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3

Clinical Cases

Introduction

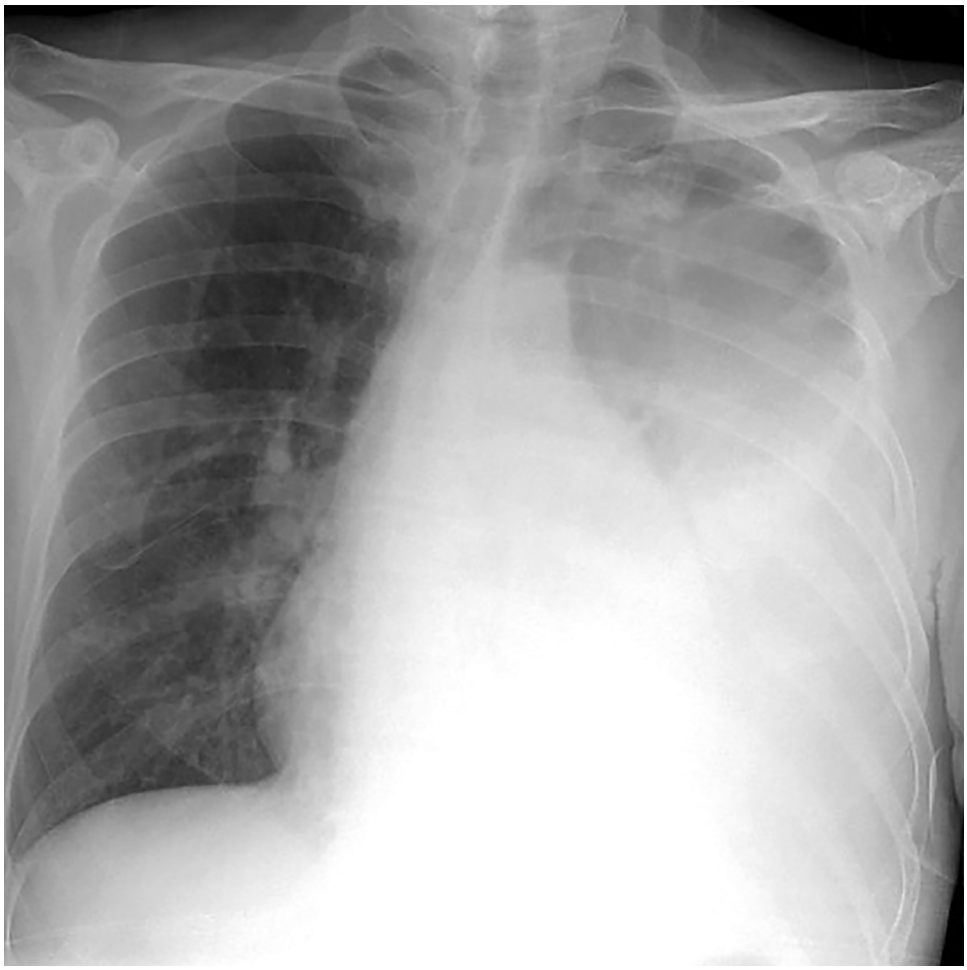
Chapter 1 provided a framework for interpreting chest radiographs and characterizing abnormalities using standard terminology. Chapter 2 illustrated the many chest radiographic abnormalities that can be caused by tuberculosis (TB). In Chapter 3, the goal is to integrate lessons learned thus far and apply that knowledge to clinical cases.

These cases are adapted from presentations gathered from U.S.-based practice but include examples of clinical problems and decision-making challenges that are applicable to any clinician diagnosing and treating TB. For each case, describe the radiographic abnormalities and answer questions relevant to the next steps in the medical evaluation and care based on the radiographic interpretation. The answers to the questions and a summary immediately follow each case.

Case #1

The patient is a 27-year-old woman who was born in Pakistan and moved to the United States at age 3. She reported 2 weeks of pleuritic chest pain, fevers, night sweats, and 5 days of a nonproductive cough. The patient had spent the previous 2 years working in Ethiopia. Two years ago, her tuberculin skin test was 3 mm and now measures 14 mm. Her chest radiograph is shown in Figure 3.1.

FIGURE 3.1.



1. **Describe the chest radiograph using standard terminology.**
2. **Which of the following should be done next?**
   - **A.** Bronchoscopy
   - **B.** Thoracoscopic lung biopsy
   - **C.** Thoracentesis
   - **D.** Treatment of latent TB infection (LTBI)

Case #1 answers

1. Homogeneous opacity occupying more than one-half of the left hemithorax and extending up the lateral chest wall. The opacity is obscuring the left hemidiaphragm and the left heart border.
2. The correct answer is **C**. Because the patient's radiograph demonstrates a large left pleural effusion, the first procedure to be done should be a diagnostic thoracentesis in addition to sputum for smears, cultures, and nucleic acid amplification test (NAAT; e.g., Xpert MTB RIF, line probe, or PCR).
    - Pleural liquid should be obtained for measurement of glucose, protein, lactate dehydrogenase, adenosine deaminase, cell counts, cytology, and microbiological studies. Consider a pleural biopsy if the diagnosis is not evident from the studies listed or if there is concern for drug-resistant TB.
    - Sputum tests remain useful for suspected pulmonary TB with pleural effusions, as the effusion may often hide the presence of parenchymal involvement.

