

Primary tuberculosis in a malnourished adolescent

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ABSTRACT

Although the overall prevalence of tuberculosis has decreased in the United States, with the increasing prevalence of tuberculosis globally, higher rates of tuberculosis in some states and localities have been reported, with some component probably related to immigrant populations. We report a case of primary pulmonary tuberculosis in a malnourished adolescent.

CASE REPORT

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A 16-year-old malnourished male with coughing and wheezing was admitted to the hospital under guardianship of child protective services for concern for malnutrition and history of excessive weight loss over 6 months. Postero-anterior and lateral chest radiographs (Fig. 1) showed diffuse reticular nodular opacities bilaterally. Additionally, there were superimposed consolidative opacities involving the upper lobes with cavitory lesions. The left perihilar and right paratracheal lymph nodes were enlarged. Overall, the findings were suspicious for tuberculosis (TB). Given the extensive findings, CT imaging was performed for further evaluation.

Axial CT showed right upper lobe cavitation and diffuse reticulo-nodular and tree-in-bud opacities throughout the lungs bilaterally (Fig. 2). The lung apices also demonstrated consolidation (Fig. 3). Notably, paucity of subcutaneous fat was suspicious for cachexia. Overall findings were most consistent with active primary TB. Patient's sputum later confirmed mycobacterium tuberculosis by DNA hybridization and detection of acid-fast bacilli (Fig. 4). Patient was started on standard regime of medications for treatment of tuberculosis including ethambutol, isoniazid, pyridoxine, pyrazinamide, and rifampin. Patient continues to be compliant on medications without complications.

DISCUSSION

Tuberculosis remains a common worldwide infection causing significant morbidity and mortality, especially in developing nations [1]. Due to effective treatment and public health measures, industrialized countries have an average annual incidence of 23 per 100,000, accounting for only 4% of total notified cases worldwide [1,2]. In developed countries, the majority of TB cases result from reactivation of a latent infection, with the highest disease rates in the elderly (age > 65) [1]. Active disease in younger individuals usually arises among racial and ethnic minorities, or in association with conditions that compromise host immunity (HIV infection, malnutrition, drug and alcohol abuse, co-existent medical conditions, corticosteroid or other immunosuppressive therapy) [1]. The prevalence of infection does not show a gender predilection until adolescence, where twice as many males are reported to have TB [3]. Primary TB progresses to active disease within one year of infection in approximately 5% of individuals [1]. With the advent of multidrug-resistant (MDR) and extensively drug-resistant TB, prompt diagnosis is especially crucial for both public health infection control measures, as well as ensuring appropriate patient management [4].

Radiologic diagnosis of TB allows for early intervention in infected patients, as acid-fast bacilli are found in the sputum of only a limited number of patients (20-55%) with active pulmonary TB, and definitive diagnosis via culture takes a

minimum of ten days [4,5,6]. Chest radiography is the primary imaging modality to evaluate TB, while CT serves to bolster the diagnosis, especially when radiographic findings are unequivocal [7]. Clinical and radiologic features of primary and postprimary (reactivation) TB can overlap, complicating diagnosis between the subtypes [2]. Furthermore, some recent studies using genotyping methods for *M. tuberculosis* have challenged the notion that clinical, pathologic, and radiologic manifestations of primary and postprimary TB are unique, emphasizing that the only independent predictor of the radiographic presentation may be the host immune response status [4,5]. In this discussion, we divide imaging findings in the classic fashion for ease of review, but emphasize that findings historically associated with primary or postprimary disease may overlap significantly.

On radiologic examination, primary TB can be subdivided into four basic manifestations: parenchymal disease, lymphadenopathy, miliary disease, and pleural effusion [2]. Parenchymal disease, consisting of granulomatous inflammation, manifests as airspace consolidation and shows no predilection for any particular lobe [2,4]. It is usually unilateral, and is present in approximately 70% of children with primary TB [4]. Of note, chest radiographs appear normal in 15% of patients with proven primary TB [7]. CT can detect subtle foci of primary infection that may be indistinguishable on plain radiograph [7]. The primary parenchymal focus will resolve without radiographic sequelae in approximately two-thirds of cases, or scar and calcify in 15% of the remaining cases, resulting in an entity termed the Ghon focus [2]. Tuberculomas are persistent mass-like opacities that are seen in approximately 9% of cases [2].

