, Oblique axial cine MR image at level of suprahepatic portion of inferior vena cava (IVC) using white blood steady-state free precession (SSFP) pulse sequence (FIESTA [GE Healthcare]; fast imaging employing steady-state acquisition sequence) without gadolinium shows filling defect (arrow) in inferior vena cava withentral flow.

G, Oblique sagittal cine MR image of heart and intrahepatic portion of IVC using white blood SSFP pulse sequence (FIESTA) without gadolinium shows filling defect (arrows) extending from inferior vena cava into right atrium.

(Fig. 1 continues on next page)
44 years). It typically occurs in parous women before meno-
pause [5, 7]. Most patients with intravenous leiomyomato-
sis have a history of uterine leiomyoma leading to hysterec-
tomy, often many years earlier [5, 7]. Patients with intra-
venous leiomyomatosis may present with symptoms related to
uterine leiomyomata, such as pelvic pain or vaginal bleed-
ing [5]. They may also present with symptoms of inferior
vena cava obstruction such as lower extremity edema. If
the tumor extends into the heart, the patient may present
with heart failure, dyspnea on exertion, pulmonary embo-
lish, syncope, or sudden death [5, 7]. Physical examination
may reveal a heart murmur related to partial obstruction
of the tricuspid valve [7].

The first imaging study is often echocardiography to eval-
uate a heart murmur. On echocardiography, a mass may be
visible in the right atrium, as occurred in our patient. Careful
inspection will reveal that the mass extends into the right
atrium from the inferior vena cava. Subsequent studies often
include CT and MRI. On contrast-enhanced CT and MRI, an
enhancing mobile intraluminal filling defect is usually depicted. Establishing the diagnosis on CT or MRI depends on vi-
sualizing the connection between the intravenous mass and

Fig. 1 (continued)—48-year-old woman with palpitations, chest pain, heart
murmur, and right atrial mass seen on echocardiography.
H, Axial cine MR image at level of right atrium using white blood SSFP pulse
sequence (FIESTA) without gadolinium shows filling defect (arrow) along right
lateral wall of right atrium during systole.
I, Axial cine MR image at level of right atrium using white blood SSFP pulse se-
quence (FIESTA) without gadolinium shows filling defect (arrow) prolapsing
across tricuspid valve during diastole.
J, Inferior vena cavagram obtained using left common iliac vein injection shows
linear filling defect (arrows) extending from left internal iliac vein into left com-
mon iliac vein and up into inferior vena cava.
Right Atrial Mass

the uterus [5]. However, in most patients who have previously undergone hysterectomy, that connection cannot be shown. If the previous hysterectomy specimen showed a pathologic diagnosis of intravenous leiomyomatosis, then it is likely that a subsequently visualized intravenous mass represents recurrence and spread of intravenous leiomyomatosis. The differential diagnosis of intravenous leiomyomatosis includes other causes of tumor thrombus such as renal cell carcinoma, hepatocellular carcinoma, adrenocortical carcinoma, pancreatic carcinoma, Wilms’ tumor, renal angiomylipo, and adrenal pheochromocytoma [1, 5].

Treatment consists of complete surgical excision of the intravenous tumor along with hysterectomy and bilateral oophorectomy [5]. Surgery can be performed as a two-stage operation with separate resections of the intracardiac tumor and the abdominopelvic tumor, or as a one-stage operation with total resection of the entire tumor [7]. The recurrence rate after resection is 30%. Therefore, surveillance imaging every few months may be useful to assess for recurrent disease [5, 7].

Objective

The educational objective of this article is to describe the imaging findings and clinical characteristics of intravenous leiomyomatosis.

Conclusion

Intravenous leiomyomatosis is a rare growth pattern of uterine leiomyomata in which the histologically benign uterine tumors grow into and extend up the draining veins. When an inferior vena caval or right atrial mass is discovered in a woman with a history of hysterectomy for uterine leiomyomata or who currently has uterine leiomyomata, the possibility of intravenous leiomyomatosis should be considered. Imaging should be directed toward assessing the full extent of the tumor and showing the connection between the intravenous tumor and the leiomyomatous uterus.

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AJR Teaching File: Asymptomatic Man with Giant Negative T Waves on ECG

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Keywords: hypertrophic cardiomyopathy, MRI

Case History
A 40-year-old asymptomatic man presents for a routine health maintenance examination. The physical examination is normal; in particular, he is normotensive. ECG reveals diffuse deep T wave inversion. His family history is significant for unexplained sudden cardiac death in his father. MRI was performed to further evaluate an abnormality revealed on echocardiography.

