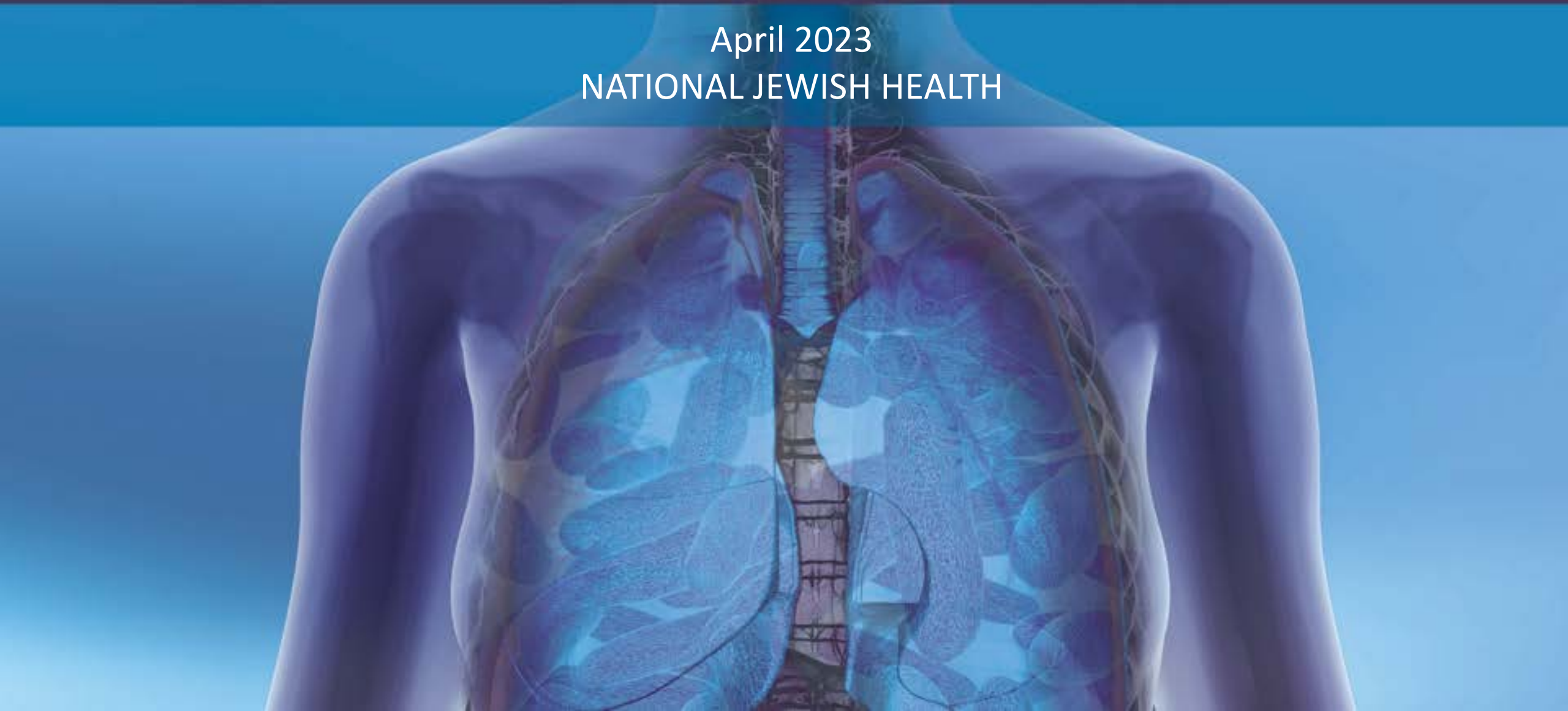
NTM Lecture Series for Providers

April 2023

NATIONAL JEWISH HEALTH



Challenging cases

NTM Provider Course

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National Jewish Health

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Disclosures

- Insmed: speaker, advisory board, investigator
- AN2: advisory board
- Paratek: speaker

