Perseverance by a Pervasive Disease (PPD)

Ramy Gorthi, MD (Associate)
Samaher Hashim, MD, Gregory T. Williams, MD

Departments of Medicine, Saint Vincent Hospital and the Reliant Medical Group, Worcester, MA
Chief Complaint

* Intermittent fever with night sweats, weight loss
* Chronic low back pain

H/O Present Illness

* 43 year old Brazilian gentleman presented with complaints of intermittent low grade fever and drenching night sweats for 8 months.

* Tmax: 101.4°F the night before admission.

* He also complained of lower lumbar pain for 3 months, non radiating, dull/aching, 6/10 intensity.
Review of Systems

* General – Positive for recurrent intermittent fevers with night sweats and significant weight loss of about 40 lbs.

* HEENT- Negative for headache, visual changes.

* Respiratory and CVS- Negative for dyspnea, cough, chest pain, palpitations.

* GI- Negative for abdominal pain, nausea, vomiting, bowel habit changes.

* Genitourinary- Negative for dysuria, hematuria, frequency or urgency.

* Neuro- Negative for weakness, numbness, paresthesias.

* Musculoskeletal- As per HPI. Negative for other arthralgias and myalgias.

* Skin- Negative for rash or ulcers.
Past Medical History

* Unremarkable.

Home Medications

* Acetaminophen PRN.

Family History

* Diabetes mellitus in father.

* Pulmonary TB in father-in-law in 1993 with positive history of exposure.
Social and Travel History

- Immigrated to the US 15 years ago at age 26.

- Last travel to Brazil (or anywhere out of the country) was 9 years ago.

- Lives with wife and son at home. Has a dog. Works in a logistics company.

- Denies history of smoking or alcohol use.

- Denies any form of recreational drug use.
Physical Examination

* General appearance: In no apparent acute distress.
* Vitals: 110/70 mmHg, pulse 108, RR 18, temp 97.7, 100% O2 on RA.
* HEENT: No lymphadenopathy. Neck supple.
* Respiratory: Clear to auscultation bilaterally.
* Cardiovascular: S1, S2 Regular rate and rhythm. No rubs, murmurs or gallops.
* GI: Soft, non tender. No organomegaly. Bowel sounds active.
* Musculoskeletal: No point tenderness along the spine. Gait normal. Limited forward flexion of the spine due to pain.
* Extremities: No skin changes. No splinter haemorrhages or needle tracks.
* Neurology: No focal neurological deficits or weakness.
Labs on Admission

<table>
<thead>
<tr>
<th>Value</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>134</td>
<td></td>
</tr>
<tr>
<td>98</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
</tr>
<tr>
<td>104</td>
<td></td>
</tr>
<tr>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td></td>
</tr>
<tr>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>9.3</td>
<td></td>
</tr>
</tbody>
</table>

- Bands = 35
- CRP = 32.7
- ESR = 20
Imaging on admission

Unremarkable CXR

Lytic lesion in the L4 vertebral body concerning for osteomyelitis.
MRI Lumbar spine showing findings consistent with osteomyelitis associated with epidural abscess in the L4-L5 region.
Course

- Laminotomy with decompression of epidural abscess and bone biopsy were done.

- Samples were negative for Gram stain, aerobic, anaerobic, fungal cultures, and smear for AFB and culture.

- In view of intermittent spikes in temperature and purulent nature of the decompressed abscess, patient was started on IV vancomycin until further microbiological data were obtained.

- Quantiferon gold: Positive.
CT Chest showing bilateral multiple nodules consistent with miliary pattern.
Course (cont)

* Patient was placed in a negative pressure room with droplet isolation precautions.

* He remained relatively asymptomatic with the exception of fevers.

* Bronchoscopy was done to obtain BAL samples and transbronchial biopsies.

* NAAT from BAL samples was negative for AFB.
Bronchial biopsy histopathology showed necrotizing granulomas with bacilli consistent with Mycobacterium.
Baseline LFTs were obtained.

Treatment with anti-TB medications – isoniazid, pyridoxine, rifampin, pyrazinamide, and ethambutol – was initiated. Within one week clinical improvement was achieved, without further febrile episodes.

Serology for Ehrlichia, Lyme, HIV, and smears for babesia, anaplasma were negative.
Miliary Tuberculosis

- All forms of progressive, widely disseminated hematogenous TB.
- Term coined from the radiologic appearance of millet seeds.
- The subacute or chronic presentations of miliary TB are more common than acute disease.
- The most common extrapulmonary sites of disease include the lymphatic system, bones and joints, and the liver.
- Patients may present with failure to thrive, fever of unknown origin, or dysfunction of one or more organ systems.
- Skeletal tuberculosis accounts for 10 to 35% of cases of extrapulmonary TB and, overall, 2.3% of all United States TB cases reported in 2013.
The most common form of skeletal TB is Pott’s disease followed by tuberculous arthritis.