Radiologic Description
Cine bright blood MR images of the heart (Figs. 1A–1F) obtained with a balanced steady-state free precession technique show thickened myocardium extending from the midventricular to the apical regions of the left ventricle (LV). The LV septum and lateral wall have a maximum end diastolic thickness of 23 mm (Figs. 1E and 1F). The basal regions of the myocardium, including the basal septum, are unaffected, and no obstruction of the outflow tract is seen (Figs. 1C and 1D). The ventricular cavity has a spadelike configuration, with the extreme apical region being spared. Review of cine images (Fig. S1) shows the extreme apical segment to be akinetic. (Supplemental video in three-chamber plane, Fig. S1, is available in supplemental data at www.ajronline.org.) A delayed contrast-enhanced image shows enhancement of the thickened myocardium at the apex of the LV extending to the anterior and inferior walls in a non-coronary-artery distribution sparing the subendocardium (Figs. 1G and 1H).

Diagnosis
The diagnosis is apical hypertrophic cardiomyopathy.

Commentary
Hypertrophic cardiomyopathy (HCM) is a relatively common form of genetic heart disease, having an incidence of 1:500 in the general population, and is the most frequent cause of sudden cardiac death in the young [1]. Familial clustering is often observed; the disease is transmitted as a Mendelian autosomal dominant trait with variable penetrance due to heterogeneous mutations involving any one of 10 genes encoding for myocardial sarcomere proteins. The characteristic feature is an inappropriate myocardial hypertrophy in the absence of an obvious cause such as systemic hypertension or aortic stenosis. Histologically, HCM is characterized by disorganization and malalignment of the myofibrils (i.e., myofibrillar disarray) and abnormal intramural coronary arteries characterized by thickened walls with increased intimal and medial collagen and narrowed lumen. Such architectural alterations of the microvasculature, as well as the mismatch between myocardial mass and coronary circulation, are likely responsible for the impaired coronary vasodilator reserve and bursts of myocardial ischemia that lead to myocyte death and repair in the form of patchy or transmural replacement scarring.

Different morphologic types of HCM exist [2]. In most patients, the ventricular septum and the anterior LV wall are preferentially involved, with abnormalities most prominent in the basal segments (asymmetrical septal hypertrophy). The LV end-diastolic septal thickness is typically greater than 15 mm. During systole, deformation and bulging of the hypertrophied septum into the left ventricular outflow tract (LVOT) produce flow acceleration and a pressure drop across the LVOT. Anterior movement and eventual apposition of the anterior mitral valve leaflet to the septum may occur (systolic anterior motion phenomenon), further contributing to the dynamic LVOT obstruction. Secondary mitral regurgitation is often observed. Other less frequent forms of HCM include the apical form, midventricular hypertrophy, and concentric LV hypertrophy patterns [2].

Apical HCM is a relatively rare form of HCM that was first described in Japan, where it represents 13–25% of the entire HCM population. Outside Japan, apical HCM is less common and has been reported in 3–11% of all HCM patients [3]. The typical features of apical HCM consist of giant T wave negativity on the ECG and hypertrophy confined...
Fig. 1—40-year-old man with giant negative T waves on ECG. See also Figure S1 in supplemental data at www.ajr.com.

A and B, Four-chamber images of heart in diastole (A) and systole (B) using balanced steady-state free precession (SSFP) MRI technique. Note thickening confined to apical portions of left ventricle, producing spadelike left ventricular cavity.

C and D, Left ventricular outflow tract images in diastole (C) and systole (D) using balanced SSFP MRI technique show thickening of apical regions of left ventricular myocardium and sparing of basal region. There is no obstruction of left ventricular outflow tract.

(Fig. 1 continues on next page)
Negative T Waves on ECG

Clinically, HCM requires an accurate diagnosis, determination of the distribution of hypertrophy and its functional consequences, and assessment of the likelihood of sudden death and progression to heart failure.

Two-dimensional and Doppler echocardiography are the most commonly used noninvasive methods for studying...
HCM. However, the 3D nature of cardiac MRI allows precise definition of the site and extent of hypertrophy and has been shown to be more accurate than echocardiography for determining regional hypertrophy and identifying the different phenotype forms. In particular, the apical form of HCM may be undetected on echocardiography because of near-field problems with the echo probe [7, 8]. Cardiac MRI can identify regions of LV hypertrophy not readily recognized by echocardiography and may be solely responsible for the diagnosis of the HCM phenotype in an important minority of patients. Cardiac MRI enhances the assessment of LV hypertrophy, particularly in the anterolateral LV free wall and apex, and is a powerful supplemental imaging test with distinct diagnostic advantages for selected HCM patients. Particularly in whom echocardiography is technically unsatisfactory, cardiac MRI should be considered the technique of choice for diagnosing and following up patients with all variants of HCM [9].