Case #1 summary

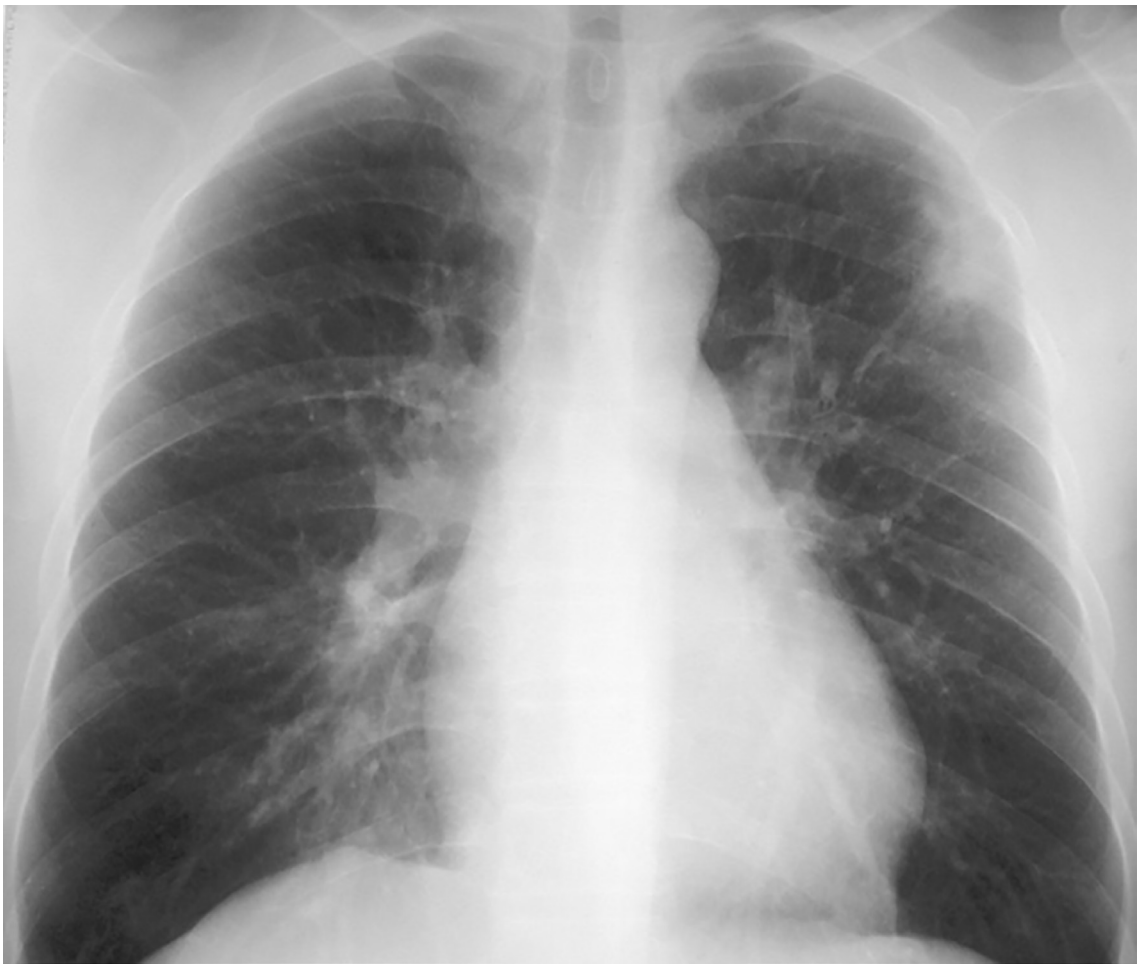
Based on the current radiographic findings, there is no immediate indication for either bronchoscopy or a thoracoscopic lung biopsy. Never start treatment for LTBI (typically with one or two medications) until active disease has been ruled out.

Pleural TB represents one of the most common forms of extrapulmonary TB. TB effusions are often unilateral and paucibacillary resulting from a hypersensitivity reaction to TB bacilli but can, on rare occasions, progress to empyema. The fluid is characterized by an exudative, lymphocyte-predominate pleural fluid. The diagnosis can be difficult to establish because pleural liquid cultures are often negative (culture yield 23-58%). In this case example, sputum and pleural fluid smear and cultures were all negative (NAAT not obtained). Culture of the pleural biopsy later revealed *M. tuberculosis* resistant to isoniazid (INH).

Case #2: Part 1

The patient is a 30-year-old woman from the Philippines who was noted to have an abnormal chest radiograph (Figure 3.2) when she underwent TB screening prior to employment in a healthcare facility. She had a documented positive IGRA test several years earlier and received 6 months of INH treatment. She denies having symptoms, has no underlying medical conditions, and is a non-smoker.