Objectives

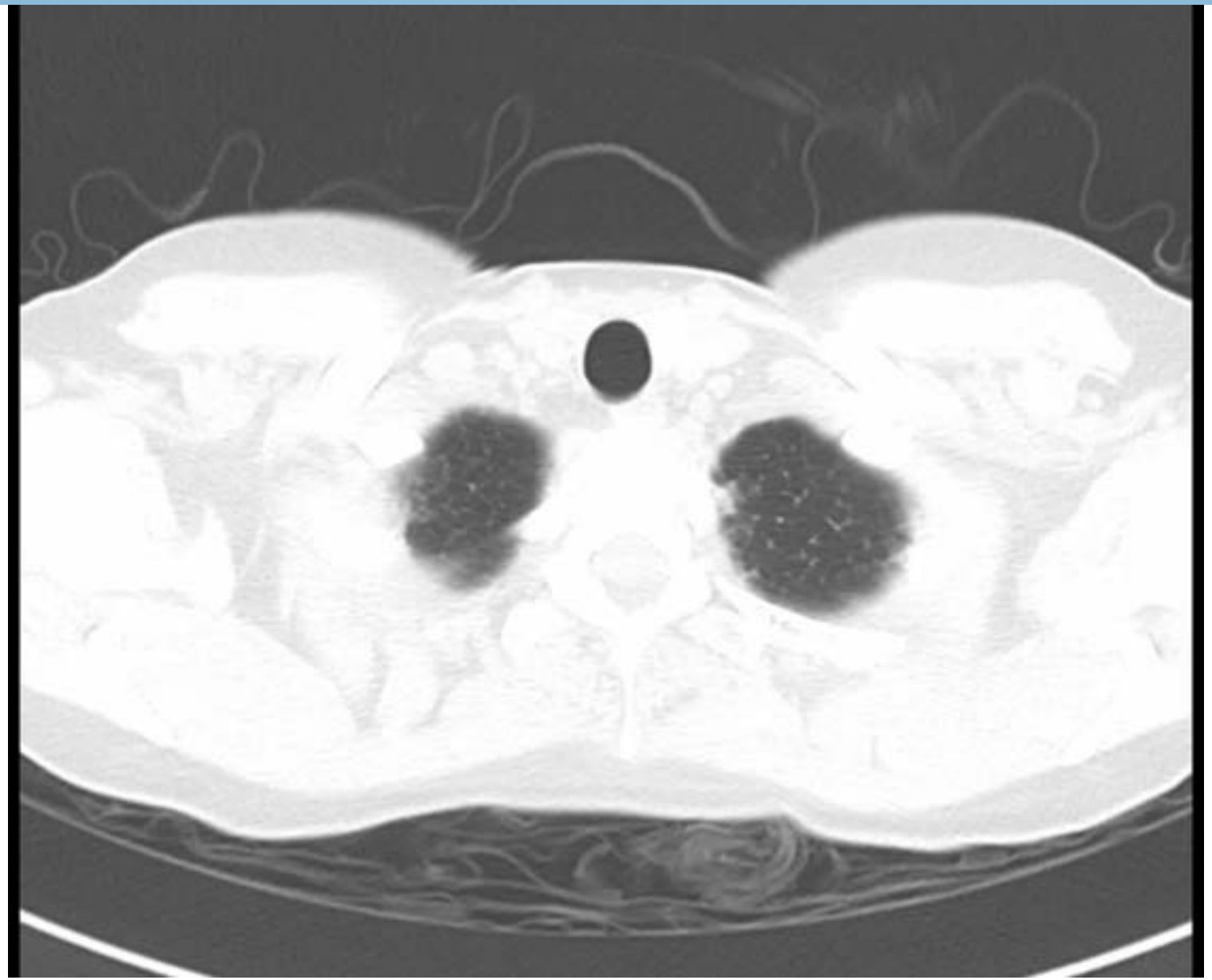
- Recognize underlying host vulnerability to bronchiectasis
- Appreciate diagnostic tools for NTM-LD
- Differentiate clinically relevant infection from non-pathogenic infection

Case One

- 40 year old female
- Healthy child
- Pneumonia at 17, 20 years old
- Pulmonary MAC diagnosed and treated on 3 separate occasions
  - First incidence at age 25
  - No culture data while on treatment
- No history of sinusitis, otitis media or other recurrent infections
- No history of infertility
- No family history of pulmonary disease

Case One

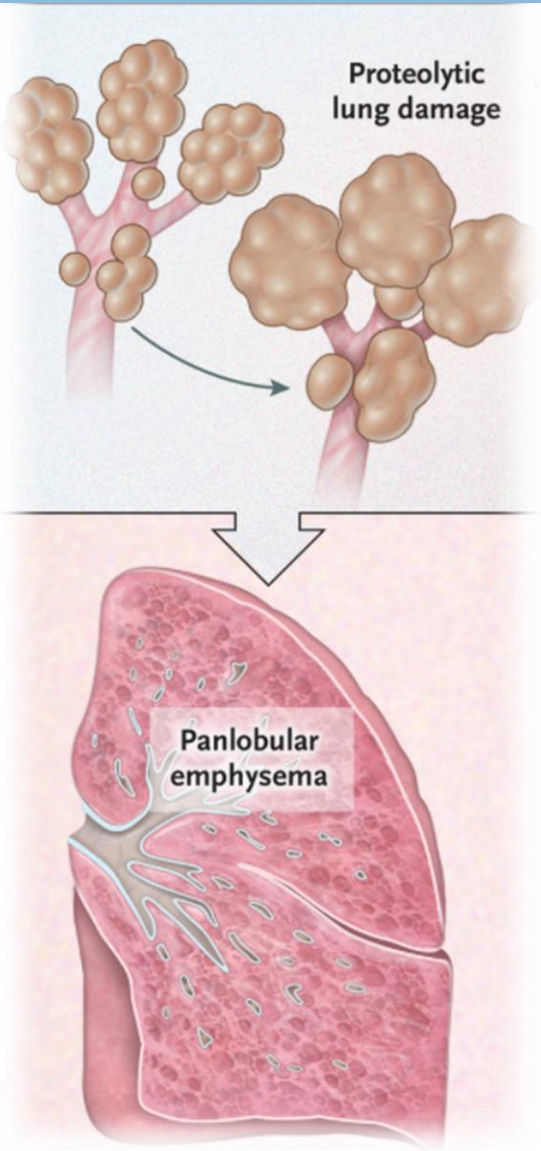
- Current symptoms of chronic cough, sputum production and fatigue
- 3/3 sputum cultures are smear -, culture + M. avium



What additional diagnostic testing is most likely to reveal her underlying susceptibility to NTM lung disease?