Lymphadenopathy (LAD) on radiologic exam is seen in up to 96% of children and 43% of adults, and is uncommon in postprimary TB [2,4]. This finding represents tubercle bacilli spread to regional hilar and mediastinal lymph nodes, and is usually unilateral and right sided, with hilar and paratracheal involvement [1,2]. One-third of cases have bilateral involvement [2]. CT has improved sensitivity for detecting LAD and has the added benefit of judging the activity of disease [2, 7]. Nodes greater than 2 cm in diameter (short axis) are highly suggestive of active disease, and typically show central low attenuation representing caseous necrosis [2,4]. The combination of calcified hilar lymph nodes and a Ghon focus is termed a Ranke complex, and suggests previous TB [2,4].

Clinically significant miliary disease affects between 1%-7% of patients with TB, and may arise during either primary or postprimary stages of disease [1,2]. Miliary spread occurs when a collection of tubercle bacilli enter into a blood or lymph vessel and spread to distant capillary beds in various organs before an adequate immune response to the bacilli is mounted [1]. The lung is most commonly affected [1]. Conventional radiography appears normal at the onset of symptoms, and may take up to six weeks to become apparent [1, 7]. CT becomes crucial in this regard, as it may help in earlier detection of miliary TB [7]. Characteristic CT findings demonstrate countless, 1- to 3-mm diameter nodules scattered throughout both lungs [4]. Each of these foci represents a local

granulomatous response consisting of a necrotic center with palisading epithelioid histiocytes and fibrous tissue [4]. Other findings include thickening of interlobular septa, as well as diffuse or localized ground-glass opacities, which may forewarn of acute respiratory distress syndrome [4].

Pleural effusion occurs in one-fourth of patients with proven primary TB, and usually manifests 3-7 months after initial exposure [2]. Effusions are generally unilateral, and complications such as empyema formation and fistulization are rare [2]. This finding is uncommon in infants, but is a common finding in children [2,8]. Pleural effusions are seen in approximately 18% of cases of postprimary TB, and are generally small effusions associated with parenchymal disease [2].

As aforementioned, features of primary and postprimary TB can overlap [2]. However, findings classically associated with postprimary TB include an affinity for the upper lobes, cavitation, and absence of LAD [2]. Multiple cavities are common, and are imposed upon an area of consolidation. Air-fluid levels should raise suspicion of anaerobic or gram negative superinfection [7]. Endobronchial spread is the most common means of spread in postprimary TB, and results in tree-in-bud opacities on CT. These findings appear as branching linear and nodular opacities which mimic a branching tree, with buds at tips of the branches [2,4]. Both cavitation and the tree-in-bud sign are signs of an active disease process [4]. It is important to re-emphasize that while these signs are commonly seen in postprimary TB, they can be signs of active primary disease, as demonstrated in this case report. Indeed, a recent study has reported upper lobe nodules, consolidation, and/or cavitory lesions among the most commonly encountered findings in previously healthy high-school students with primary TB [8].

The differential diagnosis for TB includes: necrotizing (bacterial) pneumonia; cryptococcal pneumonia; disseminated histoplasmosis, aspergillosis; Wegener's granulomatosis; and sarcoidosis. Necrotizing pneumonia is less likely in the absence of a parapneumonic effusion/empyema [9]. Wegener's granulomatosis may be associated with renal or upper respiratory and sinus symptoms, with radiographic findings including bilateral, randomly distributed nodules, cavitation (50% of cases), diffuse ground-glass opacities (50%) and CT halo and atoll signs [10]. Cryptococcal pneumonia findings include nodular opacities, consolidation, interstitial pattern, cavitation, lymphadenopathy, and pleural effusion [9]. Potential findings of acute histoplasmosis include scattered patchy or diffuse interstitial opacities, a solitary pulmonary nodule, miliary pattern, hilar or mediastinal lymphadenopathy, and with chronic cases, cavitation [9]. Radiographic signs of invasive aspergillosis may include macronodules, consolidation, halo sign, air-crescent sign, and cavitation [11,12]. Cryptococcal pneumonia, disseminated histoplasmosis and aspergilliosis should be considered if there is appropriate clinical history, as radiographic signs may overlap. Sarcoidosis imaging findings include hilar and/or mediastinal LAD, pulmonary infiltrates with upper lobe predominance, and characteristic CT findings of granulomas distributed along lymphatic vessels, as evidenced by multiple

small nodules in a perivascular distribution, with irregular thickening of bronchovascular bundles and interlobular septa [13].

