Mycobacterium avium complex

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No relevant disclosures to report
Learning Objectives

• Non-tuberculous mycobacteria species
• Prevalence of non-tuberculous mycobacterial disease
• Patient populations at risk for disease
• Clinical syndromes
• Methods of detection
• Classic case presentation
• Treatment challenges
Non-Tuberculous Mycobacteria

- Over 125 different species
  - ~40% documented to cause disease in humans
  - Some of the most common pathogenic species:
    - avium, intracellulare, abscessus, fortuitum, septicum, kansasii, gordonae, chelonae, marinum
MAC

• Mycobacterium avium complex (MAC)
  • 2 species: avium and intracellulare
  • 4 avium subspecies: avium, paratuberculosis, silvaticum, hominissuis
  • 28 serovars

• Known to form biofilms
• Can be very antibiotic resistant
• Can be resistant to many disinfectants
• Most common non-tuberculous group of mycobacteria to cause human disease
Non-Tuberculous Mycobacteria

- Ubiquitous organisms
  - Found in soil and water
  - Need to correlate with clinical picture

- Opportunistic infection
  - Most patients are immune compromised or have preexisting damage

- Populations at risk for disease
  - Transplant, cancer, autoimmune suppression, cavitary lung lesions, skin damage, very old and very young

- Prevalence increasing worldwide
  - 10x more prevalent than Tuberculosis
Clinical Syndromes

- Progressive pulmonary disease
- Lymphadenitis
- Disseminated disease
- Skin and soft tissue infections
Methods of detection

• Clinical presentation

• Radiology

• Acid fast stains
  • Kinyoun, Ziehl-Neelsen, Auramine-rhodamine

• Culture
  • Slow growing, possibly pigmented, usually rough or dry colonies

• PCR
Case history

• 23 year old HIV positive male
• Congenitally acquired HIV
• Foster care and treatment started at 6 months
• Only a single rise in HIV before his 18th birthday
Case history

• Shortly after his 18th birthday he attempted suicide by overdosing on HIV medications
• He then stopped taking all anti-retrovirals and stopped coming to clinic
• Social workers tried continually to get him back in clinic- “I’m just not ready yet”
• Ultimately returned after a 5 year absence
Clinical presentation

- Agreeable to re-start antiretroviral treatment (ART)
- Generally feels well
- Reports a 100 lb weight loss over last 4 months despite little change in eating habits or activity level
- Occasional diarrhea and night sweats
- Started on antimicrobial prophylaxis
Blood results

HIV 77,400 copies/mL
ND after only a month

CD4 of 2 upon return
Infectious disease results- Negative

- CMV
- Chlamydia
- Gonorrhoeae
- Syphilis
- Hepatitis A, B, and C
- Parvovirus B19
- Toxoplasma
- Mycobacterial culture from blood
Clinical history- 2 months since ART

- Reports increasing diarrhea, night sweats, chills
- Enlarging right inguinal lymph node
  - 2 cm x 2 cm and tender
- Undergoes needle biopsy of the lymph node
  - Routine fungal and bacterial stains and cultures are negative
Pathology

- Necrotizing granulomatous inflammation with numerous acid fast bacilli

Kinyoun at 100x

Hematoxylin and eosin at 20x
Mycobacterial results- 2 months since ART

- >9 AFB reported on smear at WSLH
- MAC and Tb PCRs negative
- QuantiFERON-TB gold and PPD are negative
- Chest X rays ordered, unremarkable
- MAC identified in culture 2 weeks later
- Treated with ethambutol, rifabutin, and azithromycin
# Susceptibility Profile

<table>
<thead>
<tr>
<th>Drug</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clofazimine</td>
<td>Susceptible</td>
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<td>Ethambutol</td>
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Clinical history continued

- Initially responds to treatment
- Begins to feel worse after 4 months of ART
- Develops cellulitis near the enlarging lymph node
- Develops a cough, fever, headaches
- Has worsening sweats and fatigue
Radiographic findings