1. Sweat testing
2. Alpha 1 antitrypsin level and phenotype
3. Quantitative immunoglobulins
4. Interferon gamma auto-antibody testing

- Sweat chloride: 21 mmol/L (within normal)
- Quantitative immunoglobulins: normal
- Alpha 1 level: undetectable
- Alpha 1 phenotype: ZZ



NEJM. , 2020, Vol.382(15), p.1443-1455

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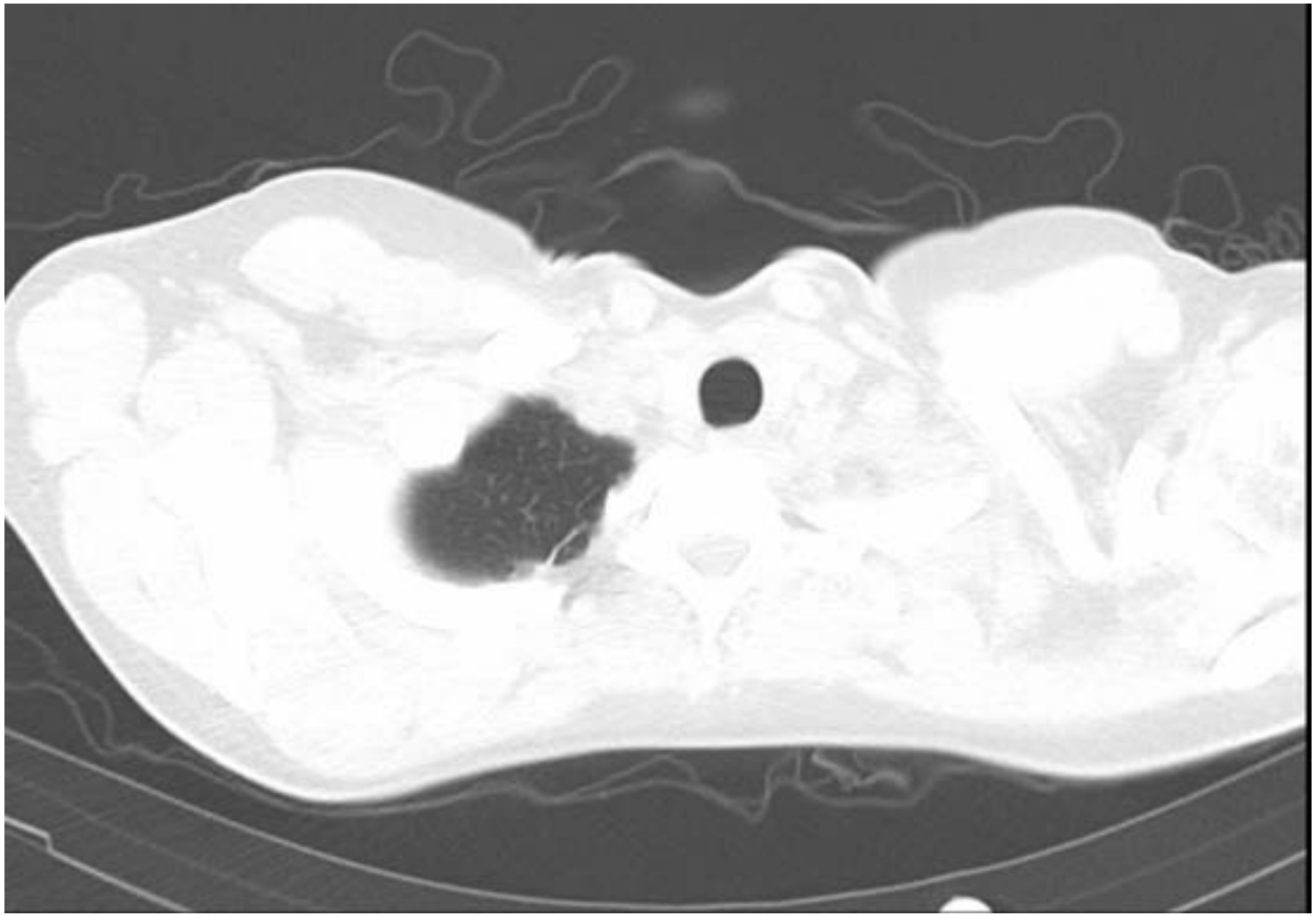
Follow up 5 years later

- Patient is receiving Alpha 1 augmentation (Prolastin-C) therapy
- She completed 18 months of MAC treatment
  - With 12 months of negative cultures
  - No evidence of recurrence
- Airway clearance: vest, aerobika, hypertonic saline twice daily
- Chronic lower respiratory infection with MRSA

Case Two

- 38-year-old female presented to NJ for an evaluation of severe asthma
- Childhood asthma, recurrent pneumonia, chronic sinusitis
- Hemoptysis at age 36, hospitalized with pneumonia
- First CT imaging at age 38



Diagnostic evaluation

- Smear +, culture + for MAC (3/3)
- Bacterial cultures + pseudomonas aeruginosa
- FEV1 57% predicted (ratio 60)
- IgE >5000

