

Pulmonary Tuberculosis: Up-to-Date Imaging and Management

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OBJECTIVE. Pulmonary tuberculosis (TB) is a common worldwide infection and a medical and social problem causing high mortality and morbidity, especially in developing countries. The traditional imaging concept of primary and reactivation TB has been recently challenged, and radiologic features depend on the level of host immunity rather than the elapsed time after the infection. We aimed to elaborate the new concept of the diagnosis and treatment of pulmonary TB, to review the characteristic imaging findings of various forms of pulmonary TB, and to assess the role of CT in the diagnosis and management of pulmonary TB.

CONCLUSION. Fast and more accurate TB testing such as bacterial DNA fingerprinting and whole-blood interferon- γ assay has been developed. Miliary or disseminated primary pattern or atypical manifestations of pulmonary TB are common in patients with impaired immunity. CT plays an important role in the detection of TB in patients in whom the chest radiograph is normal or inconclusive, in the determination of disease activity, in the detection of complication, and in the management of TB by providing a roadmap for surgical treatment planning. PET scans using ¹⁸F-FDG or ¹¹C-choline can sometimes help differentiate tuberculous granuloma from lung malignancy.

Keywords: lung CT, lung disease, lung infection, tuberculosis, pulmonary

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Tuberculosis (TB) is an airborne infectious disease caused by *Mycobacterium tuberculosis* and is a major cause of morbidity and mortality, particularly in developing countries [1–3]. In 2005, 8.8 million people developed active TB and 1.6 million died of the disease [4]. Most cases occur in Southeast Asia and Africa.

Patients with active pulmonary TB may be asymptomatic, have mild or progressive dry cough, or present with multiple symptoms, including fever, fatigue, weight loss, night sweats, and a cough that produces bloody sputum. If TB is detected early and fully treated, people with the disease quickly become noninfectious and eventually cured. However, multidrug-resistant (MDR) and extensively drug-resistant TB, HIV-associated TB, and weak health systems are major challenges. The World Health Organization is making an effort to dramatically reduce the burden of TB and to halve TB deaths and prevalence by 2015, through its Stop TB Strategy and supporting the Global Plan to Stop TB [5].

The prompt diagnosis of TB is essential for community public health infection con-

trol measures as well as for ensuring the appropriate therapy for infected patients. Unfortunately, acid-fast bacilli are found in the sputum in a limited number of patients with active pulmonary TB [6]. Therefore, the imaging diagnosis would provide an appropriate therapy for infected patients before the definitive diagnosis by the bacteriology. The aim of this article is to elaborate new concepts in the diagnosis and treatment of pulmonary TB in the 21st century, to review the characteristic imaging findings of various forms of pulmonary TB, and to assess the role of CT in the diagnosis and management of pulmonary TB.

Development of Infection and Pathogenesis

M. tuberculosis is an aerobic, nonmotile, non-spore-forming rod that is highly resistant to drying, acid, and alcohol. It is transmitted from person to person via droplet nuclei containing the organism and is spread mainly by coughing. A person with active but untreated TB infects approximately 10–15 other people per year. The probability of transmission from one person to another depends on the number of infectious droplets

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expelled by a carrier, the duration of exposure, and the virulence of the *M. tuberculosis*. The risk of developing active TB is greatest in patients with altered host cellular immunity, including extremes of age, malnutrition, cancer, immunosuppressive therapy, HIV infection, end-stage renal disease, and diabetes.

TB infection begins when the mycobacteria reach the pulmonary alveoli, where they invade and replicate within alveolar macrophages. Inhaled mycobacteria are phagocytized by alveolar macrophages, which interact with T lymphocytes, resulting in differentiation of macrophages into epithelioid histiocytes [7]. Epithelioid histiocytes and lymphocytes aggregate into small clusters, resulting in granulomas. In the granuloma, CD4 T lymphocytes (effector T cell) secrete cytokines, such as interferon- γ , which activate macrophages to destroy the bacteria with which they are infected. CD8 T lymphocytes (cytotoxic T cell) can also directly kill infected cells [8]. Importantly, bacteria are not always eliminated from the granuloma, but can become dormant, resulting in a latent infection. Another feature of human TB granulomas is the development of necrosis in the center of the tubercles.

The primary site of infection in the lungs is called the Ghon focus [9]. It either enlarges as disease progresses or, much more commonly, undergoes healing. Healing may result in a visible scar that may be dense and contain foci of calcification. During the early stage of infection, organisms commonly spread via lymphatic channels to regional hilar and mediastinal lymph nodes and via the bloodstream to more distant sites in the body. The combination of the Ghon focus and affected lymph nodes is known as the Ranke complex. The initial infection is usually clinically silent. In approximately 5% of infected individuals, immunity is inadequate and clinically active disease develops within 1 year of infection, a condition known as progressive primary infection [10]. For most infected individuals, however, TB remains clinically and microbiologically latent for many years.

In approximately 5% of the infected population, endogenous reactivation of latent infection develops many years after the initial infection (this has also been called "postprimary TB") [10]. The reactivation TB tends to involve predominantly the apical and posterior segments of the upper lobes and the superior segments of the lower lobes. This location is likely due to a combination of relatively higher oxygen tension and impaired lymphat-

ic drainage in these regions [11]. As distinct from primary infection site, in which healing is the rule, reactivation TB tends to progress. The main abnormalities are progressive extension of inflammation and necrosis, frequently with development of communication with the airways and cavity formation. The endobronchial spread of necrotic material from a cavity may result in TB infection in the same or in other lobes. Hematogenous dissemination may result in miliary TB.

Diagnosis

A definitive diagnosis of TB can only be made by culturing *M. tuberculosis* organisms from a specimen taken from the patient. However, TB can be a difficult disease to diagnose, mainly because of the difficulty in culturing this slow-growing organism in the laboratory. A complete evaluation for TB must include a medical history, a chest radiograph, a physical examination, and microbiologic smears and cultures. It may also include a tuberculin skin test and a serologic test.

The treatment of latent TB infection to prevent progression to active disease has been an essential component of public health efforts to eliminate TB [12]. Currently, latent infection is diagnosed in a nonimmunized person by a tuberculin skin test (TST), which yields a delayed-hypersensitivity-type response to purified protein derivatives of *M. tuberculosis*. However, the TST, which has been used for years for the diagnosis of latent TB infection, has many limitations, including false-positive test results in individuals who were vaccinated with bacille Calmette-Guérin (BCG) and in individuals who have infections not related to *M. tuberculosis* [13, 14].

