The Radiographic Appearance of Pulmonary Tuberculosis

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Patients History
A clinic in rural Haiti

- CM, a 34-year-old male Haitian peasant farmer p/w 2 months of fever, night sweats, fatigue, weight loss, and 2 episodes of hemoptysis
- CXR was obtained
CXR revealed a RUL infiltrate with three right perihilar cavitary lesions.
DDx of upper lobe infiltrates and cavitation:

- Tuberculosis
- Atypical mycobacteria
- Sarcoidosis
- Silicosis
- Wegner’s granulomatosis
- Collagen vascular disease
- Adenosquamous cancer
- Lymphoma (esp. Hodgkin’s)
- Actinomycosis
- Histoplasmosis

Source: Clinic Bon Sauveur, Cange, Haiti
Sputum microscopy revealed numerous acid-fast bacilli

Pt started on a four drug anti-tuberculous regimen (INH, RIF, PZA, ETH)
## Symptoms of Pulmonary TB

<table>
<thead>
<tr>
<th>Respiratory</th>
<th>Constitutional</th>
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</thead>
<tbody>
<tr>
<td>Cough (initially dry, later productive)</td>
<td>Malaise</td>
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<tr>
<td>Chest pain</td>
<td>Lassitude</td>
</tr>
<tr>
<td>Hemoptysis (sparse early, heavy w/ cavitation)</td>
<td>Fever</td>
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<tr>
<td>Shortness of breath</td>
<td>Sweats</td>
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<td></td>
<td>Anorexia</td>
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</table>
Diagnosis

- **Smear microscopy**
  - Ziehl-Neelsen
  - Kinyoun
  - Rhodamine auramine

- **Culture**
  - Can take up to six weeks to identify positive cultures (TB doubling time is 15-24 hours)

- **Chest radiography**
  - Suggestive, not diagnostic

- **Bronchoscopy**

- **Tuberculin skin testing**
  - Does not differentiate latent infection or BCG vaccination from active disease
Histopathology

Ziehl Neelsen smear of acid fast
*Mycobacterium tuberculosis*

Culture of *Mycobacterium tuberculosis* on Lowenstein-Jensen medium

Note: *Mycobacterium tuberculosis* is an aerobic, acid-fast Gram positive rod

Small PM, Fujiwara PI. *NEJM* 2001; 189-200, p. 191.

Epidemiology

- One third of the world’s population—two billion people—is infected with the tubercle bacillus
- Eight million people per year develop active disease
- Two million deaths per year are attributable to *M. tuberculosis*
- Tuberculosis remains the world’s leading infectious cause of adult mortality
- Estimates for the next 20 years include one billion new infections, 200 million with active disease, and 35 million deaths
Global Incidence of Tuberculosis, 1997

Estimated tuberculosis incidence rates, 1997

Reported TB Cases
United States, 1953 - 1998

*Change in case definition

Transmission and Pathogenesis

- Tuberculosis is an airborne infection spread by droplet nuclei (5-10µm)
- When inhaled, droplet nuclei are deposited in terminal airspaces of the lung
- Macrophages ingest the bacilli and transport them to regional lymph nodes
- Further dissemination occurs via lymphohematogenous routes to other parts of the lungs and extrapulmonary sites

Inhalation and deposition of the tubercle bacillus leads to one of three possible outcomes:

- Immediate clearance of the organism
- Primary disease
- Active disease many years after initial infection (post-primary disease)
Transmission of Tuberculosis and Progression of Latent Infection

Small PM, Fujiwara PI. NEJM 2001; 189-200, p. 192.
Primary Tuberculosis

- Most often a childhood infection in endemic settings
- Few clinical symptoms in immunocompetent hosts
- Lymphangitic spread to hilar and paratracheal nodes result in enlargement of these structures
- Often the only residua of primary infection is a positive skin test and the Ranke complex
- Primary progressive tuberculosis occurs in a minority of cases
## The natural history of primary tuberculosis in adults

<table>
<thead>
<tr>
<th>Event</th>
<th>Time</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar deposition of tubercle bacilli</td>
<td>0</td>
<td>Bacilli engulfed by alveolar macrophage</td>
</tr>
<tr>
<td>Bacilli proliferate and disseminate</td>
<td>3-8 weeks</td>
<td>Tuberculin skin test becomes reactive; chest x-ray may become abnormal</td>
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<tr>
<td>Some patients develop pleurisy; A minority develop miliary disease</td>
<td>8-26 weeks</td>
<td></td>
</tr>
<tr>
<td>High-risk period for pulmonary and Extrapulmonary disease</td>
<td>26-156 weeks</td>
<td>10% infected will develop TB</td>
</tr>
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Iseman MD. *A clinical guide to tuberculosis*, 1999, p. 130
**Primary Tuberculosis**

- **Lymphadenopathy** is the hallmark of primary disease in childhood, seen in up to 90% of cases.
- Usually affects the hilum and right paratracheal regions.
- Bilateral adenopathy occurs in one third of cases.
- Adenopathy usually seen in association with parenchymal consolidation or atelectasis.
- Lymphadenopathy can be the only manifestation of TB in young children.
- Adenopathy resolves slowly, and nodal calcification may occur six months after the initial infection.
- Pleural effusion may occur in a minority of cases.