Management of TB requires long-term, multiple drug therapy that is divided into an initial intensive phase designed to kill actively growing and semi-dormant bacilli, as well as a continuation phase. Monotherapy should never be attempted, nor should a single drug be added to a failing regimen. The initial intensive phase requires the two bactericidal drugs isoniazid and rifampin for nine months, but pyrazinamide and ethambutol may be considered as additional therapy. Treatment of suspected or confirmed cases of drug-resistant disease is more aggressive, with current guidelines recommending three to four oral drugs plus one injectable drug for 3-6 months, followed by at least three effective oral drugs for 15-18 months [14]. Recent pooled estimates of mortality due to TB indicate a 9% mortality rate and 3% mortality rate for HIV positive and HIV negative patients, respectively. However, due to variable study follow-up times, a time period was not established for these percentages. All-cause mortality during TB treatment equaled 18.8% and 3.5% in HIV positive, and HIV negative individuals respectively [15].

TEACHING POINT

It is essential to maintain a high index of suspicion for primary tuberculosis in the adolescent and adult population to facilitate early diagnosis, especially in immunocompromised individuals. Host immune response status may be a better predictor of radiographic findings than classification by primary and postprimary tuberculosis, since radiographic features such as cavitation, ground-glass opacities, and tree-in bud sign may be present in either manifestation of disease.

REFERENCES

1. Leung AN. Pulmonary tuberculosis: The essentials. *Radiology* 1999;210:307-322. PMID:10207408
2. Burrill J, Williams CJ, Bain G, Conder G, Hine AL, Misra, RR. Tuberculosis: A radiologic review. *RadioGraphics*. 2007;27:1255-1273. PMID:17848689.
3. Connolly M, Nunn P. Women and tuberculosis. *World Health Stat Q*. 1996;49(2):115-9. PMID:9050189
4. Jeong YJ, Lee KY. Pulmonary tuberculosis: Up-to-date imaging and management. *AJR*. 2008; 191:834-844. PMID:18716117.
5. Badak FZ, Kiska DL, Setterquist S, Hartley C, O'Connell MA, Hopfer RL. Comparison of mycobacteria growth indicator tube with BACTEC 460 for detection and recovery of mycobacteria from clinical specimens. *J Clin Microbiol*. 1996;34(9):2236-9. PMID:8862591.

6. Lee KS, Im JG. CT in adults with tuberculosis of the chest: characteristic findings and role in management. *AJR*. 1995; 164(6):1361-1367. PMID:7754873
7. Beigelman C, Sellami D, Brauner M. CT of parenchymal and bronchial tuberculosis. *Eur. Radiology*. 2000;10:699-709. PMID:10823618.
8. Koh WJ, Jeong YJ, Kwon OJ, Kim HJ, Cho EH, Lew WJ, Lee KS. Chest radiographic findings in primary pulmonary tuberculosis: observations from high school outbreaks. *Korean J Radiol*. 2010;11:612-617. PMID:21076586.
9. Gadkowski LB, Stout JE. Cavitory pulmonary disease. *Clin Microbiol Rev*. 2008 Apr;21(2):305-33. PMID: 18400799
10. Martinez F, Chung JH, Digumarthy SR, et al. Common and Uncommon Manifestations of Wegener Granulomatosis at Chest CT: Radiologic-Pathologic Correlation. *Radiographics*. 2012 Jan;32(1):51-69. PMID: 22236893.
11. Kuhlman JE, Fishman EK, Siegelman SS. Invasive pulmonary aspergillosis in acute leukemia: characteristic findings on CT, the CT halo sign, and the role of CT in early diagnosis. *Radiology*. 1985 Dec;157(3):611-4. PMID: 3864189.
12. Kuhlman JE, Fishman EK, Burch PA, Karp JE, Zerhouni EA, Siegelman SS. CT of invasive pulmonary aspergillosis. *AJR Am J Roentgenol*. 1988 May;150(5):1015-20. PMID: 3258702.
13. Koyama T, Ueda H, Togashi K, Umeoka S, Kataoka M, Nagai S. Radiologic manifestations of sarcoidosis in various organs. *Radiographics*. 2004;24(1):87-104. PMID:14730039
14. Lawn SD, Zumla AI. Tuberculosis. *Lancet*. 2011;378(9785):57-72. PMID:21420161
15. Straetemans M, Glaziou P, Bierrenbach AL, Sismanidis C, van der Werf MJ. Assessing tuberculosis case fatality ratio: a meta-analysis. *PLoS One*. 2011;6(6):e20755. Epub 2011 Jun 27. PMID:21738585