Discovery of the role of T lymphocytes and interferon- γ in the immune process has led to the development of an in vitro assay for cell-mediated immune reactivity to *M. tuberculosis* [15]. Recently, this whole-blood interferon- γ assay has been introduced for the diagnosis of latent TB infection and has shown a higher diagnostic accuracy than the TST [13, 16]. These new TB tests are being developed with the hope of cheap, fast, and more accurate TB testing. These new tests use polymerase chain reaction detection of bacterial DNA and whole-blood interferon- γ assay [17]. Individuals with a positive TST or whole-blood interferon- γ assay, especially HIV-infected persons or those who have chest radiographic or CT findings consistent with TB, should be considered for treatment of a latent infection [18].

New Concept of Radiologic Manifestations of Tuberculosis

Patients who develop disease after initial exposure are considered to have primary TB, whereas patients who develop disease as a result of reactivation of a previous focus of TB are considered to have reactivation TB. Traditionally, it was believed that the clinical, pathologic, and radiologic manifestations of reactivation TB were quite distinct from those of primary TB. This concept has been recently challenged on the basis of DNA fingerprinting.

DNA fingerprint pattern with restriction fragment length polymorphism (RFLP) analysis of *M. tuberculosis* isolates can give clinicians an insight into the transmission of TB [19]. Isolates from patients infected with epidemiologically unrelated strains of TB have different RFLP patterns, whereas those from patients with epidemiologically linked strains generally have identical RFLP patterns. Therefore, clustered cases of TB, defined as those in which the isolates have identical or closely related genotypes, have usually been transmitted recently. In contrast, cases in which the isolates have distinctive genotypes generally are a reactivation of infection acquired in the distant past [20, 21].

A recent study based on genotyping *M. tuberculosis* isolates with RFLP showed that the radiographic features are often similar in patients who apparently have a primary disease and those who have a reactivation TB [22, 23]. Therefore, time from acquisition of infection to the development of clinical disease does not reliably predict the radiographic appearance of TB. The only independent predictor of radiographic appearance may be integrity of the host immune response; namely, severely immunocompromised patients show a tendency to have the primary form of TB, whereas immunocompetent patients tend to have the reactivation form [22, 23]. Because this result is preliminary and most published data are based on the traditional concept of primary and reactivation disease, we follow the traditional outline in this article.

Radiologic Manifestations in Immunocompetent Hosts

Primary Tuberculosis

The initial parenchymal focus of TB may enlarge and result in an area of airspace consolidation or, more commonly, undergo healing by transformation of the granulomatous tissue into mature fibrous tissue. Primary TB

occurs most commonly in children but is being seen with increasing frequency in adults [24]. The most common abnormality in children is lymph node enlargement, which is seen in 90–95% of cases [25, 26]. The lymphadenopathy is usually unilateral and located in the hilum or the paratracheal region. On CT, the enlarged nodes typically show central low attenuation, which represents caseous necrosis, and peripheral rim enhancement, which represents the vascular rim of the granulomatous inflammatory tissue [27, 28] (Fig. 1).

Airspace consolidation, related to parenchymal granulomatous inflammation and usually unilateral, is evident radiographically in approximately 70% of children with primary TB [26]. It shows no predilection for any particular lung zone [26]. On CT, the parenchymal consolidation in primary TB is most commonly dense and homogeneous but may also be patchy, linear, nodular, or mass-like [29] (Fig. 2).

Pleural effusion is usually unilateral and on the same side as the primary focus of TB. The effusion may be large and occur in patients without evidence of parenchymal disease on chest radiographs [30].

Reactivation Tuberculosis

The most common radiographic manifestation of reactivation pulmonary TB is focal or patchy heterogeneous consolidation involving the apical and posterior segments of the upper lobes and the superior segments of the lower lobes [29, 31]. Another common finding is the presence of poorly defined nodules and linear opacities, which are seen in approximately 25% of patients [31]. Cavities, the radiologic hallmark of reactivation TB, are evident radiographically in 20–45% of patients [29–31]. In approximately 5% of patients with reactivation TB, the main manifestation is a tuberculoma, defined as a sharply marginated round or oval lesion measuring 0.5–4.0 cm in diameter [29, 31]. Histologically, the central part of the tuberculoma consists of caseous material and the periphery, of epithelioid histiocytes and multinucleated giant cells and a variable amount of collagen. Satellite nodules around the tuberculoma may be present in as many as 80% of cases [32]. Because of active glucose metabolism caused by active granulomatous inflammation, tuberculomas sometimes have been reported to accumulate ^{18}F -FDG and to cause PET scans to be interpreted as false-positive for malignancy [33] (Fig. 3). Unlike ^{18}F -FDG

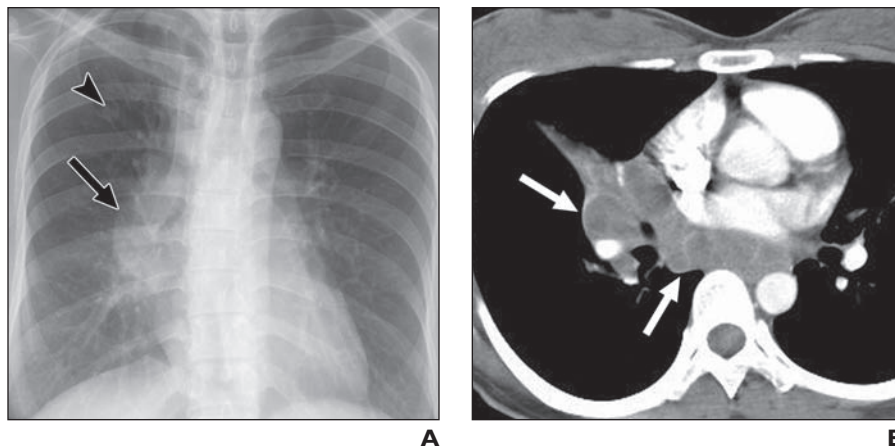


Fig. 1—Primary tuberculosis manifesting primarily as lymphadenopathy in 26-year-old woman.

A, Posteroanterior chest radiograph shows right hilar mass (arrow). Note smaller nodule (arrowhead) in right upper lung zone.

B, Contrast-enhanced transverse CT scan (5.0-mm section thickness) obtained at level of basal trunk using mediastinal window setting shows enlarged right hilar and subcarinal lymph nodes (arrows), central necrotic low attenuation, and peripheral rim enhancement.

