Extrapulmonary Tuberculosis

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No financial conflicts

Sites of Extrapulmonary TB
US 1993-2006

Clin Infect Dis 2009;49:1350-7
Lymph node TB (TB lymphadenitis)

- Classic presentation: Isolated chronic painless lymphadenopathy
- The overlying skin may be indurated
- Systemic symptoms are uncommon
- TB lymphadenitis in the cervical region is known as “scrofula”
- Intra-thoracic lymphadenitis usually occurs as a complication of primary TB

42 yo woman from Vietnam with a 6-week history of slowly enlarging lymph nodes.
Extrapulmonary Tuberculosis

TB lymphadenitis: Diagnosis

- AFB smear and culture AND histopathology of lymph node material
- Fine needle aspiration (FNA) is appropriate for initial evaluation of cervical lymphadenopathy (use a 21 to 23 gauge needle: micro and cytology) → yield up to 80%
- Excisional lymph node biopsy when FNA is not diagnostic, or other diagnosis is likely (e.g., lymphoma)
- Excisional biopsy is preferred over incisional biopsy (sinus tract formation)
Paradoxical reaction

- Increase in lymph node size and/or enlargement of additional lymph nodes in up to 20% of patients during or after discontinuation of TB treatment
- Most paradoxical reactions occur between 3 weeks and 4 months after initiation of treatment
- Repeat cultures are usually negative → it is not treatment failure

Paradoxical reaction

- DDx: treatment failure due to resistance or noncompliance, another infection, or an alternative diagnosis
- Management: observation, aspiration, surgical excision, or a trial of NSAIDs or corticosteroids
Pleural TB

- Early in the course of TB infection, a few organisms may gain access to the pleural space → hypersensitivity response → pleural effusion
- Symptoms:
  - Fever, pleuritic chest pain (“primary TB”)
  - If advanced, dyspnea
  - can be asymptomatic
- TST/IGRA: negative in > 20%

Pleural TB: pleural fluid analysis

- Exudate: lymphocyte-predominant
- Mesothelial cells: rare
- AFB smears almost always negative
- Culture positive in ~40% of cases
  - NAAT/PCR: close to culture results
- ADA (adenosine deaminase) level:
  - if very low, probably not TB (high sensitivity)
  - If high, can be TB, but low specificity
Pleural TB: pleural fluid analysis (Guidelines)

- NAAT should be measured (*conditional recommendation*, *very low-quality of evidence*: NAAT sensitivity 55%)
- ADA levels and free IFN-gamma levels should be measured (*conditional recommendation*, *low-quality of evidence*)
  - Sensitivity ~70%, specificity ~80%
  - Caution:
    - Neither ADA nor IFN-\(\gamma\) levels are standardized
    - Provide only supportive evidence

Sputum exam

- **With infiltrates**, AFB smears (+) in ~50%, and culture positive in ~90%
- **Without infiltrates**, sputum AFB smears are almost always negative, and culture positive in ~20%
Pleural TB: diagnosis

- Closed pleural biopsy
  - Culture (+) in 60-80%
  - Combination of culture and pathology establishes the Dx in 90-95% of cases
Miliary TB

- Pathology: lesions = yellowish granulomas 1 - 2 mm in diameter that resemble millet seeds

28 yo woman from Somalia with a 3-week history of dry cough, fever, and weight loss.

*Courtesy E. Stern, MD*
Extrapulmonary Tuberculosis

Hospitalized.
Sputum x 3: AFB smear all negative
BAL: smear and NAAT negative
Miliary TB

- Hematogenous dissemination
- Sputum smear positive in only 1/3
- Dx: obtain specimens from multiple sites (e.g., sputum, gastric aspirate, pleural fluid, ascites, urine) and mycobacterial blood cultures (lysis centrifugation techniques)
  - consider bronchoscopy
- Treatment duration: 6 months
  - Longer duration may be considered in children, immunocompromised, slow microbiologic or clinical response, CNS involvement

Skeletal TB (TB of the Bones and/or Joints)

- The most common form of skeletal TB
- TB of the spine (“Pott’s disease”)
  - From anterior aspect of the intervertebral joints → slowly reaches the adjacent vertebral body
  - Then, infection enters the intervertebral disc → vertebral narrowing and subsequent vertebral collapse → Gibbus deformity
- Sx: Pain. Systemic symptoms rare.
62 yo man from Ethiopia with back pain for a year presented with weakness of the legs → Emergent surgery

Pott’s disease

- Paravertebral “cold” abscess may be seen (e.g., psoas abscess)
- Surgical intervention (consult the orthopedic surgeon):
  - Partial paralysis of the legs due to a large abscess is a medical emergency and requires rapid drainage
  - Worsening neurological deficits despite treatment
  - Kyphosis >40 degrees at the time of presentation
Genitourinary TB

- Primarily involves the urinary collecting system (including renal pelvis, calyces, ureters, and bladder)
- Renal parenchymal lesions – less common
- Symptoms: urinary frequency, dysuria, hematuria, flank or abdominal pain (can be asymptomatic). Systemic symptoms rare.