FIGURES

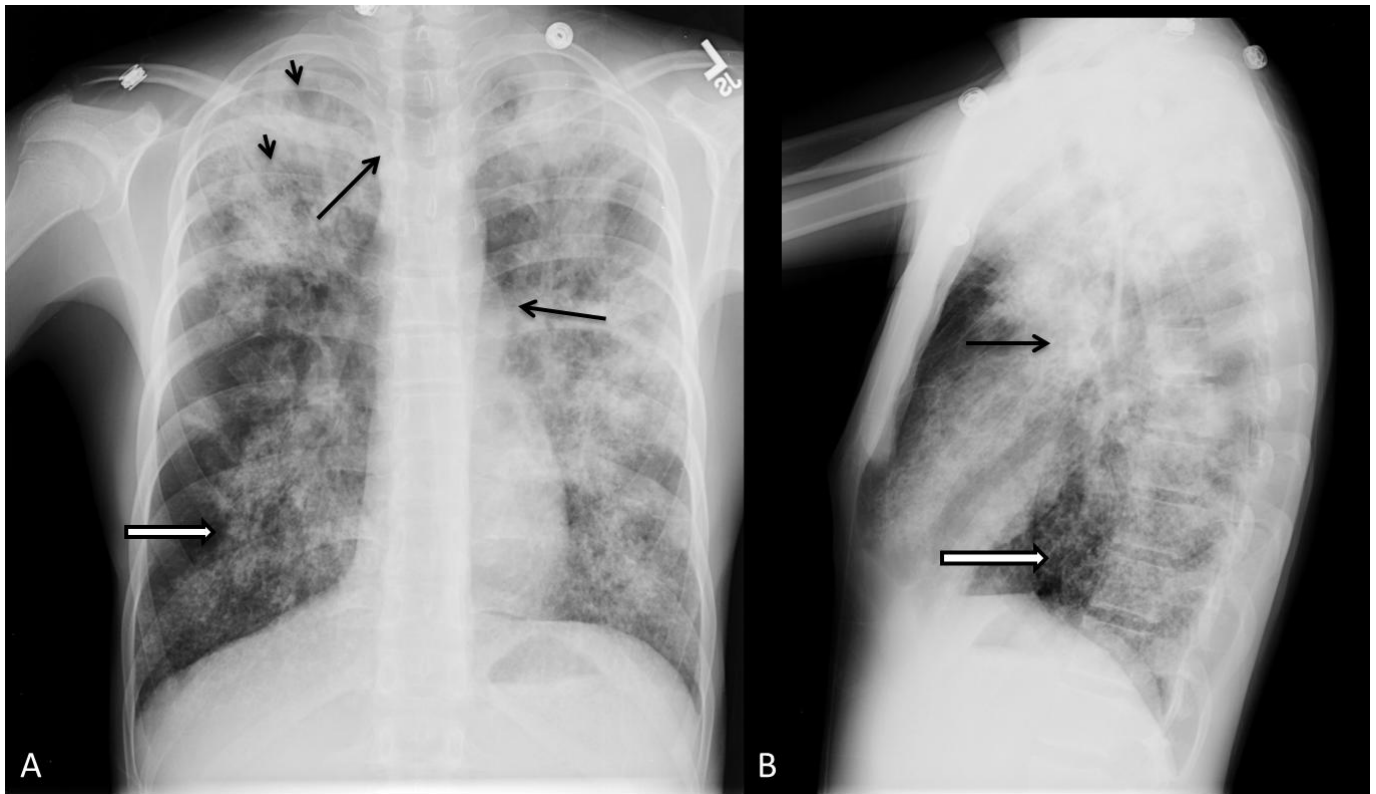


Figure 1: 16 year old male with primary active tuberculosis. Posteroanterior and lateral chest radiographs: Diffuse interstitial and nodular pattern seen throughout both lung fields (white arrows). Paratracheal (Fig 1A) and left perihilar lymphadenopathy (Fig 1 A,B) is seen (long arrows). Focal areas of lucency projecting over the right upper lung indicate areas of cavitation (short arrows, Fig 1A).

