Nontuberculous Mycobacterial Lung Disease

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Introduction

• Over 125 known species of nontuberculous mycobacteria (NTM)
• Only small number of NTM species are known to cause lung disease
• Distribution of NTM varies across geographic locales

Objectives

• Review epidemiology of NTM lung disease
• Describe clinical manifestations of NTM lung disease
• Illustrate imaging patterns associated with NTM lung disease

Epidemiology

• Exact incidence and prevalence unknown
  – Not reportable diseases
• Number of NTM infections increasing
  – Studies showing increased sensitization to M. intracellulare
  – Increasing number of NTM isolates reported in laboratories

Epidemiology

• NTM ubiquitous in environmental reservoirs
  – Water
  – Soil
  – Food
  – Animals
• No known human-human or animal-human transmission

Disclosures

• Consultant
  – Perceptive Informatics
• Royalties (book author)
  – Amirsys, Inc.
  – Wolters Kluwer
  – Springer
Epidemiology

<table>
<thead>
<tr>
<th>Species</th>
<th>Geographic Distribution</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. intracellulare &amp; M. avium (MAC)</td>
<td>Worldwide</td>
<td>Most common cause of NTM lung disease</td>
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<tr>
<td>M. kansasii</td>
<td>US, Europe, S. Africa</td>
<td>Similar to TB, associated with mining and municipal water sources</td>
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<tr>
<td>M. abscessus</td>
<td>Worldwide</td>
<td>Cystic fibrosis; difficult to eradicate with medical therapy alone</td>
</tr>
<tr>
<td>M. xenopi</td>
<td>Europe, Canada</td>
<td>Hot water systems</td>
</tr>
<tr>
<td>M. chelonae</td>
<td>Worldwide (likely)</td>
<td>Underlying lung disease</td>
</tr>
<tr>
<td>M. fortuitum</td>
<td>Worldwide (likely)</td>
<td>Associated with aspiration</td>
</tr>
<tr>
<td>M. marmoreum</td>
<td>UK, Northern Europe</td>
<td></td>
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</tbody>
</table>

Adapted from Taiwo B. Infect Dis Clin N Am 2010 and American Thoracic Society

Epidemiology

<table>
<thead>
<tr>
<th>Location</th>
<th>Species</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York¹</td>
<td>M. avium complex 79%</td>
<td>Rapidly growing mycobacteria (RGM):</td>
</tr>
<tr>
<td></td>
<td>M. xenopi 6%</td>
<td>M. abscessus</td>
</tr>
<tr>
<td>South Korea²</td>
<td>M. kansasii 5%</td>
<td>M. fortuitum</td>
</tr>
<tr>
<td></td>
<td>M. abscessus 33%</td>
<td>M. chelonae</td>
</tr>
<tr>
<td></td>
<td>M. fortuitum 11%</td>
<td></td>
</tr>
<tr>
<td>South Africa³</td>
<td>M. kansasii 68%</td>
<td>Cohort consisted of predominantly miners with TB or silicosis</td>
</tr>
</tbody>
</table>

¹Bodle EE et al. Emerg Infect Dis 2008
²Koh WJ et al. Chest 2006
³Corbett EL et al. Int J Tuberc Lung Dis 1999

Epidemiology

- Host factors
  - Immunologic
  - Body shape
  - Structural lung disease

Epidemiology

- Macrophage
- Interleukin-12
- Interferon gamma
- Neutrophil and macrophage activation

Epidemiology

- Body shape
  - Narrow AP chest diameter
  - Scoliosis
  - Pectus excavatum
  - Mitral valve prolapse

Epidemiology

- Body shape
  - Decreased force of cough
  - Underlying connective tissue disease
  - Phenotypic marker of genetic predisposition to NTM infection
Epidemiology

• Structural lung disease
  – Emphysema
  – Cystic fibrosis
  – Bronchiectasis
  – Smoking

Clinical Presentation

• Nonspecific respiratory tract signs and symptoms
  – Common
    • Cough
    • Dyspnea

Clinical Presentation

• Nonspecific respiratory tract signs and symptoms
  – Uncommon
    • Hemoptysis
    • Night sweats
    • Weakness

Clinical Presentation

• 3 distinct prototypical forms
  – Fibrocavitary disease
  – Nodular bronchiectatic disease
  – Hypersensitivity syndrome
  • Largely based on Mycobacterium avium complex (MAC)

Imaging

• Reflects prototypical forms
• Chest radiograph usually initial imaging study
  – May be normal in up to 6% of patients with sputum culture + MAC infection\(^1\)
• HRCT better detects presence and extent of abnormalities\(^2\)

Fibrocavitary Disease

• “Classical” pattern
  – Similar appearance to tuberculosis
• Middle-age or older men with structural lung disease
  – Emphysema
  – Bronchiectasis
  – Pneumoconiosis
  – Previous tuberculosis
  – Sarcoidosis

\(^1\)Christensen EE et al. AJR Am J Roentgenol 1978
\(^2\)Lynch DA et al. J Comput Assist Tomogr 1995
Fibrocavitary Disease