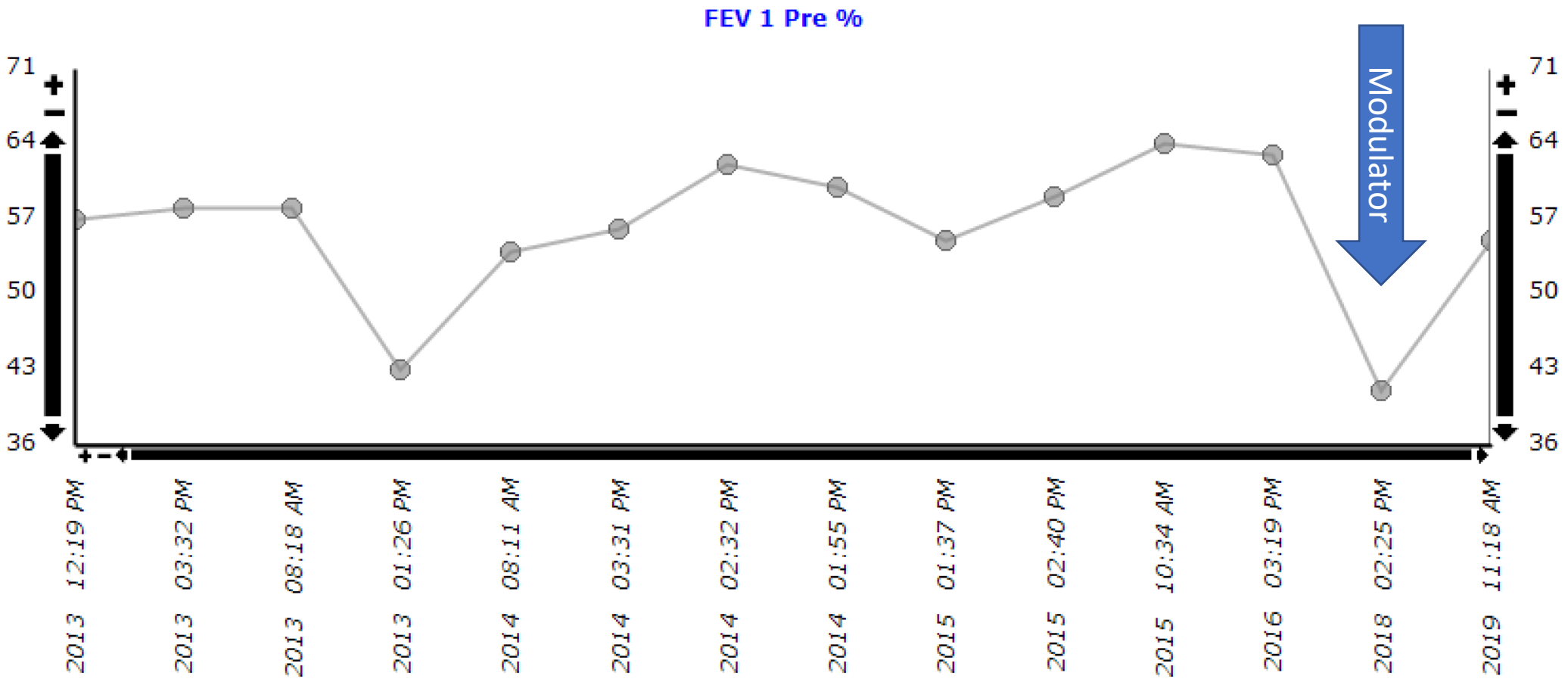
What is the most likely diagnosis

- Asthma
- APBA
- Cystic fibrosis
- All of the above

Follow up

- Sweat chloride 26, 39 mmol/L (above normal range)
- CFTR: deltaF508, R117H mutations

- She completed 12 months of negative cultures for MAC
- While on treatment for MAC, she began isolating *M. abscessus*
- She completed an additional 12 months of *M. abscessus* therapy
- 2018 she started modulator therapy


FEV 1 Pre %
Modulator
71
64
57
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36
2013 12:19 PM
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2014 02:32 PM
2014 01:55 PM
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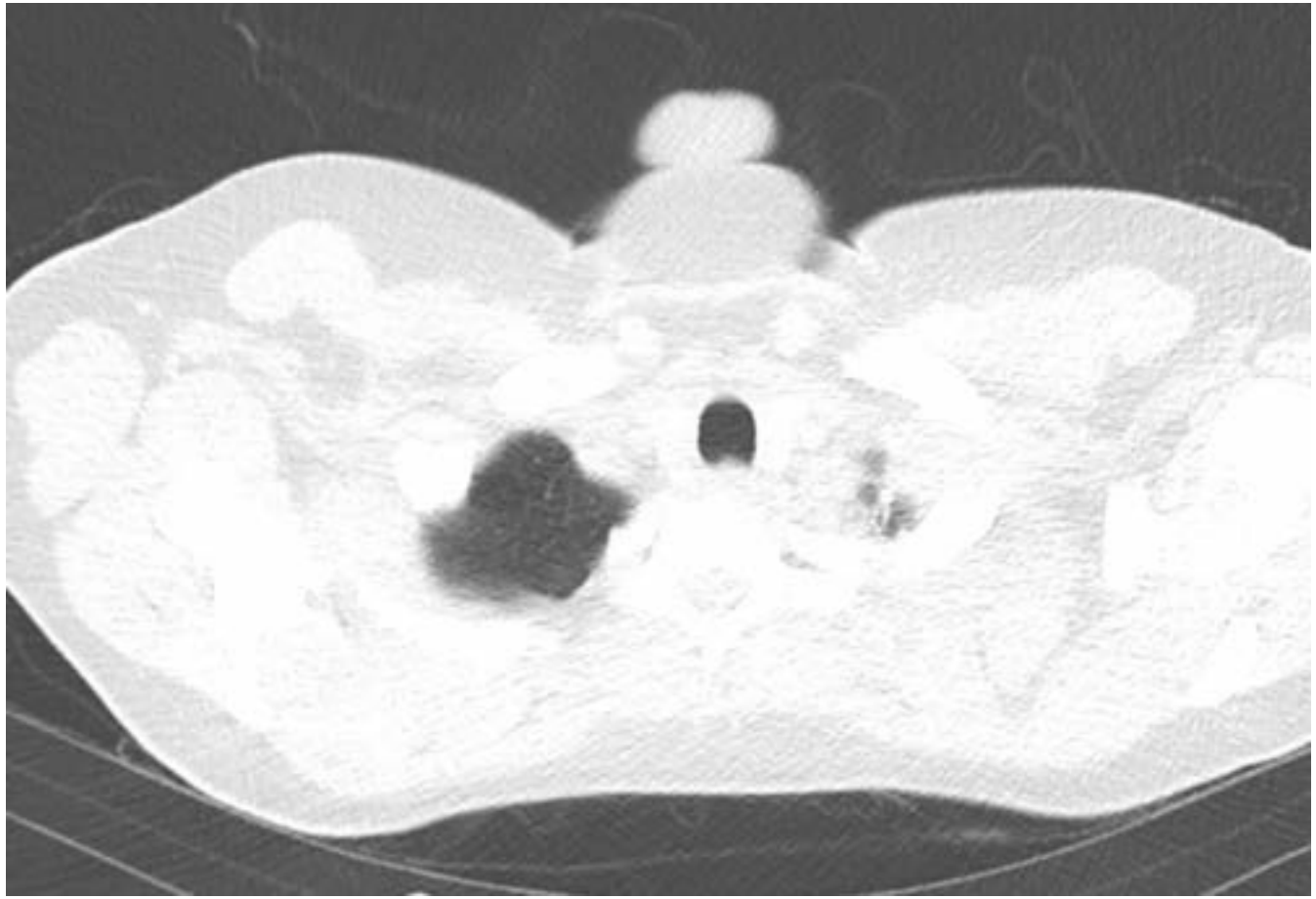
2015 10:34 AM
2016 03:19 PM
2018 02:25 PM
2019 11:18 AM