Pott’s disease most commonly affects the lower thoracic and upper lumbar region.

Treatment of musculoskeletal tuberculosis consists of antimicrobial therapy.

For most patients receiving first-line agents, 6 to 9 months of therapy is sufficient. A longer duration of therapy (9 to 12 months) is warranted for patients on regimens that do not include rifampin and/or for patients with extensive or advanced disease, particularly if it is difficult to assess the response to therapy.

Surgical intervention is warranted for advanced neurological defects, worsening defects while on therapy.
Diagnosis of Tuberculosis

- Tuberculin skin test - supportive test.

- Acid-fast smear and culture - stains used are acid-fast fluorochrome dye, auramine-O, and Ziehl-Nielsen stain.

- Histopathology - showing necrotizing (caseating) granulomas.

- Molecular tests - NAAT
  - Amplified MTD test
  - Amplicor (Roche)
  - Xpert MTB/RIF assay-NAA plus rifampin resistance
  - PCR
# Frequency of positive smear or culture in patients with miliary tuberculosis

<table>
<thead>
<tr>
<th>Site</th>
<th>Maartens, 1990</th>
<th>Kim, 1990</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum smear</td>
<td>33*</td>
<td>36</td>
</tr>
<tr>
<td>Sputum culture</td>
<td>62</td>
<td>76</td>
</tr>
<tr>
<td>BAL smear</td>
<td>27</td>
<td>9</td>
</tr>
<tr>
<td>BAL culture</td>
<td>55</td>
<td>54</td>
</tr>
<tr>
<td>Gastric aspirate smear</td>
<td>43</td>
<td>0</td>
</tr>
<tr>
<td>Gastric aspirate culture</td>
<td>100</td>
<td>75</td>
</tr>
<tr>
<td>Urine smear</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Urine culture</td>
<td>33</td>
<td>59</td>
</tr>
<tr>
<td>CSF smear</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>CSF culture</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>Serosal smear</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Serosal culture</td>
<td>44*</td>
<td>14Δ</td>
</tr>
</tbody>
</table>
WHO Guidelines for TB Treatment

- **Pulmonary and Extrapulmonary TB are treated with the same drug regimens:**
- **2HRZE/4HR**
  - Isoniazid and Rifampicin for entire therapy course
  - First 2 months of therapy should also include 2 of these first-line drugs: pyrazinamide, ethambutol, or streptomycin
- **Duration of treatment varies by type:**
  - New pulmonary TB = 6 months
  - TB of bones or joints = 9 months
  - TB meningitis = 9-12 months
Tuberculin skin test

IGRA

Close contacts of patients with active pulmonary TB should undergo a second TST test 8 to 12 weeks later if the first test is negative.

Treatment of LTBI should be initiated only once active TB has been excluded.
## Treatment of Latent TB Infection

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Children &lt;12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Standard regimen:</td>
<td>Standard regimen:</td>
</tr>
<tr>
<td></td>
<td>300 mg PO daily for nine months</td>
<td>10 to 15 mg/kg PO daily for nine months; not to exceed 300 mg/day</td>
</tr>
<tr>
<td>Alternate regimens:</td>
<td>300 mg PO daily for six months</td>
<td>Alternate regimen:</td>
</tr>
<tr>
<td></td>
<td>900 mg PO twice weekly(^\Delta) for nine months</td>
<td>20 to 30 mg/kg PO twice weekly for nine months; not to exceed 900 mg/day</td>
</tr>
<tr>
<td></td>
<td>900 mg PO twice weekly(^\Delta) for six months</td>
<td></td>
</tr>
<tr>
<td><strong>Isoniazid and rifapentine</strong></td>
<td>Isoniazid (orally once weekly for 12 doses, given by direct observation)</td>
<td>(Further study needed)</td>
</tr>
<tr>
<td></td>
<td>15 mg/kg, rounded up to the nearest 50 or 100 mg; 900 mg maximum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifapentine (orally once weekly for three months, given by direct observation)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 to 14 kg: 300 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.1 to 25 kg: 450 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.1 to 32 kg: 600 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32.1 to 49.9 kg: 750 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;50 kg: 900 mg maximum</td>
<td></td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>600 mg PO daily for four months</td>
<td>10 to 20 mg/kg PO daily for four months; not to exceed 600 mg/day</td>
</tr>
<tr>
<td><strong>Isoniazid and rifampin(^\S)</strong></td>
<td>Isoniazid 300 mg PO daily for three months</td>
<td>Isoniazid 10 to 15 mg/kg PO daily for three months; not to exceed 300 mg/day</td>
</tr>
<tr>
<td></td>
<td>Rifampin 600 mg PO daily for three months</td>
<td>Rifampin 10 to 20 mg/kg PO daily for three months; not to exceed 600 mg/day</td>
</tr>
</tbody>
</table>
Thank You
Questions