FIGURE 3.2.



1. **How would you describe the chest radiograph?**
2. **Based on your interpretation of the chest radiograph, which of the following are appropriate next steps?** (Choose all that apply)
   - **A.** Collect 3 sputum specimens for acid-fast smears, NAAT, and mycobacterial cultures
   - **B.** Begin treatment for LTBI
   - **C.** Repeat the IGRA
   - **D.** Look for the records and radiographs from her previous evaluation to determine if the radiographic abnormality was present at that time

Case #2 answers: Part 1

1. Left upper-lobe peripheral airspace opacity.
2. The correct answers are **A** and **D**. When a patient has a positive TB skin test or IGRA and an abnormal chest radiograph consistent with TB, the first step should always consist of collecting sputum (if not already done) to assess the possibility of active TB. Based on the information provided, chest imaging should have been done when she was evaluated for the previous positive IGRA. An image showing that the lesion was unchanged might lessen the need for additional evaluation, whereas progression of the lesion would indicate the need for further evaluation. Even if the lesion is stable, obtain sputum for microbiological evaluation to confirm no active disease is present, particularly if LTBI treatment is indicated.

Case #2: Part 2

An earlier chest radiograph could not be found and initial test results revealed negative smears and a negative NAAT. She was started on 4 antituberculosis medications pending the results of sputum cultures. After 2 months, the culture results were negative. A repeat chest radiograph was obtained (Figure 3.3).

FIGURE 3.3. **After 2 months of treatment for TB**

3. **How would you describe the chest radiograph?**
4. **Which of the following would be the most appropriate next step?**
   - **A.** Continue multidrug therapy for TB
   - **B.** Obtain a chest CT scan
   - **C.** Perform a fine-needle aspiration of the nodule
   - **D.** Perform bronchoscopy to obtain a better respiratory specimen

Case #2 answers: Part 2

3. Left upper-lobe peripheral opacity is nearly resolved compared with the chest radiograph from 2 months ago.
4. The correct answer is **A**. Because the radiographic abnormality decreased in size and there was no other etiology identified, the patient is considered a clinical (culture-negative) case of TB. Therefore, the multidrug regimen should be continued and the patient treated for active disease.

Case #2 summary

In a patient at increased risk for TB who has an abnormal chest radiograph consistent with TB, the first step should be to obtain sputum for acid-fast smears, NAAT, and mycobacterial cultures. Sputum examination for mycobacteria is necessary because it is not possible to determine if the lesion is residual scarring from previous TB or currently active TB on the basis of a single radiograph.

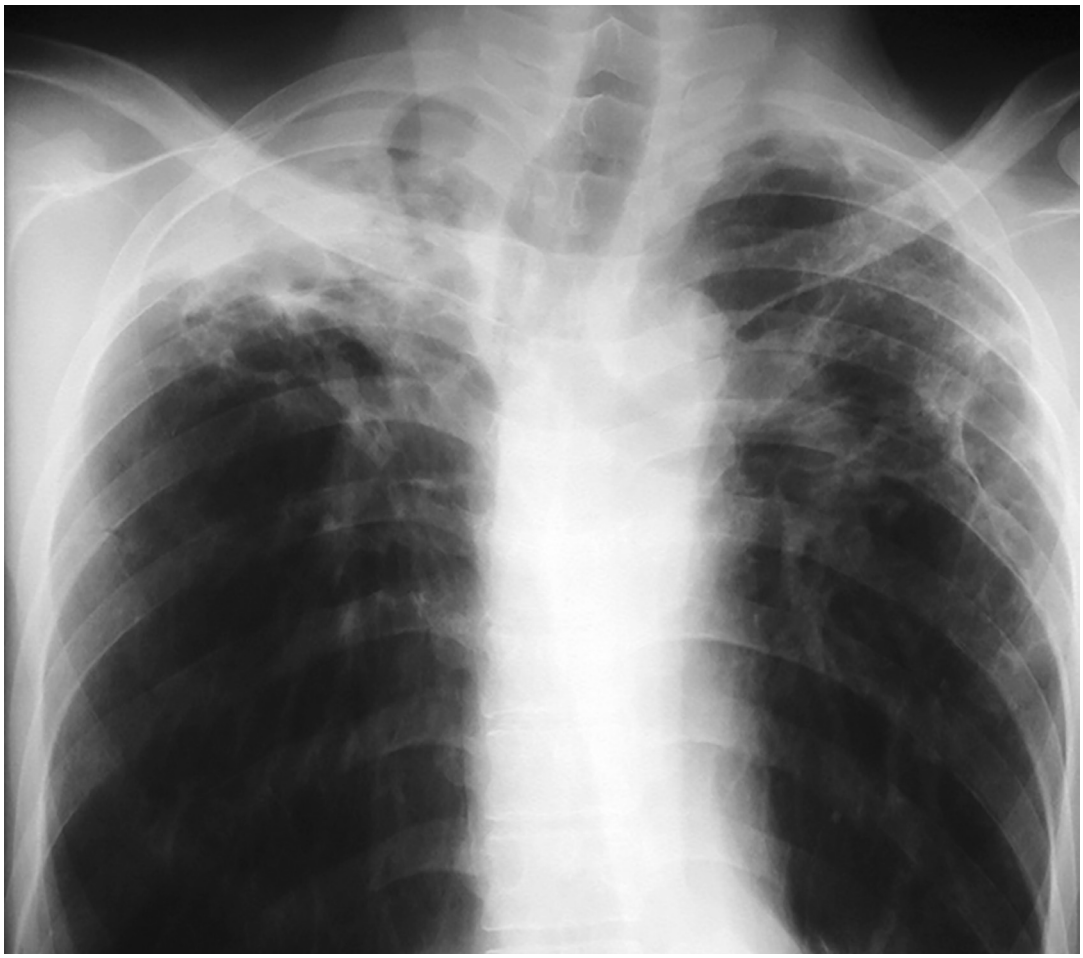
Negative cultures do not necessarily exclude a diagnosis of active TB; usually 15-20% of reported cases in the United States each year are culture negative. Presumably, the negative microbiological tests are due to a low bacillary load. These cases are best managed by follow-up clinical and radiographic evaluation after 2-3 months of multidrug therapy to determine if there has been a response.