Follow up CT scan 6 years later- 2019



Case three

- 23 year old female
- In Thailand teaching English
- 18 months (7/16) into stay: 3 weeks of dry cough without fever/chills/NS/wt loss

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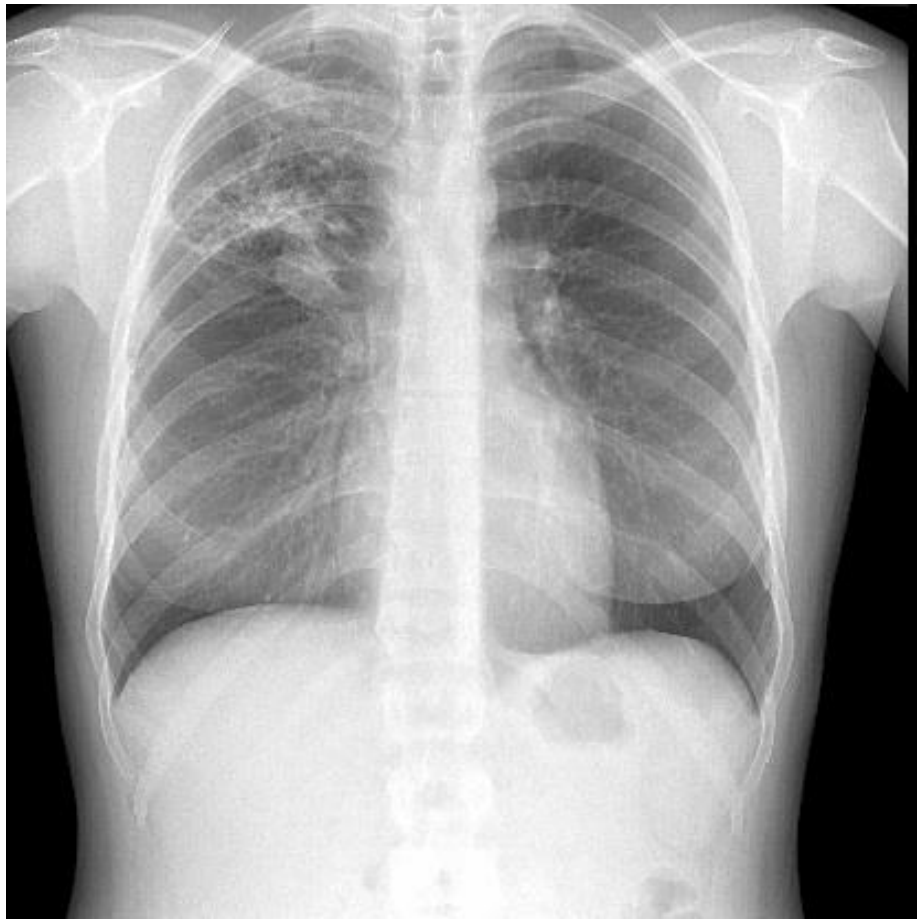
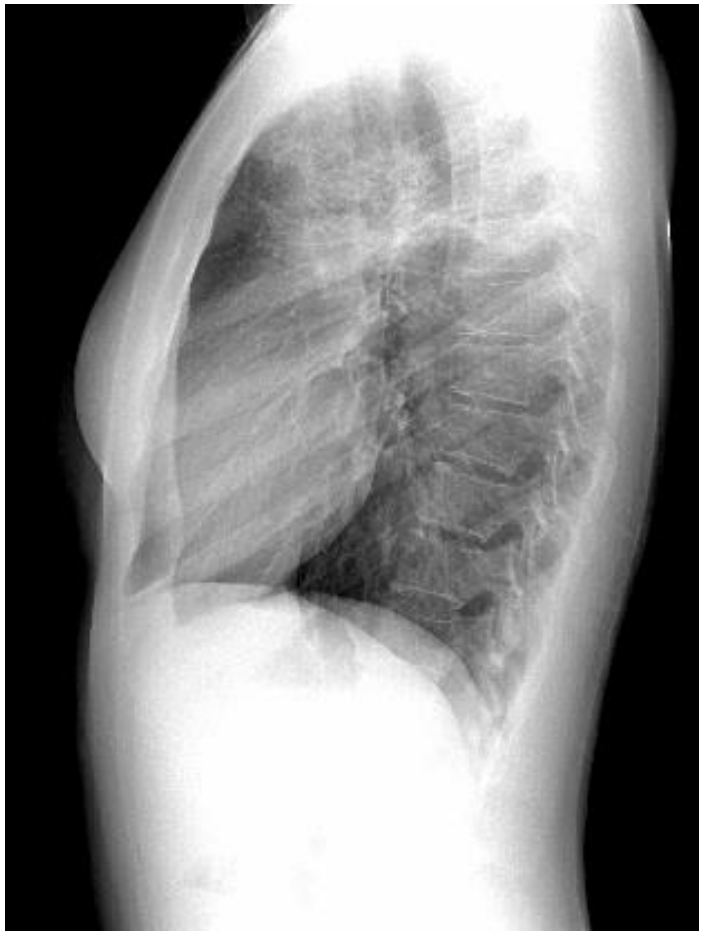
Initial CXR

