Nontuberculous Mycobacterial Lung Disease: When and Why to treat

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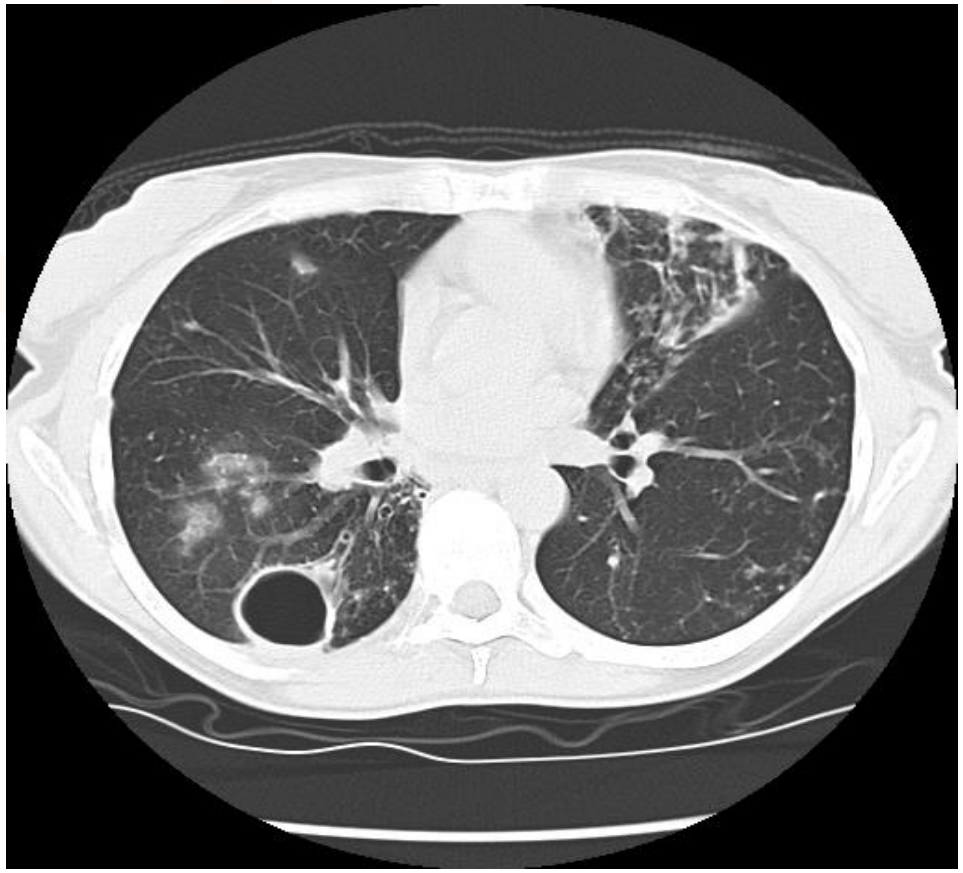
Factors Influencing the Decision to Treat NTM Lung Disease

- This risk/benefit analysis evaluates multiple factors:
  - Is the NTM lung disease associated with cavities?
  - What is the NTM respiratory pathogen?
  - How symptomatic is the patient?
  - What are the patient's pulmonary co-morbidities and are they compensated?
    - Bronchiectasis
  - What is the patient's short- and long-term prognosis?
  - What does the patient want to do?

When to treat

- Square 1: Fibrocavitary disease is invariably progressive and must be treated.
- There is no advantage to a period of observation for fibrocavitary disease patients.