If a patient exhibits either a clinical response or significant improvement in the radiograph after 2-3 months of treatment and no other etiology is identified, treatment should be continued for a total of 4 months for culture-negative, active TB. However, in some individuals a 6-month regimen may be indicated.

Case #3

A 60-year-old woman, who immigrated from China 1 month ago, is screened for TB She denies symptoms and has no history of previous TB treatment or other significant medical history. Her IGRA, done as part of her immigration evaluation before arriving to the U.S., was positive. Her immigration chest radiograph done 6 months ago in China is shown in Figure 3.4.

FIGURE 3.4.



1. **How would you describe the chest radiograph?**

Pre-immigration acid-fast smears and cultures of sputum (x 3) were documented as negative in her immigration forms. A repeat chest radiograph now remains unchanged.

2. **What would be the most appropriate next step?**
   - **A.** Obtain sputum for smear, NAAT, and culture. If all tests return as negative for *M. tuberculosis*, treat for LTBI
   - **B.** Treat as culture-negative TB disease with a multidrug regimen for 4 months
   - **C.** Monitor chest radiograph every 3-6 months for 2 years
   - **D.** Obtain chest CT

Case #3 answers

1. Right greater than left upper-lobe fibronodular opacities with volume loss and bilateral hilar retraction. Pronounced right apical pleural thickening.
2. The correct answer is **A**. While the abnormalities described may represent residual damage from prior TB, diagnostic sputum tests should still be done to investigate for active TB disease. Current U.S. TB program practices vary regarding whether overseas sputum results are relied upon before starting LTBI treatment or are repeated when a new immigrant arrives with abnormal chest radiographic findings. Empiric multidrug treatment or a CT scan are not currently indicated given the lack of clinical symptoms and the reassuring lack of interval radiographic change compared to image taken 6 months ago.

Case #3 summary

Patients with a positive IGRA or TB skin test who have radiographic evidence of prior TB and who have not received prior treatment are at increased risk for the subsequent progression to active TB.

- The radiographic findings that constitute evidence of prior TB are upper-lobe opacities or fibrosis, often with volume loss. Other radiographic findings due to prior TB may include bronchiectasis or pleural thickening. In many instances of resolved TB, the chest radiographic findings revert to normal.
- Individuals with LTBI and limited radiographic findings of healed primary TB (e.g., calcified solitary pulmonary nodules, calcified hilar lymph nodes, and pleural thickening without associated parenchymal opacities or fibrosis) are not at increased risk for progression to active TB compared with persons with LTBI and normal chest radiographs.

Disease activity cannot be determined from a single chest radiograph. Unless previous radiographs show that the abnormality has not changed, sputum examination should be performed to assess the possibility of active TB. Once active TB has been excluded, consider LTBI treatment for individuals who have not had prior treatment.

The decision to initiate multidrug antituberculosis treatment at the initial evaluation should be based on the degree of clinical suspicion for active TB. If suspicion is high, multidrug therapy should be initiated before smear/culture results are known. If suspicion is low, treatment can be deferred until additional data have been obtained to clarify the diagnosis.

Case #4

A 32-year-old male patient with AIDS presents with a history of fever, cough, dyspnea, and night sweats for the past 3 weeks. His last CD4 lymphocyte count was 550 cells/μL. His radiograph is shown in Figure 3.5.

FIGURE 3.5.