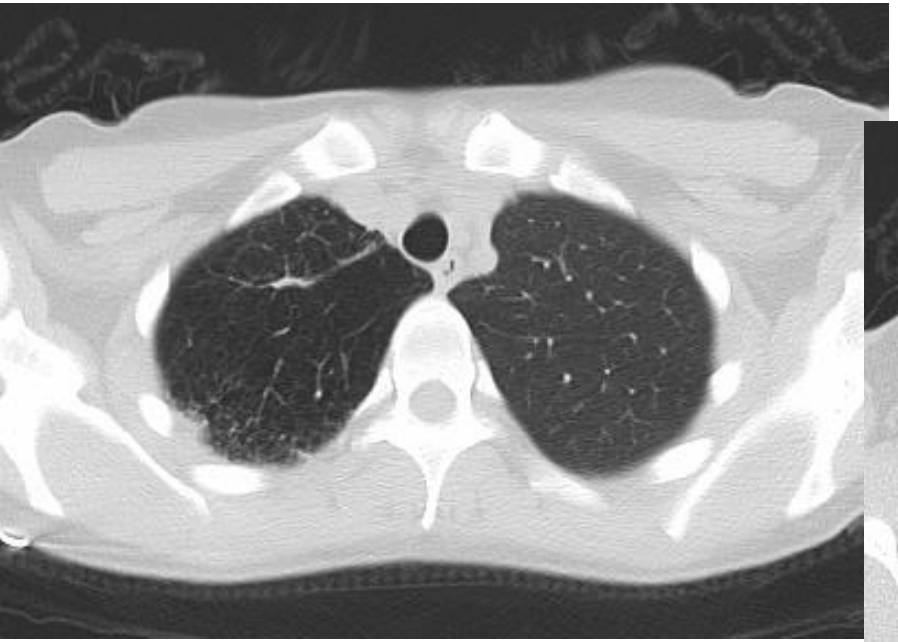


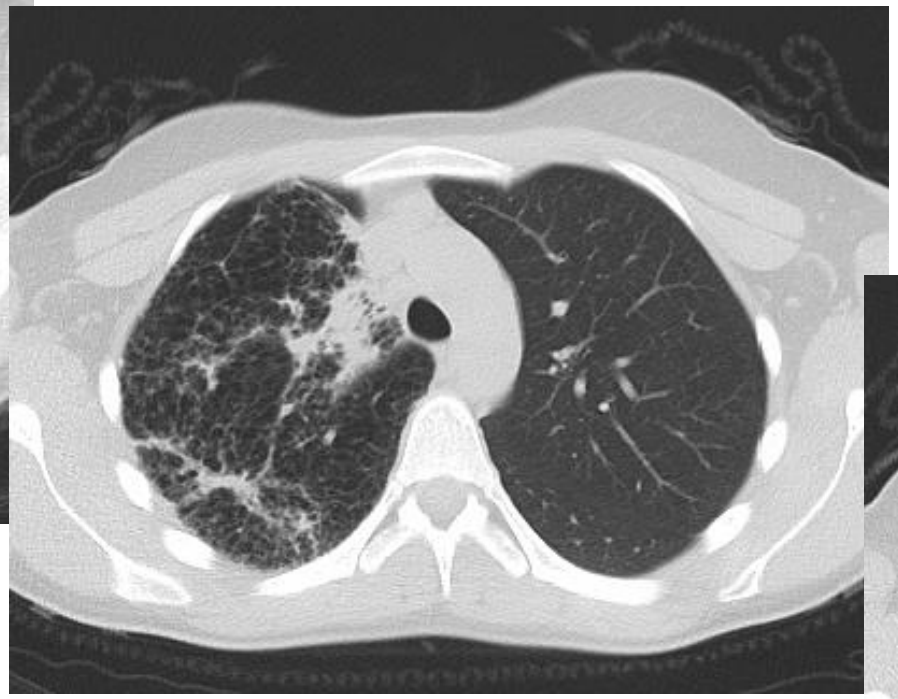


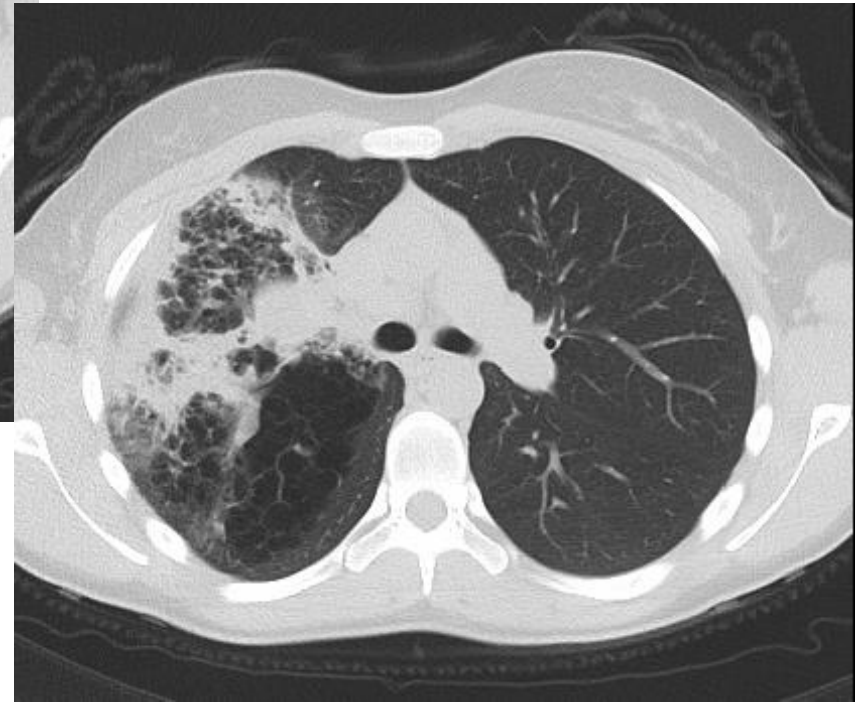
Initial evaluation (Thailand)