- 3 x 5 x 6 cm mass with rim enhancement.
- Skin thickening and surrounding inflammation.
- Multiple enlarged lymph nodes
- Right upper lobe consolidation
- Left lower lobe nodules
Laboratory Results

<table>
<thead>
<tr>
<th></th>
<th>Pre Absence</th>
<th>On Return</th>
<th>2 months Post ART</th>
<th>4 months post ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>6.8</td>
<td>2.1 <strong>L</strong></td>
<td>5.6</td>
<td>11.3 <strong>H</strong></td>
</tr>
<tr>
<td>CD4</td>
<td>748</td>
<td>2 <strong>LL</strong></td>
<td>27 <strong>L</strong></td>
<td>68 <strong>L</strong></td>
</tr>
<tr>
<td>Abs Neutrophils</td>
<td>3910</td>
<td>1000 <strong>L</strong></td>
<td>4200</td>
<td>9930 <strong>H</strong></td>
</tr>
<tr>
<td>Platelets</td>
<td>294</td>
<td>195</td>
<td>434 <strong>H</strong></td>
<td>409 <strong>H</strong></td>
</tr>
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- Diagnosed with IRIS
IRIS (Immune reconstitution inflammatory syndrome)

• Paradoxical symptomatic relapse despite treatment

• Immune reconstitution during an infection causes an increased inflammatory response.

• Unmasking of infections
  • Symptoms develop around 8 weeks after the start of ART

• Develops in about 13% of patients starting ART
IRIS

HIV copies and CD4 cells over time with different treatments:
- Healthy
- Healthy + MAC
- HIV
- HIV + MAC
- HIV + MAC + HAART

Immune response graph showing the effects of different treatments on HIV levels.
Diagnostic criteria

- HIV positive with response to ART
- Low starting CD4 count (<100 cell/μL)
- Inflammation following start of ART
- Identified co-infection
- Pathogen is not resistant to therapy
- Good patient compliance with treatment
## Different treatment strategies

### Treat MAC before HIV

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<td>Reduce the risk and severity of IRIS</td>
<td>Risk of HIV disease progression</td>
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<td>Slow clearance of MAC without help from immune system</td>
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<td>Starting and stopping ART can lead to HIV resistance</td>
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### Treat HIV and MAC simultaneously

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<td>Immune system can help fight MAC</td>
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IRIS Risk Factors

- CD4 < 100 cells/mL
- 2.5 log drop in HIV copies/mL at start of ART
- Type and severity of co-infection
Most common pathogens associated with IRIS

- Mycobacterium tuberculosis
- Mycobacterium avium complex
- Cytomegalovirus
- Cryptococcus
- Pneumocystis
- Herpes simplex
- Hepatitis B
- Human herpes virus 8 (Kaposi sarcoma)
Clinical history continued

- Pain worsens, node becomes necrotic and swells.
- Node bursts open and drains thick whitish material
- Patient presents to ED in 4 months after starting ART
  - Undergoes surgical resection of node
- Pathology reports few AFB
- Culture grows MAC again
  - Isolate shows increased resistance profile
Susceptibility Profiles

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1\textsuperscript{st} treatment: Ethambutol, rifabutin, and azithromycin
2\textsuperscript{nd} treatment: Clindamycin, cefazolin, azithromycin, ethambutol,
Case conclusion

• Symptoms have resolved
• HIV viral load well controlled but CD4 count is still slow to return to normal
Question Time

What are risk factors for IRIS?

a. Low CD4 count and an HIV co-infection
b. High white blood cell count
c. Foster care
d. Age and weight
Question Time

How much more prevalent are non-tuberculous mycobacteria compared to Tb?

a. They are less common
b. 5x more
c. 10x more
d. 100x more
Question Time

What are methods for diagnosing MAC?

a. PCR
b. Clinical picture and radiographic findings
c. Kinyoun stain
d. All of the above
Question Time

What puts you at greater risk for non-tuberculous infections?

a. Hot air balloon rides
b. Suntanning
c. Immune compromise
d. How well you do on this test