1. **How would you describe the chest radiograph?**
2. **Based on the clinical presentation and your reading of the chest radiograph, what would be the least likely diagnosis?**
   - **A.** TB
   - **B.** Fungal infection
   - **C.** *Pneumocystis jirovecii* pneumonia
   - **D.** *Mycobacterium avium* disease

Case #4 answers

1. Right perihilar consolidation with a focus of cavitation and possible right hilar lymphadenopathy.
2. The correct answer is **C**. Infection with *P. jirovecii* does not usually cause lymphadenopathy, although cavitation can occur. TB is a classic cause of cavitation and lymphadenopathy, but nontuberculous mycobacteria such as *M. avium* may on occasion present with identical radiographic findings. Finally, fungal infections like cryptococcus can cause cavitation and lymphadenopathy and thus need to be included in the differential diagnosis as well.

Case #4 summary

The patient had 3 acid-fast smears which were positive, a positive NAAT for *M. tuberculosis* without rifampin resistance, and was started on directly observed therapy with 4 antituberculosis medications. Final cultures grew *M. tuberculosis.*

Patients with HIV who develop pulmonary disease often present challenging diagnostic dilemmas to clinicians. One reason is the myriad radiographic appearances that the same infection can take in an HIV-positive individual. For example, TB in a person with HIV can appear as lower-lung zone involvement, lymphadenopathy, and pleural effusion instead of the more typical post-primary reactivation pattern of upper-lobe cavitary disease. As a general rule, the more immunosuppressed the patient, the more atypical the chest radiograph findings with respect to TB. Proper interpretation of the chest radiograph is critical in such patients to help guide the diagnostic evaluation. The presence of cavitation and lymphadenopathy in this patient made TB and other mycobacterial and fungal infections much more likely than *P. jirovecii* pneumonia.

Case #5

The patient is a 4-year-old child who presents to a local hospital with fever, cough, and wheezing. The child has no underlying medical conditions. He was recently exposed to 2 family members with culture-positive TB. The organisms are pan-susceptible. His chest radiograph is shown in Figure 3.6.

FIGURE 3.6.

1. **How would you describe the chest radiograph?**
2. **What would be the most appropriate next step?**
   - **A.** Perform bronchoscopy to obtain a good respiratory specimen
   - **B.** Collect sputum specimens for acid-fast smears, NAAT, and cultures
   - **C.** Begin a broad-spectrum antibiotic for community-acquired pneumonia
   - **D.** Begin multidrug antituberculosis therapy

Case #5 answers

1. Right paratracheal and hilar lymphadenopathy and right lower-lung zone consolidation with probable middle-lobe collapse. The right heart border and medial portion of the right hemidiaphragm are not seen (silhouette sign). Note: The image is a lordotic projection (the clavicles are not seen in the image). This projection tends to make objects in the lower half of the thorax appear larger.
2. The correct answer is **D**. Generally, any child with lymphadenopathy on the chest radiograph and recent exposure to adults with TB should be started on antituberculosis therapy. The yield from bronchoscopy is low, and the procedure is not always readily available. It can be very difficult to obtain sputum specimens from a young child. The presence of lymphadenopathy is unlikely to be due to community-acquired pneumonia. Definitive microbiological diagnosis is best made in young children by obtaining aspirates of gastric secretions.

Case #5 summary

It is often challenging to establish a diagnosis of TB in children because it is difficult to obtain sputum or other diagnostic specimens. However in this instance, the epidemiological evidence plus the radiographic findings that are most consistent with TB are sufficient to make a diagnosis of TB, even though microbiological proof from the child is unlikely.

Case #6

A 71-year-old man is evaluated because of a 1-month history of a cough with occasional bloodstreaked sputum. He denies fever or weight loss. He previously smoked cigarettes but stopped 23 years ago. He thought he was treated for TB in the past, but he is unable to provide any details. Eight months ago, he arrived in the United States from China on an immigrant visa. The physical exam is unremarkable. An IGRA test is positive. No prior radiographs are available. Three sputum smears are negative for acid-fast bacilli, but the NAAT is positive (negative rifampin resistance), and cultures are pending. His chest radiograph is shown in Figure 3.7.

FIGURE 3.7.

1. **How would you describe this chest radiograph?**
2. **Which of the following would you do next?**
   - **A.** Begin INH for treatment of LTBI
   - **B.** Begin multidrug TB treatment and obtain a chest CT
   - **C.** Repeat chest radiograph in 6 months