- Sputum x 1: afb smear negative
- 9/2016 BAL:
  - smear negative for afb
  - Routine cultures negative
  - Fungal cultures and serology negative
  - Cytology negative for malignancy
  - Meloidosis serology negative
- Started on empiric TB therapy Rifampin/Isoniazid/PZA/Ethambutol
- 2 month follow up: symptoms unchanged, AFB cultures negative
- 11/16 she elected to return to the US

Initial CT 11/2016



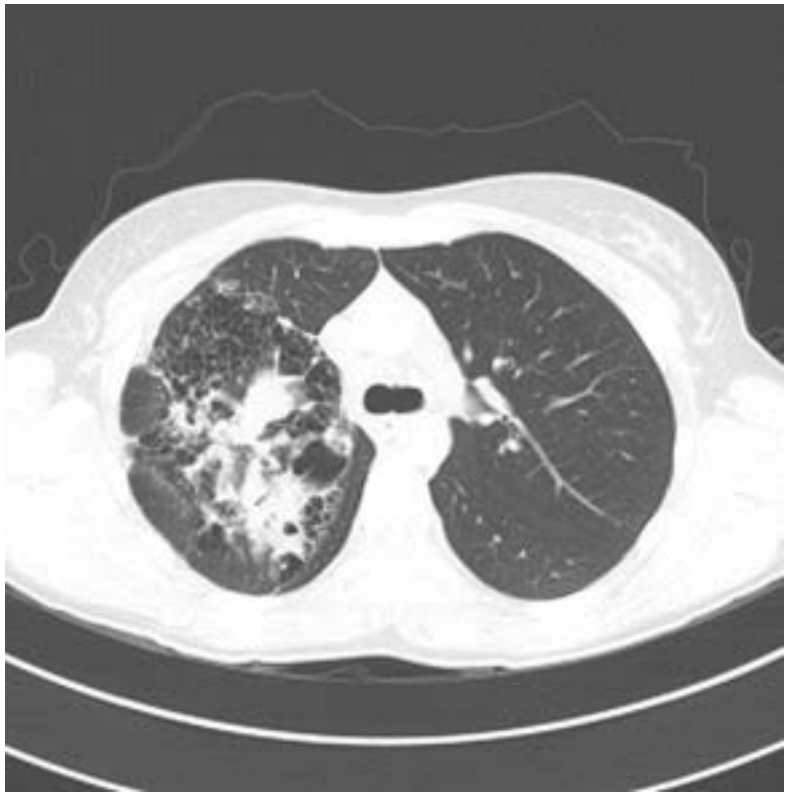




NJ Evaluation 10/2017

- Continued cough, productive

- CBC WBC 11.1, Hgb 11.7, Plt 338
- No eosinophilia
- CMP normal
- HIV negative
- Immunology evaluation normal
- Fungal serologies negative
- QFT negative

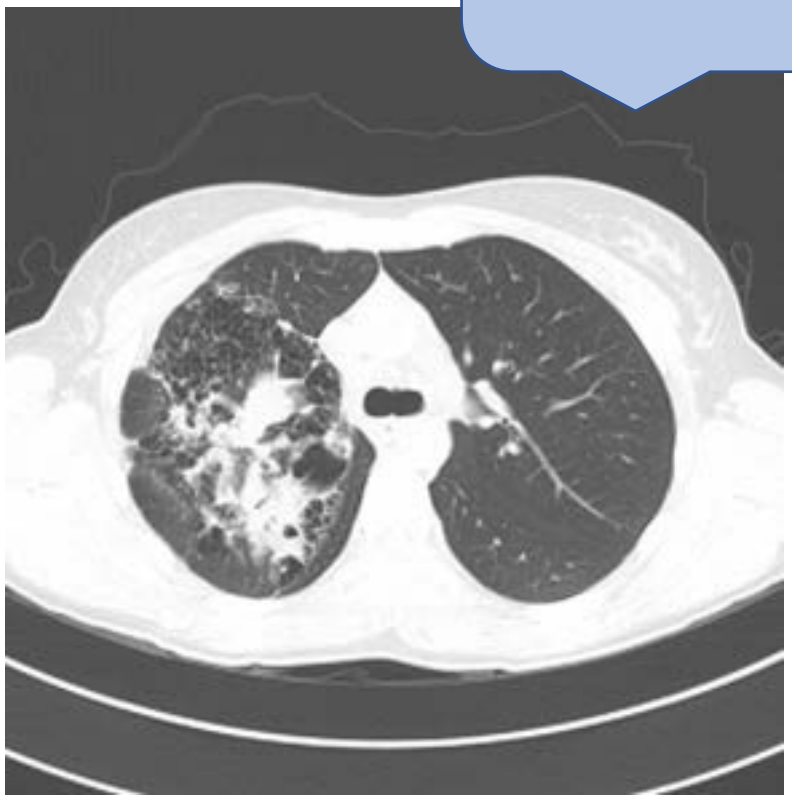


As an NTM suspect-What additional testing would be indicated?