Source: Dr. Seymor Shalek, BIDMC
Radiographic Residuals of Primary Infection

Primary Tuberculosis

Ranke’s Complex

Simon Foci


Source: Clinic Bon Sauveur, Cange, Haiti
Post-Primary Tuberculosis

- Post-primary TB represents 90 percent of adult cases in the non-HIV-infected population
- Results from reactivation of a previously dormant focus seeded at the time of primary infection
- Apical-posterior segments of the upper lobes (80 to 90 percent of patients), followed in frequency by the superior segment of the lower lobes and the anterior segment of the upper lobes
- The original site of spread is occasionally associated with Simon foci—residual uni- or bilateral apical fibronodular shadows from primary infection
- Post-primary disease also known as reactivation TB, recrudescent TB, chronic TB, endogenous reinfection, and adult type progressive TB
Post-Primary Tuberculosis

The radiographic appearance of post-primary disease can include:

- Upper lobe infiltrates
- Cavitary lesions
- Tuberculomas
- Absence of lymphadenopathy
- Complete lobar or lung opacification and lobar collapse in severe cases
- Complications, including effusion, empyema, bronchiectasis, mililiary pattern, and spontaneous pneumothorax
Post-Primary Tuberculosis

Post-Primary Tuberculosis

Bilateral upper lobe involvement seen in this patient with post-primary disease

Advanced post-primary tuberculosis in an immunocompetent host

Source: Dr. Seymor Shalek, BIDMC

Source: Clinic Bon Sauveur, Cange, Haiti
Cavitary Disease

- A characteristic finding of post-primary disease
- Cavitation implies a high bacillary burden and high infectivity
- Cavity size ranges from a few mm to several cm
- Variable wall thickness
- Air fluid levels rare, and may be an indication of bacterial or fungal superinfection
Cavitary Disease

Source: Socios en Salud, Lima, Peru
Pathology

- Gross specimen of upper lobe cavitary disease and endobronchial spread to both upper and lower lobes
- Infected bronchi appear as small, pale nodules with a hyperemic border
Cavitary Disease

Source: Dr. Seymor Shalek, BIDMC

Source: Socios en Salud, Lima, Peru
Tuberculoma

- Single or multiple rounded, well-circumscribed, focal lesions
- Manifestation of primary or post-primary disease
- Easily mistaken for coin lesions or metastatic disease on chest radiograph
- Vary in size from a few millimeters to 5 or 6 cm in diameter but usually range from 1 to 3 cm.
- They may or may not contain calcium

Post-Primary Tuberculosis

Interval improvement of a 4 x 2 cm cavitary mass abutting the right hilum after 4 months of effective therapy
Role of CT in Pulmonary Tuberculosis

- Chest radiography remains the first choice of initial evaluation of patients with tuberculosis
- CT may be helpful in the patients who initially present with a normal chest radiograph and high suspicion of active disease
- Various patterns of primary and post-primary disease may necessitate CT as a diagnostic tool in pulmonary tuberculosis
- CT facilitates differentiation of pulmonary tuberculosis from lung cancer or other granulomatous lung disease
Role of CT in Pulmonary Tuberculosis

CT reveals 4 x 3 cm right hilar cavitary mass poorly seen on chest X-ray

Source: BIDMC
Complications of Post-Primary Tuberculosis

- Tuberculous effusion
- Tuberculous empyema
- Bronchostenosis
- Broncholithiasis
- Spontaneous pneumothorax
- Dissemination to other organs
Tuberculous effusion

Pre-thoracentesis

Post-thoracentesis

Source: Clinic Bon Sauveur, Cange, Haiti
Spontaneous pneumothorax

End-inspiration

Source: Dr. Seymour Shalek, BIDMC

End-expiration

Source: Dr. Seymour Shalek, BIDMC
Miliary Tuberculosis

- Results from hematogenous dissemination of tubercle bacilli
- Seen in both primary and post-primary disease
- Occurs more frequently in young children and immunocompromised patients