Case #6 answers

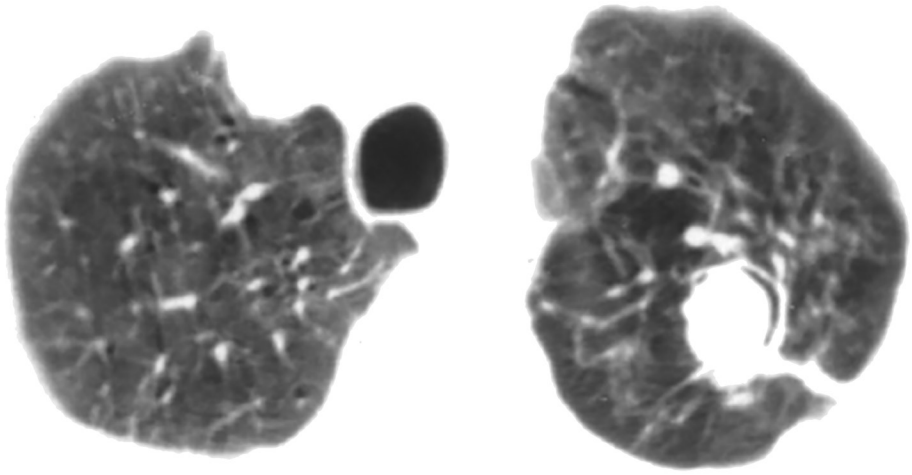
1. Left upper-lobe focal rounded mass with crescent-shaped air collection in its superior aspect.
2. The correct answer is **B**. INH alone should not be started in someone suspected of having potential active TB. A repeat chest radiograph in 6 months would be too long an interval for follow-up.

Case #6 summary

The first step in approaching a patient with a positive IGRA and an abnormal chest radiograph is to obtain sputum for acid-fast smears, NAAT, and cultures. The positive NAAT suggests active disease is likely and multidrug therapy is indicated. An air crescent within the cavity suggests a mycetoma and can be better visualized with a chest CT.

The CT scan (Figure 3.8) indicates that the radiographic abnormality is a mycetoma, which is a fungus ball that develops in a preexisting cavity (in this case, due to prior TB). When a patient with a mycetoma develops massive hemoptysis, embolization or lung resection may be considered for definitive treatment of the hemoptysis. This patient will require treatment for both his active TB and the mycetoma.

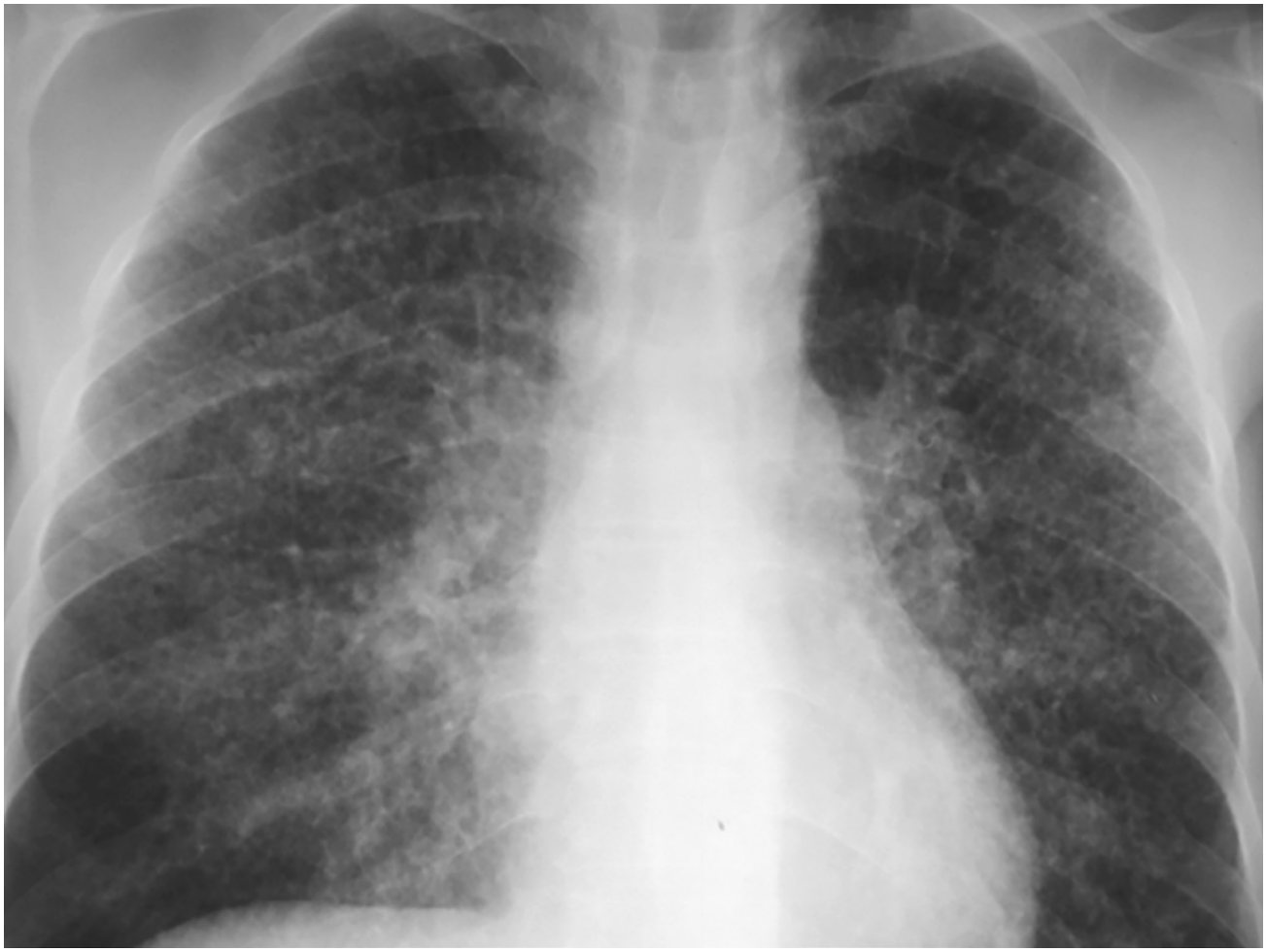
FIGURE 3.8.