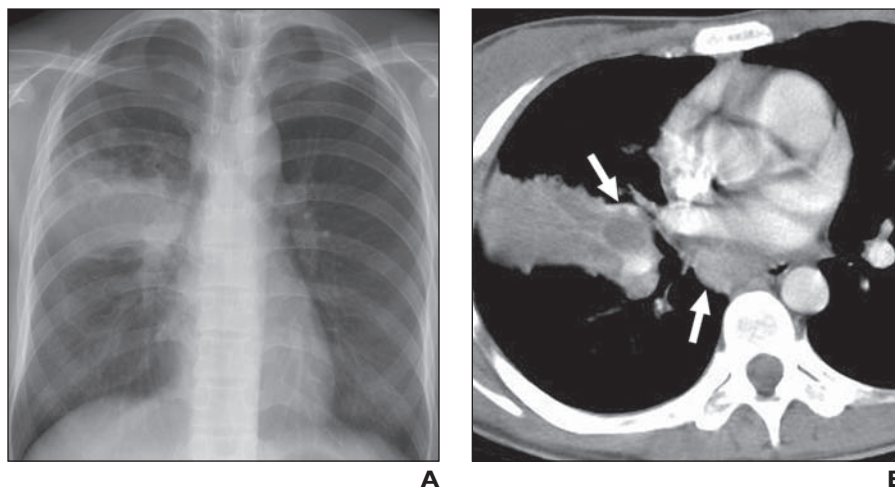


Fig. 2—Primary tuberculosis presenting with consolidation and lymphadenopathy in 21-year-old woman.

A, Posteroanterior chest radiograph shows airspace consolidation in right middle lung zone.

B, Contrast-enhanced transverse CT scan (5.0-mm section thickness) obtained at level of right middle lobar bronchus using mediastinal window setting shows airspace consolidation in right middle lobe. Note enlarged right hilar and subcarinal lymph nodes (arrows). Hilar node has necrotic low attenuation.

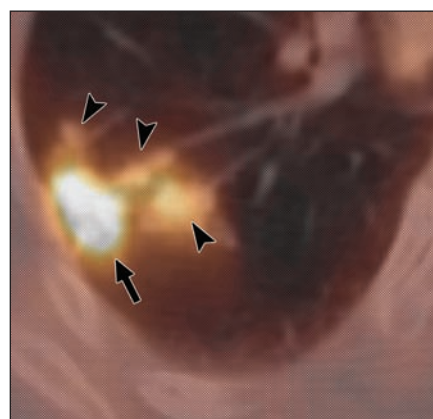


Fig. 3—Tuberculous granulomas in 58-year-old man. ^{18}F -FDG PET/CT scan shows increased FDG uptake in nodules—well-defined predominant nodule (arrow) and surrounding smaller satellite nodules (arrowheads)—in right upper lobe with maximum standard uptake value of 6.1.

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PET scans, ^{11}C -choline PET scans can help differentiate between lung cancer and tuberculoma [34]. The standard uptake value of tuberculoma is low in ^{11}C -choline PET scans.

Hilar or mediastinal lymphadenopathy is uncommon in reactivation TB, being seen in approximately 5–10% of patients [30, 31]. Pleural effusion, typically unilateral, occurs in 15–20% of patients [35].

The most common CT findings of reactivation pulmonary TB are centrilobular small nodules, branching linear and nodular opacities (tree-in-bud sign), patchy or lobular areas of consolidation, and cavitation [24, 36, 37]. The centrilobular small nodules and tree-in-bud sign reflect the presence of endobronchial spread and are due to the presence of caseous necrosis and granulomatous inflammation filling and surrounding terminal and respiratory bronchioles and alveolar ducts [36, 38] (Fig. 4). These tree-in-bud signs are considered a reliable marker of the activity of the process [6]. Cavitation is also a sign of an active disease process and usually heals as a linear or fibrotic lesion.

Although it is usually accompanied by parenchymal abnormalities, pleural effusion may be the sole imaging manifestation of TB. In this particular situation, the determination of pleural fluid adenosine deaminase (ADA) level (elevated in TB pleurisy) can be helpful for the characterization of the pleural fluid; the ADA assay has a sensitivity of 92% (95% CI, 90–93%) and a specificity of 90% (89–91%) for diagnosing TB pleurisy [39]. New subpleural lung nodules may develop during medication for TB pleural effusion. It should not be regarded as treatment failure. These paradoxical subpleural nodules will eventually show improvement with continued medication [40].

Miliary Tuberculosis

Miliary TB refers to widespread dissemination of TB by hematogenous spread. It occurs in 2–6% of primary TB and also occurs somewhat more frequently in reactivation TB [41]. In the latter situation, miliary TB may be seen in association with typical parenchymal changes or may be the only pulmonary abnormality. Each focus of miliary infection results in local granulomas that, when well developed, consist of a region of central necrosis surrounded by a relatively well-delimited rim of epithelioid histiocytes and fibrous tissue.

The characteristic radiographic and high-resolution CT findings consist of innumerable, 1- to 3-mm diameter nodules randomly

distributed throughout both lungs [41–44] (Fig. 5). Thickening of interlobular septa and fine intralobular networks are frequently evident [37]. Diffuse or localized ground-glass opacity is sometimes seen, which may herald acute respiratory distress syndrome [43–45] (Fig. 6).

Airway Tuberculosis

The most common cause of inflammatory stricture of the bronchus is TB. Tracheobronchial TB has been reported in 10–20% of all patients with pulmonary TB [24, 46]. The principal CT findings of airway TB are circumferential wall thickening and luminal narrowing,

with involvement of a long segment of the bronchi [46, 47]. In active disease, the airways are irregularly narrowed in their lumina and have thick walls, whereas in fibrotic disease, the airways are smoothly narrowed and have thin walls [46, 47]. The left main bronchus is involved more frequently in fibrotic disease, whereas both main bronchi are equally involved in active disease [46] (Fig. 7).

Radiologic Manifestations in Immunocompromised Hosts

Impaired host immunity has been regarded as a predisposing factor in TB. Known risk factors for development of active TB

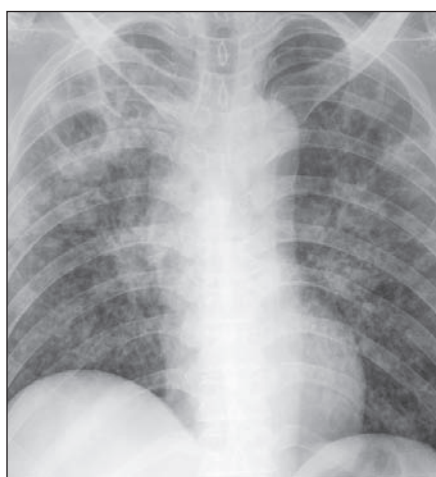
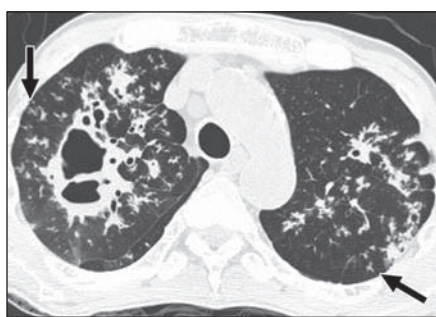
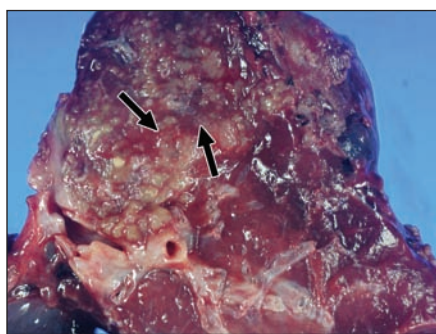


Fig. 4—Reactivation tuberculosis in 55-year-old man. **A**, Anteroposterior chest radiograph shows cavitary consolidation in right upper lung zone and multiple ill-defined nodules in both lungs.