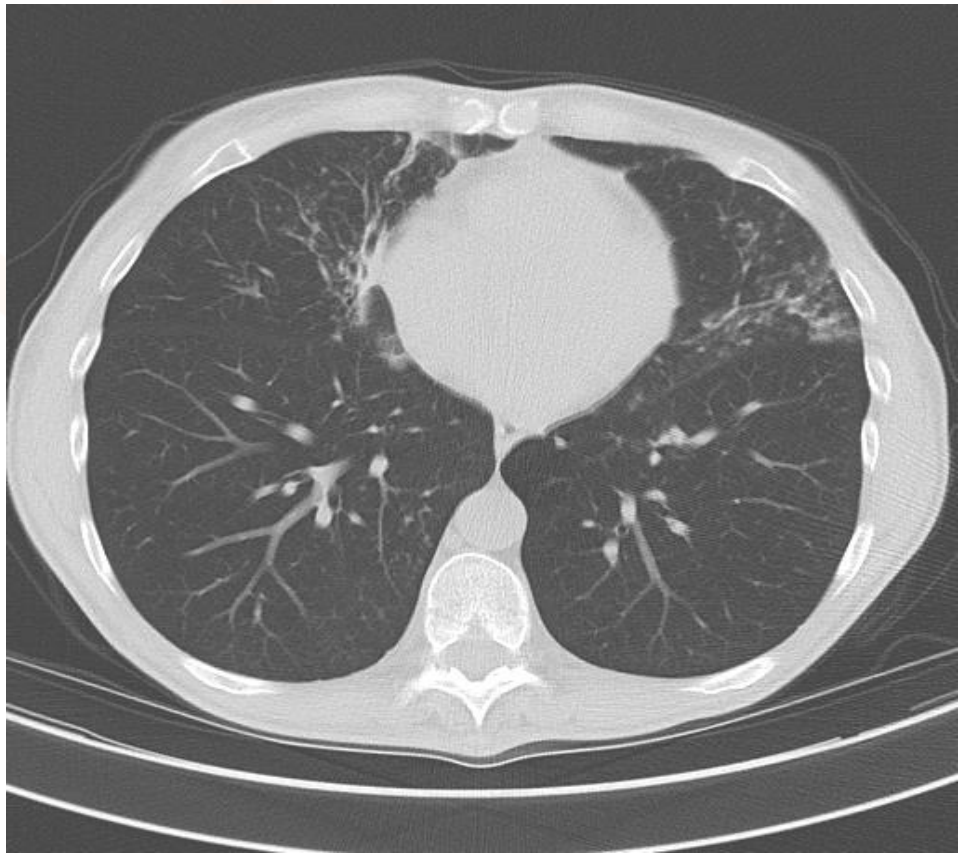
Mixed fibrocavitary and nodular/bronchiectatic MAC lung disease



Square 2: Addressing Respiratory Co-morbidities

- Major challenges of underlying lung diseases (especially bronchiectasis)
  - Symptom overlap
    - Cough, sputum production, fatigue, weight loss
    - Impact on NTM treatment evaluation
  - Infectious exacerbation of bronchiectasis/COPD
  - Pneumonia
  - Hemoptysis (+/- mycetoma)
  - Bronchospasm and/or bronchospastic exacerbation of bronchiectasis/COPD

Nodular/bronchiectatic MAC lung disease



Semiquantitative Culture Analysis during Therapy for Mycobacterium avium Complex Lung Disease.

Griffith DE and Adjemian J, AJRCCM 2015, 192:754

- 180 NB MAC LD patients undergoing macrolide-based therapy with symptomatic, radiographic, and semiquantitative mycobacterial culture analysis.
- Bronchiectatic exacerbations during MAC therapy
  - Sputum conversion within 6 months starting therapy
    - 42% at least one exacerbation
    - 33% at least 2 exacerbations
  - Sputum conversion after 6 months or no sputum conversion
    - 81% at least one exacerbation
    - 74% at least 2 exacerbations

Factors Influencing the Decision to Treat Nodular/bronchiectatic NTM Lung Disease

- 10-15% of patients diagnosed with MAC lung disease have spontaneous conversion of sputum to AFB culture negative
  - High BMI
  - Sputum AFB smear negative
  - Nodular/bronchiectatic disease

When to treat

- When to treat
  - Patient symptoms
  - Microbiologic Results
    - Smear and culture positivity
    - NTM isolated: *M. kansasii, M. szulgai, M. xenopi, MAC, M. abscessus, M. simiae, M. fortuitum*
  - Radiographic Appearance: Fibrocavitary vs nodular/bronchiectatic
- Cystic Fibrosis Model

Factors Influencing the Decision to Treat (Nodular/bronchiectatic) NTM Lung Disease

- It is clear that not all patients with MAC lung disease require immediate initiation of anti-mycobacterial therapy
- Optimization of therapy for underlying lung disease
- Prospective evaluation of sputum AFB analysis, chest radiography
- No statute of limitations for NTM lung disease

Why to treat?

Semiquantitative Culture Analysis during Therapy for Mycobacterium avium Complex Lung Disease.
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- 180 NB MAC LD patients undergoing macrolide-based therapy with symptomatic, radiographic, and semiquantitative mycobacterial culture analysis.
- Improvement in semiquantitative culture score, cough and radiographs was highly predictive of sputum long-term conversion status.