Case #7

The patient is a 62-year-old man from India with a 3-month history of fevers, night sweats, intermittent cough, and a 10-kilogram weight loss. His chest radiograph is shown in Figure 3.9.

FIGURE 3.9.



1. **How would you describe this chest radiograph?**
2. **Which of the following diagnostic tests has the highest sensitivity for identifying *M. tuberculosis* in this patient?**
   - **A.** Mycobacterial cultures of blood
   - **B.** Mycobacterial cultures of sputum
   - **C.** Mycobacterial cultures of transbronchial biopsies
   - **D.** Mycobacterial cultures of bronchoalveolar lavage fluid

Case #7 answers

1. Miliary pattern of multiple well-defined, small nodules, mostly 2-3 mm in diameter, that are widespread in distribution.
2. The correct answer is **C**. The diagnostic yield of tuberculosis from transbronchial biopsy (combining both histology and culture) is 50-70% in patients with miliary disease. This pattern is found in patients with disseminated TB and can also be seen in disseminated fungal infections and some malignancies.

Case #7 summary

A miliary pattern is indicative of disseminated disease. It consists of diffuse small nodules the size of millet seeds, about 2 mm in diameter. In TB, the miliary pattern results from hematogenous dissemination of tubercle bacilli, which explains its widespread distribution. A miliary pattern is not specific for TB and can also be seen in disseminated fungal infections and some malignancies (e.g., renal cell carcinoma). Because the miliary pattern is an example of an interstitial pattern, transbronchial tissue provides the highest diagnostic yield. Transbronchial tissue should be examined for the presence of granulomas and cultured for mycobacteria (yield: 50-70%). Sputum samples should be collected as part of the initial evaluation, but more extensive sampling is usually required. Because miliary TB almost always involves other organs, diagnostic alternatives include biopsies of bone marrow (especially in patients with cytopenias) and liver (especially in patients with elevated serum alkaline phosphatase), and cultures of urine. Given the high mortality of disseminated TB, evaluation should occur without delay.

Case #8

The patient is a 54-year-old woman with a 5-week history of fever, night sweats, and a cough productive of foul-smelling sputum. Medical problems include a history of chronic obstructive pulmonary disease and heavy alcohol use. Her last tuberculin skin test 3 years ago had 13 mm of induration. Her chest radiographs are shown in Figures 3.10A and 3.10B.

FIGURE 3.10A. **Frontal**

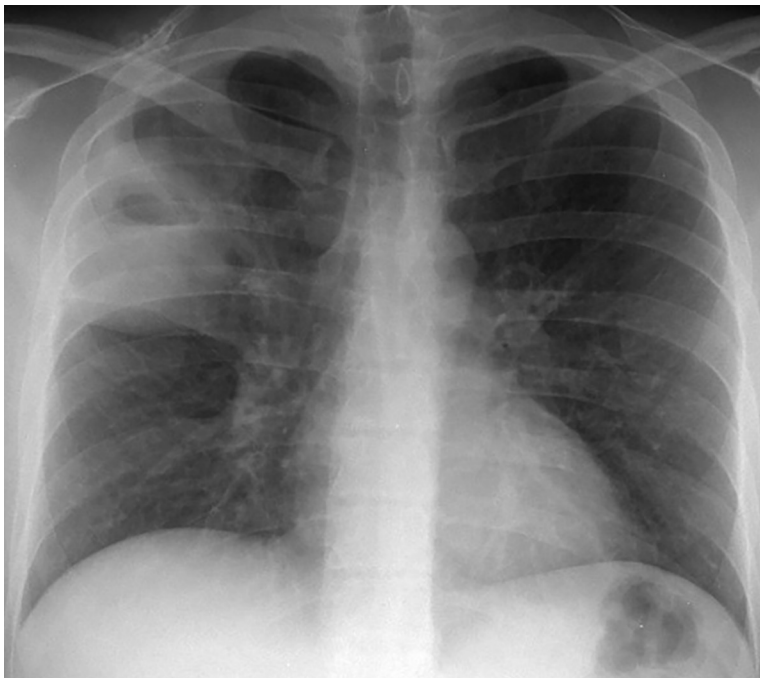
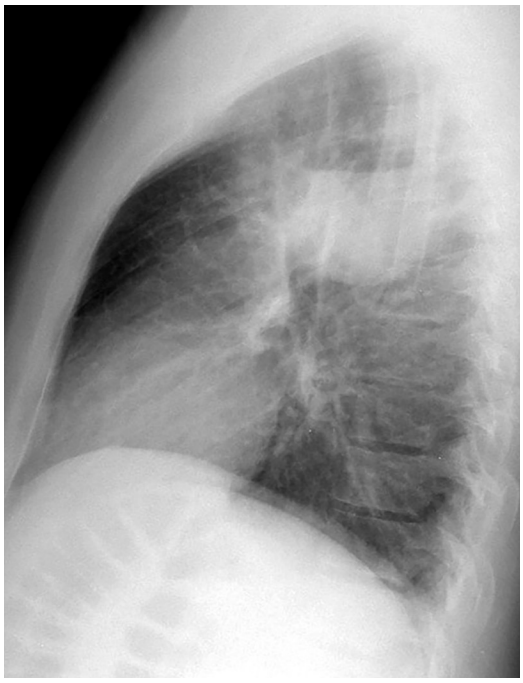