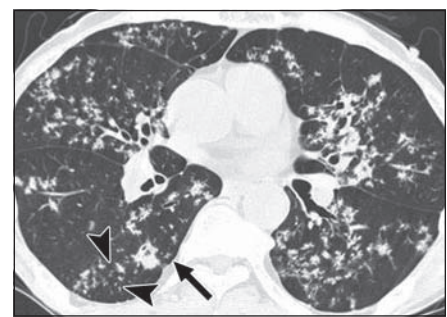


B and C, High-resolution CT scans (1.0-mm section thickness) obtained at levels of aortic arch (**B**) and proximal ascending aorta (**C**) show consolidation and acinus-sized nodules containing several cavities in both upper lobes. Note branching nodular and linear opacities (tree-in-bud signs) (arrows) and centrilobular small nodules (arrowheads, **C**) in both lungs.



D, Photograph of gross specimen obtained at lobectomy from different patient shows multiple foci of nodules and consolidation that are distinctly white, consistent with caseous necrosis. Most have nodular appearance and some appear to be branching (arrows), suggestive of airway-centered nature of lesions.

E, Photomicrograph of surgical specimen discloses multiple granulomas, each related to small membranous bronchiole (arrows). Some granulomas show central caseous necrosis (arrowhead). (H and E, $\times 40$)



include conditions that are associated with defects in cell-mediated immunity, such as HIV infection; malnutrition; drug and alcohol abuse; malignancy; end-stage renal disease; diabetes mellitus; and corticosteroid

or other immunosuppressive therapy [48]. Infliximab and etanercept (used in the treatment of Crohn's disease and rheumatoid arthritis) are human antibodies against tumor necrosis factor- α (TNF- α), which is in-

involved in the host defense against TB—killing of *M. tuberculosis* by macrophage, granuloma formation, or apoptosis and prevention of dissemination of infection to other sites. Active TB may develop soon after

Fig. 5—Miliary tuberculosis in 70-year-old man. **A**, Posteroanterior chest radiograph shows evenly distributed, discrete, uniformly sized, millet-sized nodular opacities in both lungs. **B**, High-resolution CT image (1.0-mm section thickness) at level of right upper lobar bronchus shows uniform-sized small nodules randomly distributed throughout both lungs. Note subpleural and subfissural nodules (arrows).

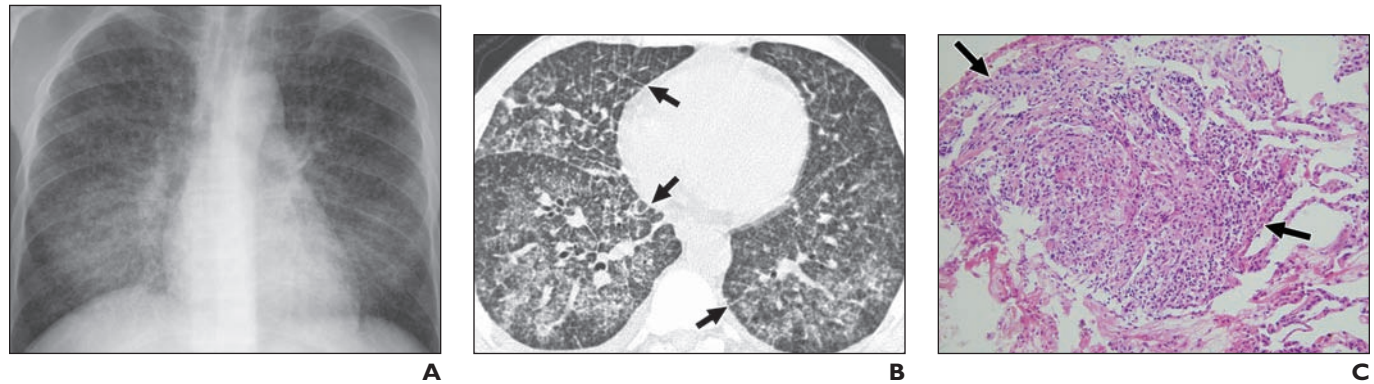
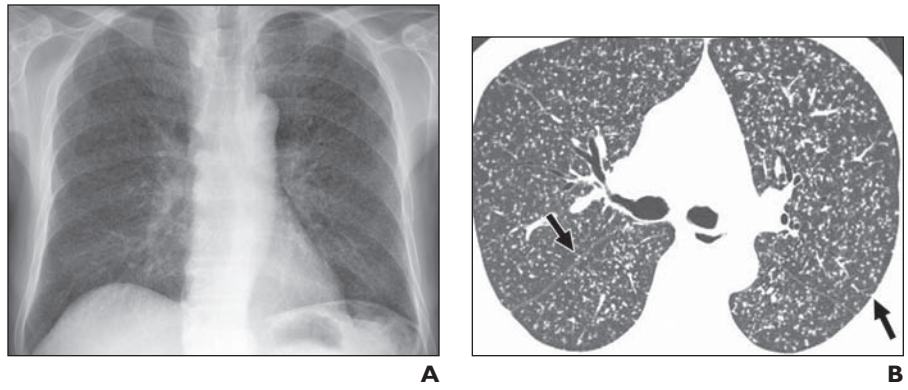


Fig. 6—Miliary tuberculosis presenting as acute respiratory distress syndrome in 47-year-old man. **A**, Posteroanterior chest radiograph shows innumerable millet-sized nodular opacities and ground-glass opacities in both lungs. **B**, High-resolution CT image (1.0-mm section thickness) obtained at ventricular level shows randomly distributed small nodules and extensive bilateral ground-glass opacity. Note interlobular septal (arrows) and intralobular interstitial thickenings in both lungs. **C**, Photomicrograph of pathologic specimen obtained with transbronchial lung biopsy discloses granuloma (arrows) in alveolar wall. Diffuse alveolar wall thickening and intraalveolar fibrin deposition (not shown) suggesting early stage of diffuse alveolar damage were also observed. (H and E, $\times 400$)