Sterile pyuria

- AFB culture of 3 morning urine specimens → diagnostic in 90% of cases
- Genital TB: more common in female
  - The fallopian tubes and the endometrium
  - Sx: infertility, pelvic pain, menstrual abnormalities
  - Dx: biopsy or culture of specimens obtained by dilation and curettage
• 25 yo man from Mexico with 2 month history of fever, chills, night sweats, cough, and 10 lb wt loss
• Also dysuria with 3+ WBC and RBC

CNS TB

1. TB meningitis
2. Intracranial tuberculoma
3. Spinal TB arachnодitis
TB meningitis

- Sub-ependymal tubercle $\rightarrow$ rupture into the subarachnoid space $\rightarrow$ intense hypersensitivity reaction
- inflammatory changes are most marked at the base of the brain (a fibrous mass encases adjacent cranial nerves)
  - Paresis of cranial nerves common (esp. ocular nerves)

19 yo man from Guatemala had a fainting spell 2 weeks PTA, then developed progressive frontal headaches with nausea and emesis.

- Exam: T 39.6 Left fourth cranial nerve palsy
- MRI with leptomeningeal enhancement in left temporal lobe

- Lumber puncture:
  - CSF WBC 338, Lymph 60%, protein 136, glucose 32
  - CSF HSV negative
  - CSF TB PCR negative
CSF Characteristics

California Encephalitis Project

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<tr>
<th>Characteristic</th>
<th>CNS TB</th>
<th>HSV-1</th>
<th>Enterovirus</th>
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<tbody>
<tr>
<td>No. Cases</td>
<td>20</td>
<td>39</td>
<td>44</td>
</tr>
<tr>
<td>CSF leukocytes per ml, median</td>
<td>201</td>
<td>47</td>
<td>85</td>
</tr>
<tr>
<td>CSF protein, mg/dl, median</td>
<td>174</td>
<td>71</td>
<td>60</td>
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<tr>
<td>CSF glucose, mg/dl, median</td>
<td>35</td>
<td>69</td>
<td>67</td>
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- All 20 CNS TB cases: culture positive
- 4/17 (24%) CSF TB PCR positive

TB meningitis

- Vasculitis with resultant aneurysm, thrombosis, and infarction
- Communicating hydrocephalus – impaired CSF circulation/resorption
TB meningitis

- If highly suspected, immediate empiric Rx and serial LP daily x 3
- Repeated lumbar punctures should be considered to monitor changes in CSF cell count, glucose, and protein, especially early in the course of therapy
- > 50% of patients with TB meningitis have abnormal CXR (old or current TB process)

TB meningitis

- Paradoxical reaction in one-third of the patients
- Adjunctive corticosteroid therapy with dexamethasone or prednisolone tapered over 6–8 weeks
- Longer treatment (total 9 – 12 months)
- Drug penetration into CSF/CNS
  - Good: INH, PZA, ethionamide, cycloserine
  - Variable: RIF, aminoglycoside
  - Pediatrics: ethionamide or aminoglycoside as the 4th drug
**Intensified Therapy in TB Meningitis**


Randomized, double-blind, placebo controlled study in Vietnam

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<th>Standard Therapy</th>
<th>Intensified</th>
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<td>3 months of INH, PZA, EMB, Rifampin (10 mg /kg)</td>
<td>Additionally the first 8 weeks of Levo 20 mg/kg and ↑ Rifampin 15mg/kg</td>
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Followed by 6 months
INH and rifampin

All received dexamethasone for 6-8 weeks

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**Pericardial TB (TB pericarditis)**

- **Onset**: often subacute (can be acute)
- **Symptoms**: dyspnea, fever, dull retrosternal pain
- **Dx**: pericardiocentesis under echo guidance
  - **Effusion**: AFB smear rarely positive, culture positive in two-thirds of the cases
  - **Pericardial biopsy**: higher yield
TB pericarditis

- Even with treatment, complications may develop
  - Chronic constrictive pericarditis with thickening of the pericardium
  - Fibrosis with calcification (visible on a CXR)

TB Pericarditis and Steroids: Changing recommendations

Multicenter randomized study comparing prednisolone vs. placebo in 1400 adults with TB pericarditis

Primary endpoint: mortality, cardiac tamponade, or constrictive pericarditis

NEJM 2014;371:1121-30
TB pericarditis: treatment

- Treatment Duration: 6 months
- Adjunctive corticosteroids should not be used routinely.
- Selective use of glucocorticoids in patients who are at the highest risk for inflammatory complications
  - Large pericardial effusions
  - High levels of inflammatory cells or markers in pericardial fluid
  - Early signs of constriction

TB Peritonitis

- > 90% of patients with TB peritonitis have ascites at the time of presentation
- More advanced "dry" phase, representing a fibroadhesive form → “doughy abdomen”
- Symptoms: ascites, abdominal pain, fever
Peritoneal TB

- 59 yo man from China with a 4-month history of progressive abdominal distention and pain
  - Peritoneal fluid:
    - AFB smear rarely positive
    - Culture positive < 20% of cases
  - Laparoscopy with biopsy → the visceral and parietal peritoneum are studded with tubercles

Sputum collection for extrapulmonary TB cases

“Unexpected Pulmonary Involvement in Extrapulmonary TB Patients”

- ~5% of XPTB patients had positive sputum culture despite normal CXR findings and negative HIV
- Weight loss in XPTB patients was associated with positive sputum culture results

(Chest 2008;134:589)
Summary: Extrapulmonary TB

- Establish TB diagnosis by obtaining specimens
  - Empiric treatment without having AFB specimens should be discouraged.
- Evaluate for pulmonary disease. CXR should be obtained even if you are not suspecting concurrent pulmonary TB (and obtain sputum specimens if possible)