Mycobacterium TB: Introduction

- Wide spread and deadly
- Infects ~ 1/3 world population
  - 15 million in US
- 21st century: ↓ TB in US
  - 2009: 11,500 cases
  - except CA, TX, FL, NY, NJ
  - cases are increasing

MTB: US Epidemiology

- HIV is greatest risk factor
  - Men age 22 - 44, US born
  - Recent TB infection
- Foreign born, high TB rates
  - Reactivation of latent TB
  - >50% cases TB in US
- Drug-resistant TB
  - Homeless, malnourished, overcrowded
  - Chronically ill or immune suppressed

Genus Mycobacterium: Microbiology: Acid Fast Bacillus

- Aerobic acid-fast rod: resists drying, acid, & alcohol

Non-MTB (NMTB): Opportunistic
- 50+ species

MTB complex (MTC): Pathogens
- Cause TB or TB-like illness
- Common ancestor
- Identical genetic profile
- Different hosts & pathogenicity

MTB
- M africanum
- M canetti
- M bovis (BCG)

Objectives

- Epidemiology in US
- Microbiology & genetic profile
- Natural history
- Tools to diagnose TB
- Role of immune status and imaging
  - Immune competent vs impaired

MTC: Unique Genetic Profile

- Blood interferon γ release assays (IGRA)
  - Lymphocytes produce IFN-γ, specific for MTB
- DNA or RNA amplification tests of AFB
  - Specific for TB, excludes NMTB
  - From sputum or culture
- DNA fingerprinting – outbreaks of TB
  - Primary – identical strains / pattern - recent
  - Reactivation – unique strain – in only 1 person
- Redefines “primary” and “reactivation”
**Tools to Diagnose Active TB**

- Clinical – patients are sick
- TB skin test (TST) or IGRA
- Chest radiograph
- Microscopy (AFB) & culture (2-8 weeks)
- Definitive Diagnosis: find MTB from culture or DNA / RNA assays from specimen
- Otherwise, “presumptive”
- TB may be difficult to diagnose

**TB: Primary Infection**

- Inhale tiny droplets into alveoli
- T-cells & macs contain infection
- If local host response fails:
  - Granulomatous response surrounds infection
  - Tubercle may enlarge, spreads to nodes
  - Lymphatic & hematogenous spread
- 2-6 week: cell-mediated immunity
  - Necrotizing granulomas

**TB: Natural History**

- Exposure to active TB
  - No infection
    - 70 - 90%
  - Infection
    - 10 – 30%
  - Active TB (1%)
    - Sick
  - Latent TB, ppd+
    - Well
    - Not infectious
    - Visible organisms
  - Reactivation TB (10%)
    - 50% within 3 years
  - Never develop TB

**TB: Utility of CXR**

- Initial +ppd – R/O active disease
- Most patients – normal CXR
- Abnormal CXR
  - CXR in 2 months for sputum-negative TB
  - CXR in 6 months after Tx as baseline
- Symptoms of worsening TB or relapse
- Annual questionnaire for ppd+ health care workers

**TB: Role of CT**

- Immunocompromised patient
- Worsening despite therapy
- Hemoptysis
- CT may play a role
  - when CXR is normal or inconclusive
  - to assess disease activity, complications
- Direct surgical resection
  - Lobectomy, pneumonectomy, transplant

**CXR Reflects Immune Response Not Time Course**

<table>
<thead>
<tr>
<th>“Post-primary / reactivation” Immune competent Typical</th>
<th>“Primary TB” Immune impaired Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Children</td>
</tr>
<tr>
<td>Reactivation or re-infection</td>
<td>Initial infection</td>
</tr>
<tr>
<td>Consolidation &amp; cavitation</td>
<td>Consolidation &amp; adenopathy</td>
</tr>
<tr>
<td>Upper lungs</td>
<td>Lower lobes</td>
</tr>
<tr>
<td>Usually progressive</td>
<td>Usually self limited</td>
</tr>
<tr>
<td></td>
<td>Milliary, effusion, extra-pulm</td>
</tr>
</tbody>
</table>
Healed TB

Findings:
- Ca++ RUL granuloma
- Ca++ mediastinal LN
Differential Dx:
- TB, NMTB, fungal
Teaching points:
- Healed granuloma
- Likely “inactive”
- Viable organisms

Active TB: Nodules

Sputum negative
Bronch negative
VATS: + MTB
Dx not always easy

TB: Nodule

RUL nodule
Pleural effusion
Volume loss

TB: Nodule

Findings:
- RUL nodule
- Tiny satellite nodules
- Pleural effusion & rind
- Trapped lung
DDx:
- TB, fungal, lung cancer
Teaching points:
- TB – solitary nodule UL
- Exudative effusion

TB: Nodules

Findings:
- Satellite RUL nodules
- Tiny hard nodules track along bronchus
Teaching points:
- TB: clustered MPN in UL
- Immune competent
- “Reactivation”

TB: Nodule Cavitary

Findings:
- Upper lung
- Cavitary nodule
- Bronchiolectasis
- Bronchogenic spread
- Immune competent
TB: Consolidation