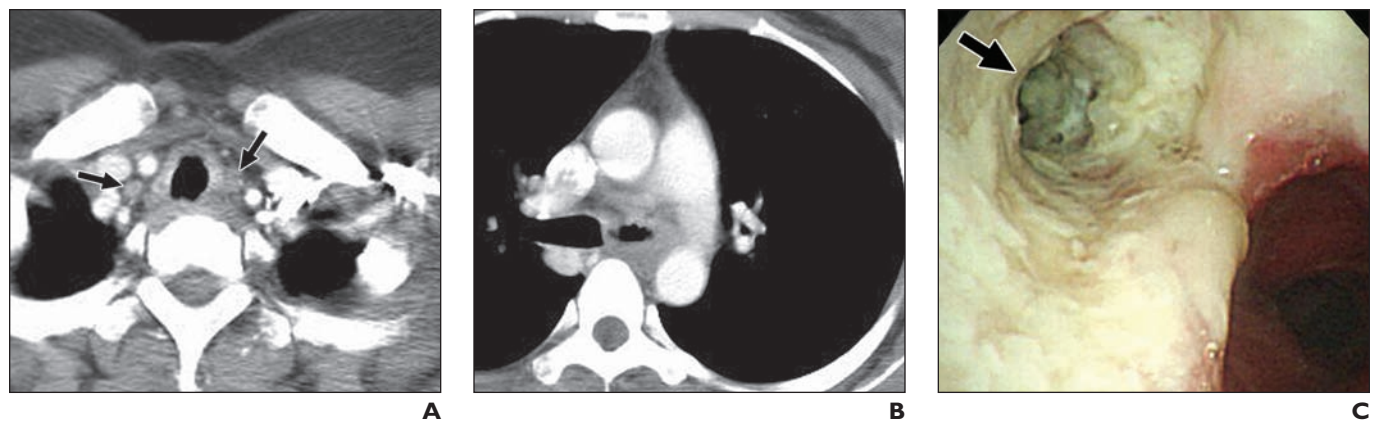


Fig. 7—Actively caseating bronchial tuberculosis in 42-year-old woman. **A** and **B**, Contrast-enhanced transverse CT scans (5.0-mm section thickness) using mediastinal window setting obtained at levels of thoracic inlet (**A**) and main bronchi (**B**) show luminal narrowing of trachea and proximal left main bronchus and irregular wall thickening. Note lymph nodes (arrows, **A**) in mediastinum. **C**, Bronchoscopy shows narrowed left main bronchial lumen with its mucosa swollen and covered diffusely with whitish cheeselike substance (arrow).

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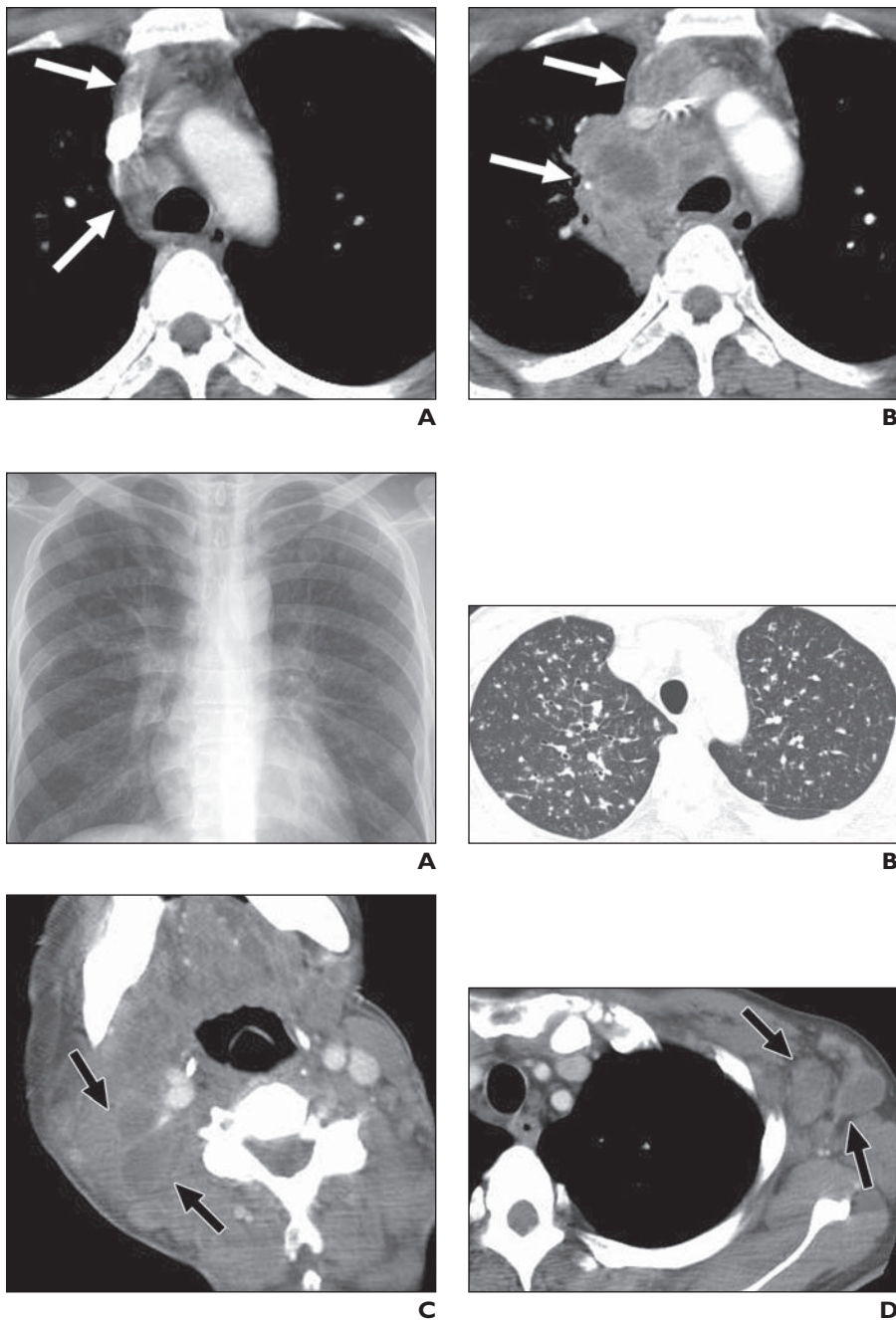


Fig. 8—Paradoxical worsening of tuberculous lymphadenitis associated with immune reconstitution inflammatory syndrome in 40-year-old woman with AIDS.