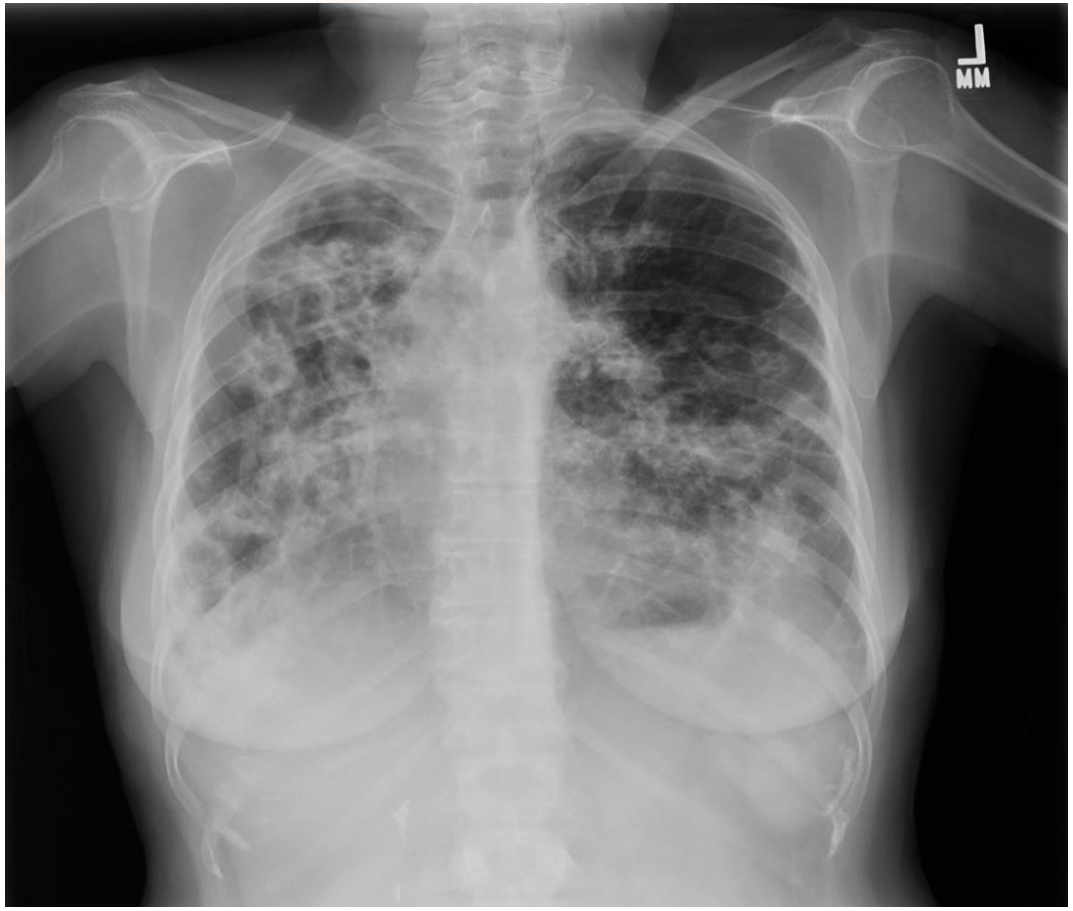
Why to treat?

- Patients with treatment failure for MAC lung disease have greater pulmonary function decline than those who do not require treatment or are treated successfully
- Patients with untreated NB MAC lung disease followed for a mean of 6 years with serial chest CT scans showed significant radiographic deterioration
- 126 MAC lung disease patients, treated and untreated, microbiologic persistence leads to an increased risk of radiographic progression

Patient mortality with pulmonary NTM disease

- Retrospective review of 106 patients treated at the NIH for pulmonary NTM disease (Fleshner et al, IJTLD 2016, 20: 582)
  - Fibrocavitary disease and pulmonary hypertension associated with significant elevated risk of mortality
- Lung cavitation is independent risk factor for NTM disease progression and mortality:
  - Hayashi M et al, 2012; Am J Respir Crit Care Med
  - Kim SJ et al, 2017; BMC Pulm Med
  - Lee MR et al, 2013; PLoS One
  - Kumagi S et al, 2017; BMC Pulm Med

64 yo female with macrolide resistant MAC
Multiple courses of antibiotics
Chronic respiratory failure



Why to treat when you choose to treat?

- Symptoms
- Pulmonary Function Decline
- Radiographic Progression
- Mortality