FIGURE 3.10B. **Lateral**



1. **How would you describe these chest radiographs?**
2. **Which of the following would be the most appropriate treatment for this patient?**
   - **A.** Doxycycline
   - **B.** Treatment for anerobic infection
   - **C.** Isoniazid, rifampin, pyrazinamide, and ethambutol
   - **D.** Fluconazole

Case #8 answers

1. Large air-filled spherical density in the right upper lobe that has an air-fluid level.
2. The correct answer is **B**. The differential diagnosis of an air-fluid level in the chest includes lung abscess and other pyogenic infections; hemorrhage into a bulla or cyst; bronchogenic cancer; and noninfectious cavitary lung disease (e.g., Wegener's granulomatosis). Although TB is on the list of diseases associated with cavitation, the presence of an air-fluid level is uncommon. In this case, lung abscess is more likely than the other diagnostic possibilities given the symptom of foul-smelling sputum, and radiographic findings of a thick-walled cavity with an air-fluid level and absence of surrounding infiltrate. Antibiotics like doxycycline do not provide sufficient anaerobic bacterial coverage to be useful for treating a lung abscess. Fluconazole (choice D) should not be used unless a fungal infection is found to be the cause.

Case #8 summary

It is important to identify and properly characterize focal lucent areas on the chest radiograph. There are many causes of focal lucent lesions, but diseases that result in cavitation are among the most important. Causes of pulmonary cavitation include TB, lung abscess, pulmonary infarction, bronchogenic cancer, and non-infectious inflammatory diseases (e.g., Wegener's granulomatosis). These diseases have different clinical presentations, so obtaining a good history is an important first step. The next step in the diagnostic evaluation is usually collecting sputum for microbiologic studies and cytologic examination. Patients should also be placed in respiratory isolation if TB is suspected on the basis of either the radiographic findings or clinical examination.

Take-home points

Proper interpretation of the chest radiograph is an essential component of the diagnostic evaluation of any person with potential TB. The radiographs and clinical case scenarios in this chapter intend to illustrate common patterns associated with pulmonary TB and to very briefly discuss how the findings fit into the sequence of diagnostic and/or therapeutic approaches. Importantly, the cases highlight some basic principles related to the role of radiography in the diagnosis of pulmonary TB. Some of these principles are:

- Chest radiographs cannot establish a diagnosis of TB, but they are highly influential in suggesting or guiding clinicians' diagnostic approaches that can confirm a diagnosis.
- An exception to this rule can occur in persons with radiographic findings consistent with pulmonary TB but with negative microbiologic tests who have positive IGRAs or TB skin tests and are given multidrug treatment empirically. If no alternate diagnosis is established and a follow-up radiograph 2-3 months after starting anti-TB treatment shows improvement, a clinical diagnosis of TB is strongly inferred.
- In general, while there are differences in the radiographic patterns of "primary" and "post-primary" TB, there is considerable overlap.
- Radiographic findings of healed primary TB (e.g., calcified solitary pulmonary nodules, calcified hilar lymph nodes, and pleural thickening without associated parenchymal opacities or fibrosis) are not indicative of an increased risk for progression to active TB.
- It is essentially impossible to diagnose "old, inactive TB" from a single chest radiograph. Appropriate specimens for microbiological testing should be obtained from any patient with an abnormal chest radiograph in whom a diagnosis of TB is being considered.
- Prior radiographs, if available, should be sought. They can help to determine if a given lesion is active (progressing) or inactive (unchanging).
- Clinical suspicion for TB in children is often based on a positive tuberculin skin test or IGRA and an abnormal chest radiograph showing lymphadenopathy as well as parenchymal abnormalities.
- People with immunocompromising conditions or treatments commonly have "atypical" chest radiographic findings with lower-lobe opacities, hilar and mediastinal lymphadenopathy, and little or no cavitation.

Although not explicitly stated, the clinical scenarios imply that communication/discussion between radiologists and clinicians is highly desirable, if not essential, to get the most information from chest radiographs.

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