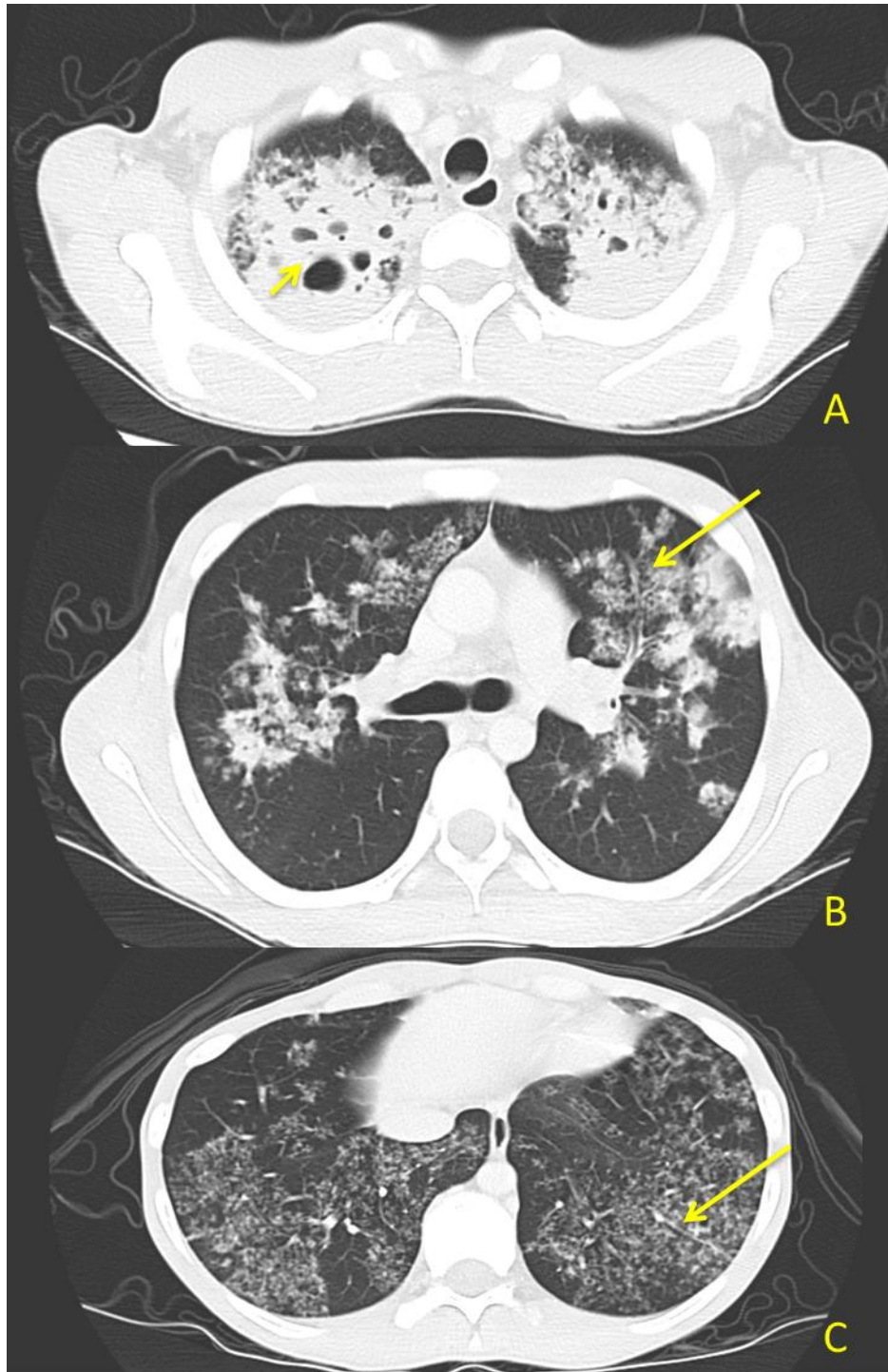


Figure 2: 16 year old male with primary active tuberculosis. Contrast enhanced axial chest CT shows right upper lobe cavitation (short arrow). Consolidation and mild bronchiectasis is notable in bilateral lung apices. Diffuse tree-in-bud opacities as well as centrilobular nodules are observed in the lower lobes (long arrows). (Protocol: GE Lightspeed VCT 64 slice, kVp 120, mAS variable, 5mm slice thickness, 91cc Optiray 320)