Findings:
- RUL consolidation
- Volume loss
- Bronchiectasis
- Cavitary
- Ipsilateral LAN

Teaching point:
Immune competent

TB: Consolidation

Findings:
- Bilateral consolidation
- Upper lungs
- Asymmetric
- Immune competent

TB: Consolidation, atelectasis

Findings:
- Bilateral consolidation
- Upper lungs
- Asymmetric
- Multi-cavitary
- Immune competent

TB: Consolidation Cavitary

Findings:
- Consolidation
- Upper lungs
- Asymmetric
- Multi-cavitary
- Bronchogenic spread

Teaching points:
Large upper lung cavity
ST tracking along bronchi

DDx:
- TB, NMTB, fungal
- Lung CA

TB: Consolidation Cavitary

Findings:
- Large upper lung cavity
- ST tracking along bronchi

DDx:
- TB, NMTB, fungal
- Lung CA

Teaching points:
Large upper lung cavity
**Consolidation Multi-cavitary**

Findings:
- Upper lung cavities
- Air-fluid level
- Bronchogenic spread

Teaching points:
- Immune competent
- Accelerated progressive
- Multiple drug resistant?

**Fibrocavitary**

UL fibrosis
- Cavities
- Bronchiectasis

**Fibrocavitary**

UL fibrosis
- Cavities
- Bronchiectasis

**Fibrocavitary: Double Lung Tx**

UL fibrosis
- Fungus ball LUL
- No source of bleeding

**Fibrocavitary: Hemoptysis Mycetoma**

UL fibrosis
- Cavities
- LAN
- End-stage

Upper lung fibrosis
- Fungus ball LUL
- No source of bleeding
**TB: Fibrocavitary Mycetoma**

Findings:
- Segmental
- Lung base
DDx:
- Pneumonia
- Immune impaired

**TB: Consolidation AIDS**

Findings:
- RLL
- LAN
DDx: CAP
- Immune impaired

**TB: Lymphadenopathy AIDS**

DDx LAN:
- Malignant
- Granulomatous
- TB
- Fungal

**TB: Fibrocavitary - Hemothysis**

Coronal MIPS

**TB: LAN AIDS**

Central necrosis
Peripheral enhancement

Courtesy of Dr. Sandy Rubin

Courtesy of Dr. Michael McCarthy
TB: LAN AIDS

TB LAN: central necrosis
Peripheral enhancement
Courtesy of Dr. Michael McCarthy

TB: Miliary - Hematogenous Renal Tx

Random distribution

TB: LAN AIDS

LAN, miliary

Courtesy of Dr. Sandy Rubin

TB: Airway Involvement

Tubercle forms in airway submucosa
=> Ulceration, fibrosis, stenosis

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>• Tracheitis</td>
<td>• Tracheal stenosis</td>
</tr>
<tr>
<td>• Tracheal compression</td>
<td>• Bronchiectasis, stenosis</td>
</tr>
<tr>
<td>• Bronchitis</td>
<td>• Broncholithiasis</td>
</tr>
<tr>
<td>• Bronchiolitis</td>
<td>• 2nd amyloid</td>
</tr>
</tbody>
</table>

TB: Broncholith

Findings:
RUL stricture
Atelectasis
Bronchiectasis
Bronchogenic spread

TB: Bronchial Stricture

Findings:
RUL stricture
Atelectasis
Bronchiectasis
Bronchogenic spread

Courtesy of Dr. Sandy Rubin
**TB: Airway Involvement**

- Bronchial stricture
- LUL atelectasis
- Tree-in-bud

**TB: Pleura**

Findings:
- RUL nodule
- Tiny satellite nodules
- Pleural effusion & rind
- Trapped lung

DDx:
- TB, fungal, lung cancer

Teaching points:
- TB – solitary nodule UL
- Exudative effusion

**Multiple Drug Resistance (MDR-TB)**

Looks like accelerated active TB
Multi-lobar cavities + consolidation

**Immune Reconstitution Syndrome (IRS)**

Paradoxical worsening of symptoms & imaging
Reflects recovery of immune surveillance
- Reported with initiation of TB therapy
- HAART for HIV infection

CXR: adenopathy, consolidation, effusions
Exclude MDR-TB, treatment failure
Supportive measures, corticosteroids
TB: Chest Radiography

Summary

<table>
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<th>Normal or healed TB</th>
<th>“Reactivation” Immune Competent</th>
<th>“Primary” Immune Deficient</th>
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Who gets TB: foreign born, HIV+, immune compromised

Imaging reflects immune status, not time course

Findings not always conclusive of TB

Most infected individuals have latent TB & normal CXR & never develop active TB

Immune Competent: “Reactive”

Upper lungs
- Solitary or clustered pulmonary nodules
- Consolidation
- Cavitation & bronchogenic spread
- +/- LAN, pleural effusion

Immune Deficient: “Primary”

Lower lungs - consolidation
- Dominant LAN
- Milary
- Pleural effusion