Cardiac function and flow dynamics at the LVOT in the event of LVOT obstruction are also well characterized by cardiac MRI. The turbulent jet across the LVOT during systole is easily detected by cine MRI, and gradients across the LVOT can be quantified using velocity-encoded techniques. The systolic anterior motion of the anterior mitral valve, a feature of the obstructive form of HCM, is readily detectable by cardiac MRI, and any consequent mitral regurgitation can be quantified. Cardiac MRI tagging may be used to identify abnormal patterns of strain, shear, and torsion in HCM, showing significant dysfunction in hypertrophic areas [10].

More recently, late-enhancement gadolinium cardiac MRI has been used in HCM to show areas of fibrosis [11–13]. Enhancement was invariably found in hypertrophied regions, with the pattern being patchy and multiple foci predominantly involving the middle third of the ventricular wall and the junction of the ventricular septum and right ventricular free wall. The extent of enhancement was positively correlated with wall thickness and inversely correlated with systolic wall thickening in the hypertrophied regions. Preliminary data in a selected group of patients suggest that a correlation exists between the extent of enhancement detected by cardiac MRI and the clinical risk factors for sudden death, LV dilatation, and heart failure in HCM patients [13]. In a more recent study of a large HCM cohort with no or only mild symptoms, myocardial fibrosis detected by cardiac MRI was associated with a greater likelihood and increased frequency of ventricular tachyarrhythmias on ambulatory ECG using a Holter monitor [14]. Identifying patients at high and low risk is an important but problematic aspect of the clinical management of HCM, particularly with the availability of an effective but not hazard-free treatment option, the implantable cardioverter-defibrillator.

Treatment strategies depend on appropriate patient selection, including drug treatment for exertional dyspnea (β-blockers, verapamil, disopyramide) and the septal myectomy–myectomy operation, which is the standard of care for severe refractory symptoms associated with marked outflow obstruction; alcohol septal ablation and pacing are alternatives to surgery for selected patients [1]. Sudden cardiac death is the most dreaded complication and is most common in adolescents and young adults who are often asymptomatic. The currently recognized major risk factors for sudden cardiac death in HCM include unexplained syncope (particularly when exertional or recurrent), a family history of HCM-related sudden death, identification of high-risk mutant genes, frequent multiple or prolonged episodes of nonsustained ventricular tachycardia on Holter monitoring, abnormal blood pressure response to exercise, and extreme degrees of LV hypertrophy (maximum LV wall thickness ≥ 30 mm) [15]. Risk stratification for sudden cardiac death is of critical importance, and high-risk patients may be treated effectively for sudden death prevention with placement of an ICD [16].

Objective

The educational objective of this article is to describe the MRI features of apical HCM and to discuss the usefulness of MRI in the diagnosis of HCM.

Conclusion

Apical HCM is a relatively rare form of HCM characterized by deep negative T waves on ECG, hypertrophy involving the apical regions of the heart not associated with LVOT obstruction, and a relatively benign prognosis in terms of cardiovascular mortality. Cardiac MRI allows precise definition of the site and extent of hypertrophy in HCM and is more accurate than echocardiography for determining regional hypertrophy and identifying different phenotypes such as the apical form of HCM, which may be undetected on echocardiography. Preliminary data have shown that MRI delayed hyperenhancement in HCM is associated with markers of sudden cardiac death and progressive disease, with possible additional prognostic information for risk stratification.

References

Negative T Waves on ECG


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A data supplement for this article can be viewed in the online version of the article at: www.ajronline.org.
In the article titled “Radiological Reasoning: Algorithmic Workup of Abnormal Vaginal Bleeding with Endovaginal Sonography and Sonohysterography,” which appeared in the December 2008 issue of AJR Integrative Imaging (AJR 2008; 191[suppl]:S68–S73), the criteria for normal endometrial thickness reported in the algorithm in Figure 3 was inaccurate. The corrected algorithm appears here.

We sincerely regret this error.

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Fig. 3—Algorithm for evaluating women with abnormal vaginal bleeding. In asymptomatic postmenopausal women, endometrial thickness of > 6 mm (for patients not undergoing hormone replacement therapy) or > 8 mm (for those receiving hormone replacement therapy) is considered abnormal and should trigger a similar workup for endometrial abnormalities [24]. Threshold for workup of asymptomatic women taking tamoxifen is controversial, with endometrial thickness cutoffs of 5–8 mm having been proposed. D&C = dilatation and curettage.