• Similarities to *M. tuberculosis*
  – Thick-walled cavities
  – Intracavitary liquid usually absent

• Differences from *M. tuberculosis*
  – More extensive pleural thickening
  – Pleural effusion less common
  – Lesser degree and extent of lymphadenopathy

M. avium complex
Fibrocavitary Disease

M. avium complex

Fibrocavitary Disease

M. avium complex

Fibrocavitary Disease

M. szulgai

Fibrocavitary Disease

M. kansasii

Courtesy of Travis Henry, M.D. (Atlanta, GA)

Fibrocavitary Disease

M. avium complex

Fibrocavitary Disease

Silicosis and M. avium complex

2008

2011

Courtesy of Howard Mann, M.D. (Salt Lake City, UT)
Fibrocavitary Disease

Silicosis and M. avium complex

2008 2011

Courtesy of Howard Mann, M.D. (Salt Lake City, UT)

Nodular Bronchiectasis

• “Non-classical” pattern
• Older Caucasian female nonsmokers
• Reinfection or coinfection with different strains of *Mycobacterium avium* complex can occur

Nodular Bronchiectasis

- Single or multiple nodules
  - Usually < 5 mm
- Bronchiectasis
  - Right middle lobe and lingula disproportionately affected
  - Can affect any or all lobes
- Tree-in-bud opacities

Nodular Bronchiectasis

M. avium complex

Nodular Bronchiectasis

M. avium complex
Nodular Bronchiectasis

M. avium complex
Hypersensitivity Syndrome

- Etiology
  - Typically *M. avium* complex
  - Hot tub or medicinal pool
  - Metal working fluid
  - Any contaminated water source
- Clinical presentation
  - Acute to subacute dyspnea and cough
  - Fever

- Concomitant hypersensitivity response
  - Temporal relationship between exposure and symptoms
  - Improvement when removed from exposure

- Infection with NTM
  - NTM sometimes cultured on tissue of affected patients
  - Increased number and better formation of granulomata
Hypersensitivity Syndrome

Indoor pool exposure

M. avium complex

After treatment

M. avium complex

Disseminated Disease

• M. bovis infection
• Intravesicular therapy
• Superficial bladder transitional cell carcinoma

M. bovis

Immune Reconstitution Inflammatory Syndrome

• Occurs when T-cell function is restored following treatment with highly active antiretroviral therapy (HAART)
• Immunologic reaction to Mycobacterial antigens
• Systemic illness with radiologic features of mycobacterial infection

Initial 3 weeks after HAART

Courtesy of Sudhakar Pipavath, M.D. (Seattle, WA)
Immune Reconstitution Inflammatory Syndrome

3 weeks after HAART
7 weeks after HAART

Courtesy of Sudhakar Pipavath, M.D. (Seattle, WA)

Diagnosis

• Clinical criteria (all 3 required)*
  – Pulmonary symptoms
  – Imaging
    • Nodules or cavities on chest radiograph
    • Multifocal bronchiectasis on CT +/- small nodules
  – Exclusion of other diseases
    • Especially tuberculosis

*American Thoracic Society

Diagnosis

• Microbiologic criteria (at least 1)*
  – Positive cultures from 2 separate sputum samples
  – Positive culture from at least 1 bronchial wash or lavage sample
  – Biopsy showing granulomatous inflammation or acid-fast bacilli + 1 positive culture

*American Thoracic Society

Treatment & Prognosis

Tree-in-bud — Nodules — Nodular bronchiectasis — Cavities (simple/bronchiectatic)
Complicates treatment — Respiratory Failure/death 2-1.2 years

Number of + Sputum Cultures | Risk of Progression to Cavitary Disease
---|---
2 | 80%—60%
≥3 | 60%-40%
≥4 | <30%

Courtesy of Loren Dentinger, M.D., Ph.D. (Madison, WI)
Treatment & Prognosis

• Side effect risk
  – Daily therapy
    • Universal on ≥ 3 drugs
    • Especially in patients > 50 years old
  – 3-times per week
    • Side effects reduced

• Three primary strategies
  – Tuberculosis and M. kansasii like strains (isoniazid regimen)
  – M. avium complex and similar strains (macrolide regimen)
  – Rapid growers (episodic intravenous therapy for severe symptoms)

• Reinfection
  – < 1 year after treatment, likely incomplete eradication
  – > 1 year after treatment, likely a new strain

Macrolide Susceptibility

Presentation M. avium complex
4 months azithromycin, ethambutol, rifabutin
6 months azithromycin, ethambutol, rifabutin, amikacin

Courtesy of Loren Denlinger, M.D., Ph.D. (Madison, WI)

Summary

• NTM are common causes of chronic pulmonary infection
• 3 main patterns have been described
  – Fibrocavitary disease
  – Nodular bronchiectasis
  – Hypersensitivity syndrome
• CT can help establish diagnosis in addition to assessing effects of treatment