Source: Brigham and Women’s Hospital, Boston, Massachusetts
Miliary Tuberculosis

- Characteristic radiographic appearance is a faint reticulonodular pattern consisting of widespread nodular opacities measuring 2-3 mm in diameter scattered diffusely throughout both lungs
- Associated lymphadenopathy seen in 95% of children, 12% of adults

Source: Dr. Seymor Shalek, BIDMC
Differential of a miliary pattern on chest radiograph or CT:

- Miliary tuberculosis
- Atypical mycobacteria
- Disseminated fungal infection (blastomycosis, histoplasmosis, etc.)
- Metastatic neoplastic disease
- Disseminated viral infection (varicella, CMV, etc.)
- Bacterial (nocardia, tuleremia, brucellosis, staphylococcus, streptococcus, etc.)
- Schistosomiasis
- Pneumoconioses
- Sarcoidosis
- Hypersensitivity pneumonitis

Source: Brigham and Women’s Hospital, Boston, Massachusetts
Miliary Tuberculosis

Millet seeds, after which the disease was named. The size of the seeds correspond to the size of the lesions seen on chest radiograph.

Gross specimen of lung demonstrating the diffuse nature of miliary disease.
Challenge Patient

61-year-old female Haitian peasant with cough, SOB, and significant weight loss over 4 months

What is the cause for the miliary pattern?

Source: Clinic Bon Sauveur, Cange, Haiti
There is a differential:

DDX:
- Miliary TB
- Sarcoidosis
- Metastatic Disease
- Diffuse fungal infection
**S/p left mastectomy for breast CA**

DDX:
- Miliary TB
- Sarcoidosis
- Metastatic Disease
- Diffuse fungal infection

Absent left breast shadow

Source: Clinic Bon Sauveur, Cange, Haiti
Other causes of Miliary patterns:

Varicella pneumonia is also part of the differential for a miliary pattern on chest radiograph.

In immunocompromised patients, one must rule out Pneumocystis carinii pneumonia as a potential etiology of a miliary pattern on chest radiograph.
## Radiographic findings for patients with pulmonary TB, according to HIV status

<table>
<thead>
<tr>
<th>Finding</th>
<th>HIV-positive (n=72)</th>
<th>HIV-negative (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal infiltrate</td>
<td>38 (53%)</td>
<td>46 (89%)</td>
</tr>
<tr>
<td>Upper-lobe infiltrate</td>
<td>19 (26%)</td>
<td>32 (62%)</td>
</tr>
<tr>
<td>One or more cavities</td>
<td>5 (7%)</td>
<td>23 (44%)</td>
</tr>
<tr>
<td>Hilar or mediastinal lymphadenopathy</td>
<td>28 (39%)</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Normal</td>
<td>8 (11%)</td>
<td>3 (6%)</td>
</tr>
</tbody>
</table>

Radiological features of pulmonary TB in 963 HIV-infected adults compared to 1000 HIV-negative adults with TB

<table>
<thead>
<tr>
<th>Radiological feature</th>
<th>HIV-positive (n=963)</th>
<th>HIV-negative (n=1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavitation</td>
<td>319 (33%)</td>
<td>784 (78%)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>253 (26%)</td>
<td>131 (13%)</td>
</tr>
<tr>
<td>Pleural effusions</td>
<td>159 (16%)</td>
<td>68 (7%)</td>
</tr>
<tr>
<td>Miliary pattern</td>
<td>94 (9.8%)</td>
<td>52 (5%)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>112 (12%)</td>
<td>237 (24%)</td>
</tr>
<tr>
<td>Consolidation</td>
<td>94 (10%)</td>
<td>32 (3%)</td>
</tr>
<tr>
<td>Interstitial changes</td>
<td>120 (12%)</td>
<td>68 (7%)</td>
</tr>
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Summary

- Pulmonary tuberculosis is a disease with protean, non-specific symptoms, but often associated with fever, weight loss, cough, night sweats, and hemoptysis
- *M. Tuberculosis* is the world’s leading infectious cause of adult mortality, with two billion infected worldwide
- Tuberculosis is an airborne infection
- After initial infection, one can develop primary TB, latent TB, or post-primary TB
- Primary TB characterized radiographically by lymphadenopathy
- Post-primary TB characterized radiographically by upper lobe infiltrates, cavitary lesions, and tuberculomas
- Although chest radiography is indicated when TB is suspected, CT can aid in the diagnosis
- Miliary TB, which can be secondary to primary or post-primary disease, is characterized by faint reticulonodular pattern consisting of widespread nodular opacities measuring 2-3 mm in diameter scattered diffusely throughout both lungs
References

References

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- [http://pathhsw5m54.ucsf.edu/case32/image327.html](http://pathhsw5m54.ucsf.edu/case32/image327.html)
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