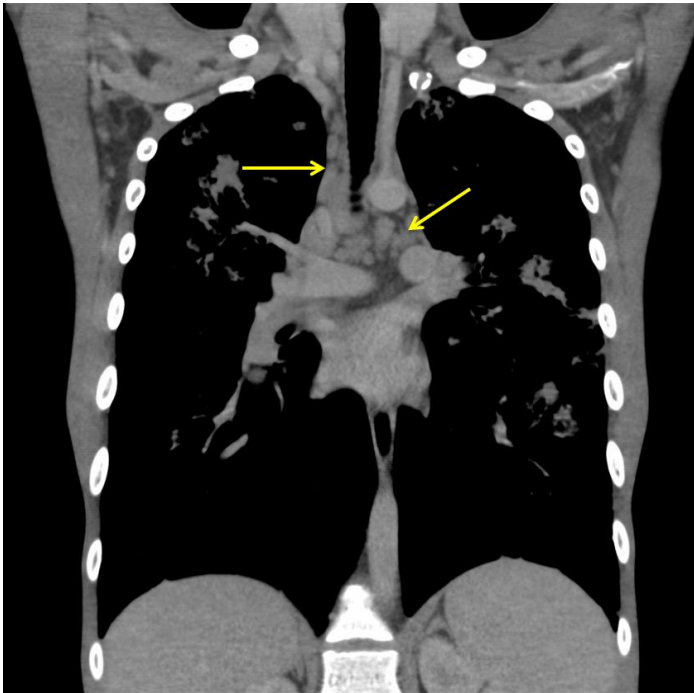


Figure 3 (left): 16 year old male with primary active tuberculosis. Contrast enhanced coronal CT shows paratracheal and perihilar lymphadenopathy (arrows). There is a notable paucity of subcutaneous fat, consistent with a cachectic state. (Protocol: GE Lightspeed VCT 64 slice, kVp 120, mAS variable, 5mm slice thickness, 91cc Optiray 320)

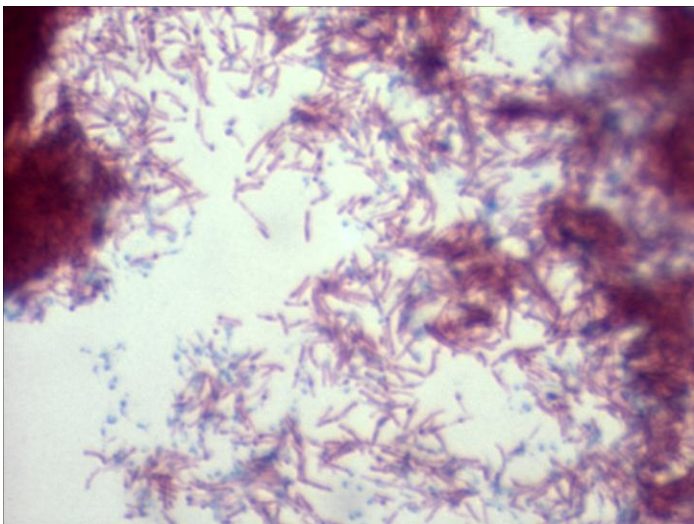


Figure 4 (left): 16 year old male with primary active tuberculosis. Ziehl-Neelsen stain of sputum showing acid-fast bacilli. Patient's sputum later confirmed mycobacterium tuberculosis by DNA hybridization and detection of acid-fast bacilli.