A, Contrast-enhanced transverse CT scan (5.0-mm section thickness) using mediastinal window setting obtained at level of aortic arch just before highly active antiretroviral therapy, shows multiple enlarged lymph nodes (arrows) with central necrotic low attenuation in prevascular and right paratracheal areas. Patient's HIV RNA viral load and CD4 counts were more than 1 million copies/mL and 35 cells/ μ L, respectively. **B**, Follow-up CT image obtained 3 months after **A** shows increased extent of necrotic lymph nodes (arrows). Patient's HIV RNA viral load and CD4 counts at this time were 433 copies/mL and 142 cells/ μ L, respectively.

Fig. 9—Pulmonary tuberculosis with lymphadenopathy and extrapulmonary involvement in 42-year-old man with AIDS. His CD4 count was 64 cells/ μ L.

A, Posteroanterior chest radiograph shows multiple small nodular opacities in both lungs, especially in upper lung zones. **B**, High-resolution CT scan (1.0-mm section thickness) obtained at level of aortic arch shows randomly distributed small nodules and interlobular septal thickenings in both lungs. **C** and **D**, Contrast-enhanced transverse CT scans (5.0-mm section thickness) using mediastinal window setting obtained at levels of mandible (**C**) and thoracic inlet (**D**) show enlarged lymph nodes (arrows), central necrotic low attenuation, and peripheral rim enhancement in right neck and left axilla.

the initiation of treatment with such drugs. Therefore, before prescribing these drugs, assessment of TB infection risk factors and a TST or interferon- γ assay are strongly recommended to determine the patient's latent TB infection status and the risk of active disease [49, 50].

TB is a major cause of death among people living with HIV infection or AIDS. In 2005, the World Health Organization (WHO) estimated that 12% of HIV deaths globally

were due to TB and that there were 630,000 new coinfections with TB and HIV [51]. Immune restoration induced by highly active anti-retroviral therapy (HAART) in developed countries has considerably improved the outcome of HIV-positive patients and reduced the prevalence of opportunistic infection and TB in these patients. However, HIV-associated TB still continues to occur in countries where HAART is widely used [52]. Furthermore, HAART may result in para-

doxical worsening or TB manifestations in patients with immune reconstitution inflammatory syndrome [53, 54] (Fig. 8).

The radiographic manifestations of HIV-associated pulmonary TB are thought to be dependent on the level of immunosuppression at the time of overt disease [55–57]. On CT, HIV-seropositive patients with a CD4 T lymphocyte count $< 200/\text{mm}^3$ have a higher prevalence of mediastinal or hilar lymphadenopathy, a lower prevalence of cavitation, and often

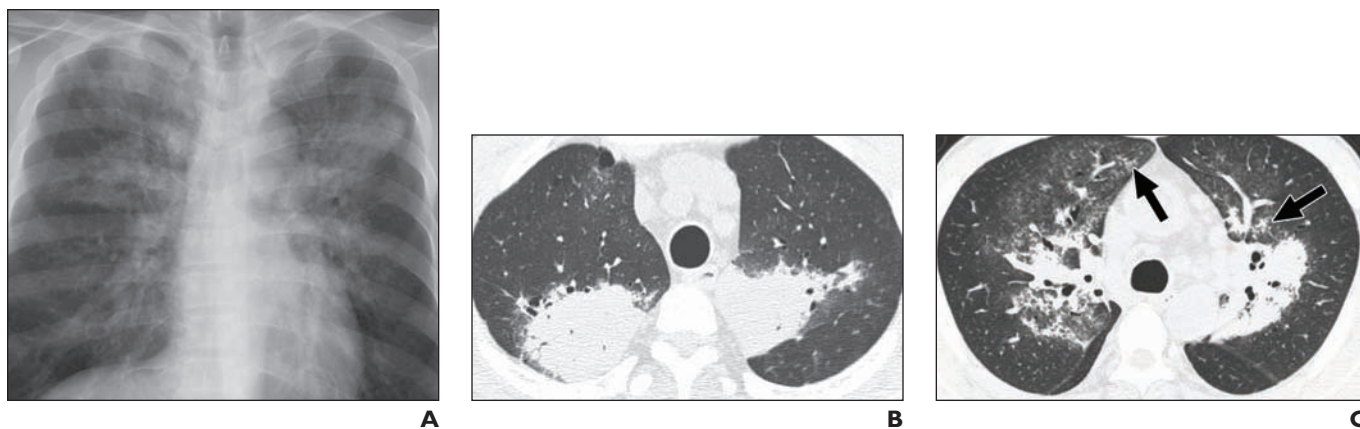
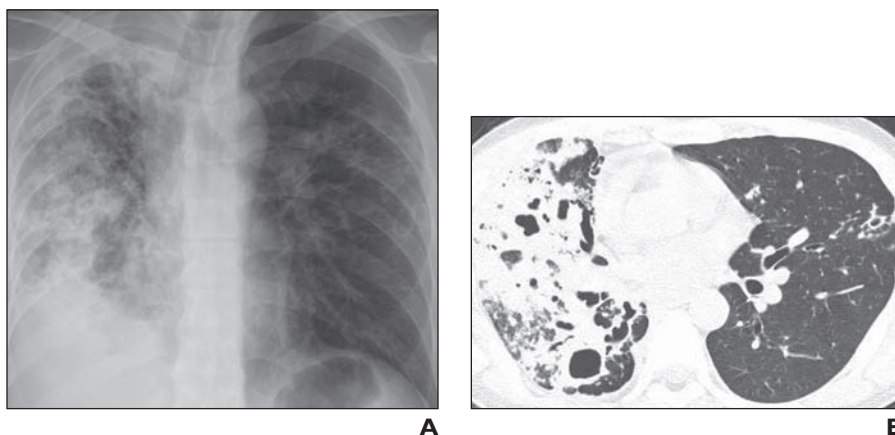


Fig. 10—Pulmonary tuberculosis in 51-year-old man with AIDS. His CD4 count was 4 cells/ μ L. **A**, Posteroanterior chest radiograph shows multifocal masslike airspace consolidation in bilateral upper lung zones. **B** and **C**, High-resolution CT scans (1.0-mm section thickness) obtained at levels of left innominate vein (**B**) and azygos arch (**C**) show masslike airspace consolidation with air bronchograms, centrilobular small nodules (arrows, **C**), and ground-glass opacity in both upper lobes.

Fig. 11—Multidrug-resistant tuberculosis in 36-year-old man.

A, Posteroanterior chest radiograph shows multiple small nodules, patchy consolidation containing several cavities, and linear opacities in both lungs. Note decreased volume in right lung and apical pleural thickening.

