Extra-pulmonary Tuberculosis

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Objectives

- How does TB spread beyond the lungs?
- How can TB present in these sites?
- How is extrapulmonary TB treated?

- DISCLOSURES: none
Figure 1 The spectrum of TB — from *Mycobacterium tuberculosis* infection to active (pulmonary) TB disease.
Indiana statistics 2013-2017

- Pleural 35 cases
- Lymphatic 33
- Bone/joint 21
- Genitourinary 13
- Peritoneal 11
- Meningeal 10
- Eye 9
- Pericardium 2

- 1 case of:
  - Bile duct
  - Small bowel
  - Stomach
  - Liver
  - Rectum
  - Salivary gland
  - Breast
A small number of tubercle bacilli enter bloodstream and spread throughout body

Is pleural TB considered extrapulmonary?

- Yes, in USA
- *No, in United Kingdom*
- Considerable overlap
- Pleural TB should have sputum examined
- Suspected pleural TB should be isolated until sputum carefully assessed
Respiratory Tuberculosis

- Active infection of lungs, pleural cavity, mediastinal lymph nodes or larynx
- British Royal College of Physicians, 2006

TB is difficult to diagnose
AFB studies of body fluids

- Pleural
- Pericardial
- Peritoneal
- Cerebrospinal
- Joint
- Urine
- Stool
- Menstrual blood
- Tissue

- AFB smear usually negative
- AFB cultures only 20-40%
- Fluids “exudative”
- PCR or NAAT?
Pleural fluid diagnosis

- pH > 7.3 usually
- Protein >4 grams
- Glucose <40 mg/mL
- WBC 300-5,000
- Lymphocyte predominance (wide range)

Pleural fluid biochemistry

- Adenosine deaminase (ADA) enzyme increased
- Inconsistent studies of ADA
Light’s Criteria

- According to Light's criteria (1972), a pleural effusion is likely exudative if at least one of the following exists:
  - The ratio of pleural fluid protein to serum protein is greater than 0.5
  - The ratio of pleural fluid LDH and serum LDH is greater than 0.6
  - Pleural fluid LDH is greater than 0.6 or $\frac{2}{3}$ times the normal upper limit for serum. Different laboratories have different values for the upper limit of serum LDH, but examples include 200 and 300 IU/l.
Patient 1

• Physical Exam:
  – 131.2 lb (baseline 167 lb) 99.6° F
  – Vision 20/25 in both eyes, color blind
  – Mild conjunctival injection Right eye
  – Dry crackles anteriorly, Right > Left
  – Right knee mildly boggy and swollen, not warm

• Pertinent Labs:
  – Glucose 118; **Creatinine 1.42**; Uric Acid 6.1
  – AST 20 ALT 19 **Alk Phos 281** Bili 0.6
  – WBC 11.2 Hg 12.5, platelets 320, **ESR 81**
  – HIV, Hepatitis C, Hepatitis B Negative

**Chest Imaging at Start of Treatment**
Patient 1

• **Started on Treatment**
  – Regimen: RIPE plus B6
  – Recent films done of right knee requested

• **F/U Visit 3 weeks**
  – Feeling better, gained 3 lbs, decreased cough, Right knee “the same”
  – **Increased redness and complaining of some pain of the Right eye;** on exam vision unchanged, Pupil reactive
  – Sputum cultures growing MTB
  – Labs: Glucose 292, Hg AIC 7.3, Uric Acid 11.5, LFTs stable, Alk phos decreasing

Back to our Question

So did this Patient with extensive Pulmonary TB and probable TB osteoarthritis of the knee also have Ocular tuberculosis?
Some Important Terminology

- **Uveitis**: Inflammatory diseases involving the uvea (includes choroid, ciliary body, iris)
- **Anterior uveitis**: Most common form: front of eye, “iritis”
- **Intermediate uveitis**: Involves ciliary body, often seen inflammatory cells in vitreous
- **Posterior uveitis**: Involves choroid and retina, includes “chorioretinitis”
- **Pan-uveitis**
- **“Granulomatous” uveitis**: Presence of large “greasy” keratitic precipitates (KPs)


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**Ocular tuberculosis masquerading as a tumor**

*Thérèse M Sassalos, Rajesh C Rao, Hakan Demirci*

*University of Michigan*
• A 31-year-old healthy woman presented with 4 days of blurry vision and 3 weeks of periorbital pain of the left eye.
• Mexico 11 years ago.
• Close contact with a friend, who was recently abroad, and who was “constantly coughing”.
• Quantiferon ++
• CXR normal
How does TB get to the eye?