Etiology	<i>Mycobacterium tuberculosis</i> infection	
Incidence	Average estimate of 23 per 100,000 in developed nations	
Gender ratio	Male:female 1:1 up to, but not including adolescence. Adolescence/post-adolescence 2:1	
Age predilection	Elderly (age ≥ 65)	
Risk factors	Age ≥ 65; Racial or ethnic minority; Immunocompromised state (HIV/AIDS, malnutrition, drug and alcohol abuse, coexistent medical conditions, corticosteroid or other immunosuppressive therapy)	
Treatment	Multi-drug regimen: Non-drug resistant – Requires Rifampin and Isoniazid for nine months if used without additional therapy. Drug-resistant – Three or more oral drugs + injectable for 3-6 months, followed by at least three oral drugs for 15-18 months.	
Prognosis	Mortality due to TB (unspecified time to follow up): HIV(+) 9%; HIV(-) 3% All-cause mortality during TB treatment: HIV(+) 18.8%; HIV(-) 3.5%	
Findings on imaging	<i>X-ray</i>	<i>CT</i>
	Airspace consolidation, Ghon focus, Ranke complex, paratracheal & perihilar lymphadenopathy, pleural effusion, cavitation	Airspace consolidation, Ghon focus, Ranke complex, paratracheal & perihilar lymphadenopathy, pleural effusion, cavitation, ground-glass opacities, tree-in bud sign

Table 1: Summary table for tuberculosis

	X-ray	CT
<i>M. Tuberculosis</i>	Airspace consolidation, Ghon focus, Ranke complex, paratracheal & perihilar lymphadenopathy, pleural effusion, cavitation	Airspace consolidation, Ghon focus, Ranke complex, paratracheal & perihilar lymphadenopathy, pleural effusion, cavitation, ground-glass opacities, tree-in bud sign
Invasive Aspergillosis	Macronodules, consolidation, halo sign, air-crescent sign, cavitation	Macronodules, wedge-shaped segmental consolidation, CT halo sign, cavitation, organizing mass on late scans
Disseminated Histoplasmosis	Acute: scattered patchy or diffuse interstitial opacities, solitary pulmonary nodule, miliary pattern, hilar or mediastinal lymphadenopathy; Chronic: cavitation	Miliary pattern of 1-3 mm nodules; enlarged lymph nodes with central necrosis
Cryptococcal pneumonia	Cryptococcoma (solitary or multiple nodules), alveolar consolidation, interstitial pattern, cavitation, lymphadenopathy, pleural effusion	Cryptococcoma (solitary or multiple nodules), alveolar consolidation, interstitial pattern, cavitation, lymphadenopathy, pleural effusion
Necrotizing pneumonia	Consider if presence of parapneumonic effusion/empyema.	Consider if presence of parapneumonic effusion/empyema.
Wegener’s granulomatosis	Nodules with possible hemorrhage or cavities with possible consolidation; subglottic stenosis	Multiple nodules (few mm up to 10 cm), usually bilateral and random. Cavitation seen in up to 50% of lesions >2 cm. CT halo and atoll signs. Diffuse ground-glass opacity and consolidation in 50% of subjects.
Sarcoidosis	Bilateral hilar and/or mediastinal LAD. Pulmonary infiltrates with upper lobe predominance.	Granulomas characteristically distributed along lymphatic vessels, demonstrating multiple small nodules in a perivascular distribution, with irregular thickening of bronchovascular bundles and interlobular septa. Upper lobe predominance. Co-existing hilar and/or mediastinal LAD.

Table 2: Differential table for tuberculosis

Findings	Primary TB	Postprimary TB
Airspace consolidation	Common (70% of children). No lobe predilection	Common. Upper lobe predilection
Cavitation	Not uncommon, but classically associated with postprimary TB (indicates active disease)	Common (indicates active disease)
Lymphadenopathy	96% of children. 43% of adults.	Characteristically absent
Miliary disease	Potential complication (1-7% of all patients with TB)	Potential complication (1-7% of all patients with TB)
Pleural effusion	Common in children. Uncommon in infants. Generally unilateral	Less common than in primary TB. Generally small effusions associated with parenchymal disease.
Tree-in-bud opacities	Less common, more characteristic of postprimary TB (indicates active disease)	Common (indicates active disease)

Table 3: Primary vs. Postprimary TB Imaging Findings

ABBREVIATIONS

CT = computed tomography
 LAD = lymphadenopathy
 MDR = multidrug-resistant
 TB = tuberculosis

KEYWORDS

Tuberculosis; Primary Tuberculosis

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