B, High-resolution CT scan (1.0-mm section thickness) obtained at level of left basal trunk shows consolidation containing several cavities in right middle lobe and right lower lobe. Note small cavitory nodule and centrilobular nodules in left upper lobe.



extrapulmonary involvement as compared with HIV-seropositive patients with a CD4 T lymphocyte count equal to or $\geq 200/\text{mm}^3$ [58] (Figs. 9 and 10). Miliary or disseminated disease has also been reported to be associated with severe immunosuppression [58] (Fig. 9).

Unusual or atypical manifestations of pulmonary TB are common in patients with impaired host immunity. In cases of active pulmonary TB, diabetic and immunocompromised patients have a higher prevalence of multiple cavities in a tuberculous lesion and of nonsegmental distribution than do patients without underlying disease [48]. The incidence of TB in patients with idiopathic pulmonary fibrosis (IPF) is more than four times higher than that of the general population. Atypical manifestations such as subpleural nodules or a lobar or segmental airspace consolidation are common in patients with IPF, which may mimic lung cancer or bacterial pneumonia [59]. Pulmonary TB in patients with systemic lupus erythematosus (SLE) has a higher incidence

and prevalence because of abnormal function of alveolar macrophages and exposure to corticosteroid and cytotoxic drugs. TB in patients with SLE tends to show radiologic findings of miliary dissemination, diffuse consolidation, or primary TB [60].

Radiologic Manifestations of Multidrug-Resistant Tuberculosis

Anti-TB drug resistance is a major public health problem that threatens the success of global TB control. The major concerns of drug resistance are fear regarding the spread of drug-resistant organisms and the ineffectiveness of chemotherapy in patients infected with the resistant organisms. In addition, MDR TB is a fatal disease because of the high mortality rate, depending on the underlying diseases, particularly in HIV-infected patients [61, 62].

Imaging findings of MDR TB do not basically differ from those of drug-sensitive TB. However, multiple cavities and findings of

chronicity, such as bronchiectasis and calcified granulomas, are more common in patients with MDR TB [63, 64] (Fig. 11). A strong correlation seems to exist between the radiologic features of MDR TB and the mode of acquisition of drug-resistance. Patients with primary drug resistance, who develop MDR TB without a history of anti-TB chemotherapy or a therapy history of less than 1 month, were found to present with noncavitary consolidation, pleural effusion, and a primary tuberculosis pattern of disease [65]. On the other hand, those who acquired MDR TB with a chemotherapy history of longer than 1 month often show cavitary consolidations and in general show a reactivation pattern of the disease.

Extensively-drug-resistant TB is defined as TB that has evolved resistance to rifampin and isoniazid, as well as to any member of the quinolone family and at least one of the following second-line TB treatments: kanamycin, capreomycin, or amikacin [66]. Extensively-drug-resistant TB is associated

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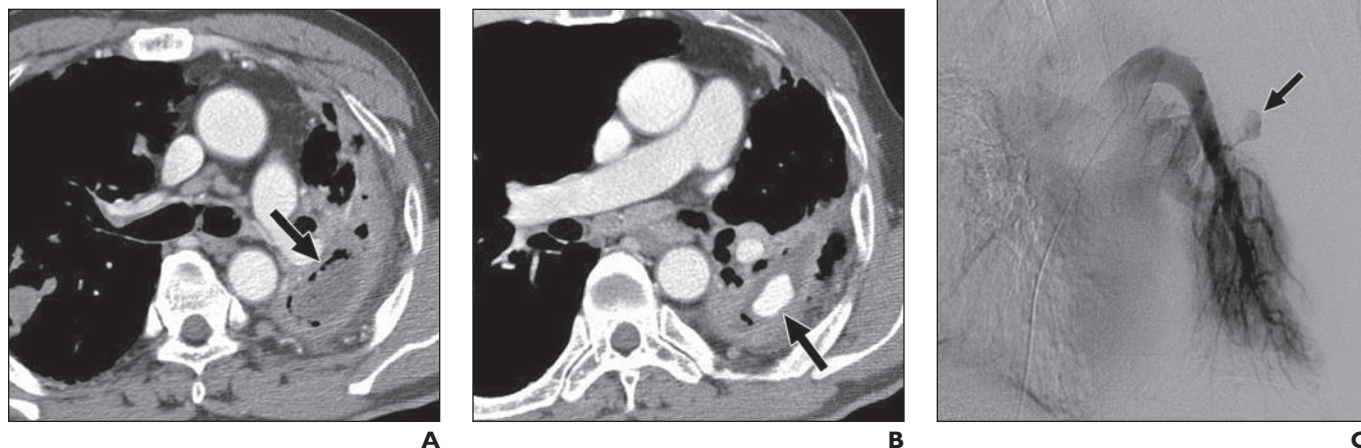


Fig. 12—Rasmussen aneurysm in chronic destructive pulmonary tuberculosis in 62-year-old man. **A**, Contrast-enhanced transverse CT scan (2.5-mm section thickness) obtained at level of main bronchi using mediastinal window setting shows cavitary consolidation with air-crescent sign (low-attenuation lesion and surrounding air) (arrow) in left upper lobe. **B**, CT scan obtained 15 mm inferior to **A** shows contrast-enhancing round vascular structure (arrow) in consolidative lesion. **C**, Left pulmonary angiogram shows contrast material filling aneurysm (arrow).

with a much higher mortality rate than MDR TB because of a reduced number of effective treatment options. The epidemiology and imaging findings of extensively-drug-resistant TB have not been well studied, but it is believed that the spread of extensively-drug-resistant TB is closely associated with a high prevalence of HIV and poor infection control [67]. There has been no report on radiologic findings of extensively-drug-resistant pulmonary TB; but in our experience, the disease manifests an advanced pattern of primary TB (extensive consolidation with or without lymphadenopathy) in AIDS patients and an advanced pattern of MDR TB (multiple cavitary lesions in consolidative or nodular lesions) in non-AIDS patients.

Complications and Sequelae of Tuberculosis

A variety of thoracic sequelae and complications from pulmonary TB may occur and may involve the lungs, airways, vessels, mediastinum, pleura, or chest wall [47, 68–71] (Appendix 1, Figs. 12 and 13).

The radiologic manifestations of acute respiratory distress syndrome secondary to TB include extensive bilateral areas of ground-glass opacity or consolidation superimposed on findings of miliary or endobronchial spread of TB. Multiple cystic lesions may develop in patients recovering from acute respiratory distress syndrome or in patients with extensive consolidation due to TB [71]. The cystic lesions may resemble pneumato-

celes or bullae, which may resolve over several months or persist [71].

Rasmussen aneurysm is a pseudoaneurysm that results from weakening of the pulmonary artery wall by adjacent cavitary TB (Fig. 12). Empyema necessitatis (Fig. 13) results from leakage of tuberculous empyema through the parietal pleura and discharge of its contents into the subcutaneous tissues of the chest wall or, less commonly, into the pericardium, vertebral column, or esophagus [69].