• Pathogenesis of Ocular Tuberculosis
  – Haematogenous spread
  – Exogenous infection
    • Direct extension from surrounding tissues
    • Self contamination from sputum
  – Immune, non-infectious syndromes
    • Inflammatory response to TB antigens?
    • Eales disease (retinal perivasculitis)
    • Serpiginous choroiditis
Detroit Metro Airport  
spring of 2017  
Arrived from Yemen, sick  

Beaumont
CT Scans April 2017

- “Large mucosal ulceration involving left pharyngeal tonsil extending to the sternocleidomastoid muscle with air along the tract compatible with fistula formation
- Cavitary lesions within bilateral lung apices”
Final diagnosis

- Cervical lymph node and cavitary pulmonary tuberculosis
- No head and neck cancer

Cerebrospinal fluid in TB meningitis

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opening pressure</td>
<td>Elevated</td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Clear early; turbid to cloudy</td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>100-500+ PMNs in early</td>
<td>Normal &lt;5</td>
</tr>
<tr>
<td></td>
<td>Up to 95% mononuclear chronic</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>100-500 mg/mL</td>
<td>Normal &lt;50</td>
</tr>
<tr>
<td>Glucose</td>
<td>40-50 mg%, rarely &lt;20</td>
<td>Compare with blood glucose</td>
</tr>
<tr>
<td>AFB smear</td>
<td>20-37%</td>
<td></td>
</tr>
<tr>
<td>AFB Culture</td>
<td>40-80%</td>
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</tbody>
</table>
2016 TB Treatment Guidelines

- PICO Question 8: Does the use of adjuvant corticosteroids in tuberculous meningitis provide mortality and morbidity benefits?
- Recommendation 8: We recommend initial adjunctive corticosteroid therapy with dexamethasone or prednisolone tapered over 6–8 weeks for patients with tuberculous meningitis (strong recommendation; moderate certainty in the evidence).

Peritoneal TB

<table>
<thead>
<tr>
<th>Finding</th>
<th>%</th>
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<tbody>
<tr>
<td>Abdominal pain</td>
<td>60%</td>
</tr>
<tr>
<td>Abdominal swelling</td>
<td>53-100%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>50-90%</td>
</tr>
<tr>
<td>Fever</td>
<td>45-100%</td>
</tr>
<tr>
<td>Concomitant respiratory TB</td>
<td>30-53%</td>
</tr>
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</table>
Pericardial TB

<table>
<thead>
<tr>
<th>Finding</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>73-93%</td>
</tr>
<tr>
<td>Paradoxical pulse</td>
<td>23-71%</td>
</tr>
<tr>
<td>Pericardial rub</td>
<td>37-84%</td>
</tr>
<tr>
<td>Neck vein distension</td>
<td>46-74%</td>
</tr>
<tr>
<td>Edema</td>
<td>24-64%</td>
</tr>
<tr>
<td>Ascites</td>
<td>30%</td>
</tr>
</tbody>
</table>
2016 TB Treatment Guidelines

- PICO Question 7: Does the use of adjuvant corticosteroids in tuberculous pericarditis provide mortality and morbidity benefits?
- Recommendation 7: We suggest initial adjunctive corticosteroid therapy **not be routinely used in patients with tuberculous pericarditis** (conditional recommendation; very low certainty in the evidence).

Genitourinary TB

- Kidneys, bladder, ureter
- Fallopian tubes, endometrium, ovaries
- Prostate, epididymis, testes
NORMAL HYSEROSALPINGOGRAM (HSG)
Uterine TB diagnosis

- Curettings from D&C
- Sent for histology, culture
- Menstrual blood cultured for AFB

Paradoxical Reactions to TB Treatment
**Immune Reconstitution Inflammatory Syndrome (IRIS)**

- Transient worsening of tuberculosis symptoms and lesions in response to antituberculous therapy
- HIV negative and HIV positive patients
- Not uncommon with treatment of lymph nodes, even after completion of treatment

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**Treatment of TB Disease (3)**

- Intensive phase should contain the following four drugs:
  - Isoniazid (INH)
  - Rifampin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)

Example of pills used to treat TB disease. From left to right: isoniazid, rifampin, pyrazinamide, and ethambutol.
Duration of Extrapulmonary TB Treatment

- TB meningitis 9-12 months
- Bone & joint TB 6-9 months
- 6 months for most other cases

In summary

- TB disease may occur in any organ of the body.
- Diagnosis is difficult, often multiple tests are needed
- Empirical TB treatment is more often necessary.