CT in Tuberculosis

Chest radiographs play a major role in the screening, diagnosis, and response to treatment of patients with TB. However, the radiographs may be normal or show only mild or nonspecific findings in patients with active disease [30]. Common causes of a missed diagnosis of TB are failure to recognize hilar and mediastinal lymphadenopathy as a manifestation of primary disease in adults, overlooking of mild parenchymal abnormalities in patients with reactivation disease, and failure to recognize that an upper lobe nodule or mass surrounded by small nodular opacities or scarring may represent TB [30].

CT is more sensitive than chest radiography in the detection and characterization of both subtle localized or disseminated parenchymal disease and mediastinal lymphadenopathy [37, 42, 72, 73]. The radiographic diagnosis of TB is initially correct in only 49% of all cases—34% for the diagnosis of primary TB and 59% for the diagnosis of reactivation TB [30].

With CT, the diagnosis of pulmonary TB is correct in 91% of patients and TB is correctly excluded in 76% of patients [74]. CT and high-resolution CT are particularly helpful in the detection of small foci of cavitation in areas of confluent pneumonia and in areas of dense nodularity and scarring [37]. In one study of 41 patients with active TB [37], high-resolution CT showed cavities in 58%, whereas chest radiographs showed cavities in only 22%.

In addition to the diagnosis of TB, high-resolution CT is useful in determining disease activity. A tentative diagnosis of active TB on CT could be based on the pattern of parenchymal abnormalities and the presence of cavitation or evidence of endobronchial spread, such as the presence of centrilobular nodules or a tree-in-bud pattern. In the series by Lee et al. [74], 80% of patients with active disease and 89% of those with inactive disease were correctly differentiated on high-resolution CT.

CT is also helpful in the evaluation of pleural complications, including tuberculous effusion, empyema, and bronchopleural fistula, and may show pleural disease that is not evident on chest radiography [75].

In addition to its major role in the diagnosis of TB, CT plays an important role in the management of TB, especially in complicated or MDR TB. MDR TB often shows multiple cavities, which lead to the expectoration of a large number of bacilli and endobronchial spread to previously unaffected areas of the lung. Limited drug penetration into the cavities that harbor large numbers of myco-

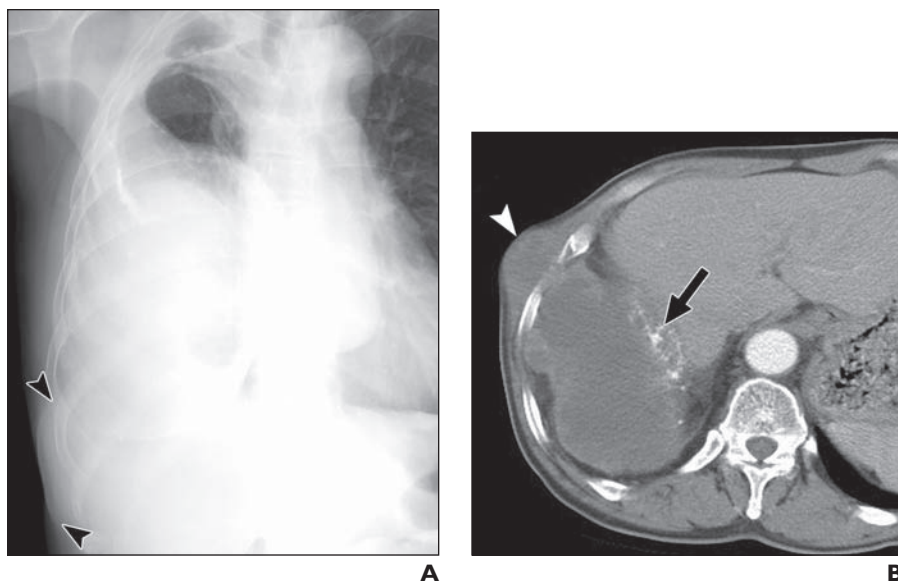


Fig. 13—Pleural and chest wall tuberculosis in 74-year-old man.

A, Posteroanterior chest radiograph shows loculated pleural fluid and pleural calcification in right hemithorax. Soft-tissue bulging opacity is also observed in right lower lateral chest wall (arrowheads). Note right upper lobe volume loss, calcifications, and cavity.

B, Contrast-enhanced transverse CT scan (5.0-mm section thickness) obtained at level of porta hepatis using mediastinal window setting shows pleural fluid collection and visceral pleural calcification (arrow) in right hemithorax, suggesting chronic tuberculous empyema. Lentiform chest wall lesion (arrowhead) showing central low attenuation, consistent with focal tuberculous chest wall abscess, is also seen.

bacteria is believed to contribute to the drug resistance. Therefore, surgery may be an adjuvant treatment for MDR TB, although present-day TB treatment relies on chemotherapy [76]. CT can locate the site of cavitation and the extent of active disease and therefore can be a roadmap for the planning of surgical treatment.

Conclusion

Although the slow reduction of the incidence of TB has been seen in developed countries, TB is still a major challenge among infectious diseases, even in the 21st century. Fast and accurate TB testing, such as bacterial DNA analysis and whole-blood interferon- γ assay, has been developed for detecting latent infection. The traditional imaging concept of primary and reactivation TB has recently been challenged on the basis of DNA fingerprinting, and radiologic features depend on the level of host immunity rather than the elapsed time after the infection. PET scans using ^{18}F -FDG or ^{11}C -choline can sometimes help differentiate a tuberculous nodule from lung malignancy. CT is an effective diagnostic method when chest radiographs are normal or inconclusive, and it provides valuable information for the diagnosis and management of TB.

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APPENDIX I: Complications and Sequelae of Thoracic Tuberculosis

Parenchymal complications

- Acute respiratory distress syndrome
- Extensive lung destruction and cicatrization
- Multiple cystic lung lesions
- Aspergilloma

Airway complications

- Bronchiectasis
- Bronchiolitis obliterans
- Tracheobronchial stenosis
- Broncholithiasis

Vascular complications

- Pulmonary and bronchial arteritis and thrombosis
- Bronchial artery pseudoaneurysm
- Pulmonary artery pseudoaneurysm (Rasmussen aneurysm)

Mediastinal complications

- Esophagomediastinal fistula
- Esophagobronchial fistula
- Fibrosing mediastinitis
- Constrictive pericarditis

Pleural complications

- Pleurisy
- Empyema
- Fibrothorax
- Pneumothorax
- Bronchopleural fistula

Chest wall complications

- Osteomyelitis
 - Chondritis
 - Spondylitis
 - Empyema necessitatis
-

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