1. Second bronchoscopy for repeat AFB cultures
2. Universal PCR on BAL fluid
3. Sputum induction x 3 for AFB smear and culture
4. Serum IgA antibodies against mycobacterial glycopeptidolipid (GPL) core antigen

NJ evaluation 10/2017

- BAL cell count: 94% neutrophils, 3% macrophage, 3% Lymph, 0 eosinophils
- BAL culture negative (bact/fungal/afb)
- BAL galactomannan negative
- 3 induced sputum: + *M. abscessus*



CT scan consistent with congenital abnormality: bronchial atresia

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ELSEVIER

Medicine and Infectious Diseases

Volume 28, Issue 12 , December 1998 , Pages 937-939

Effect of lidocaine (Xylocaine ®) on culture of tubercle bacilli in liquid medium

F. Evreux **, C. Lemort **, A. Hauchecorne **, C. Lacroix ***, A. Morel **

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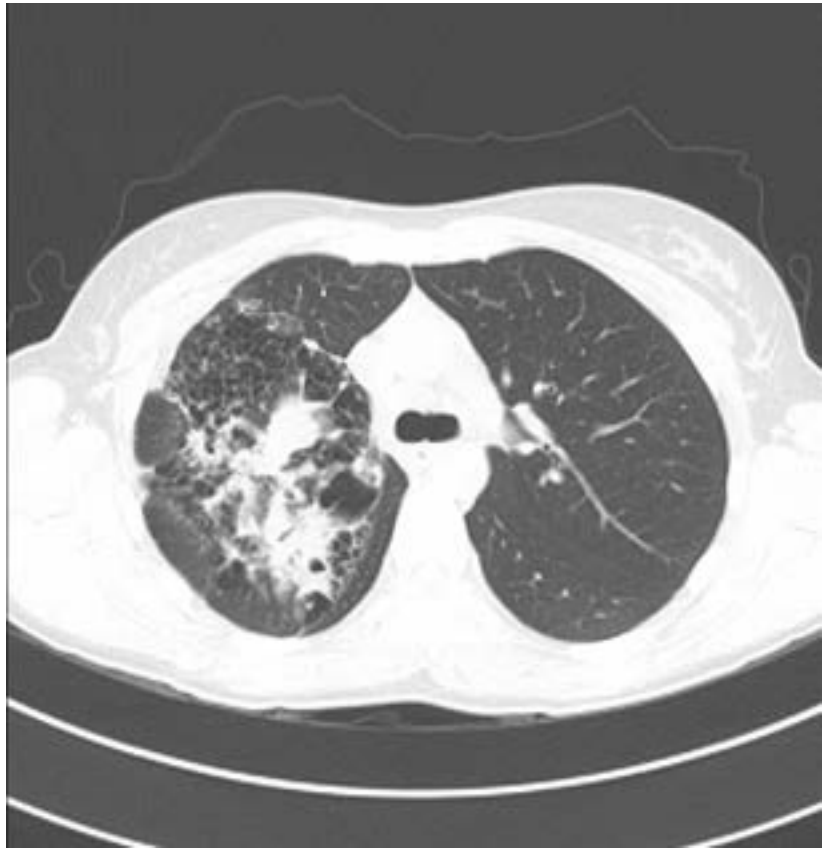
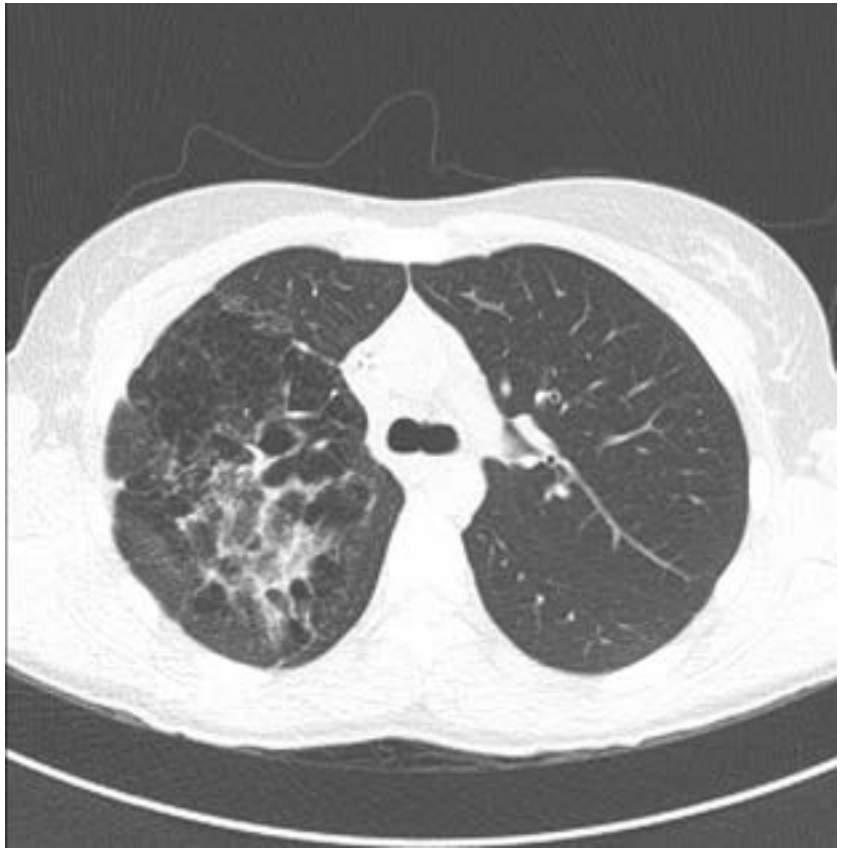
M. abscessus, subspecies *abscessus:* C28 sequevar



11/2017



1/2018

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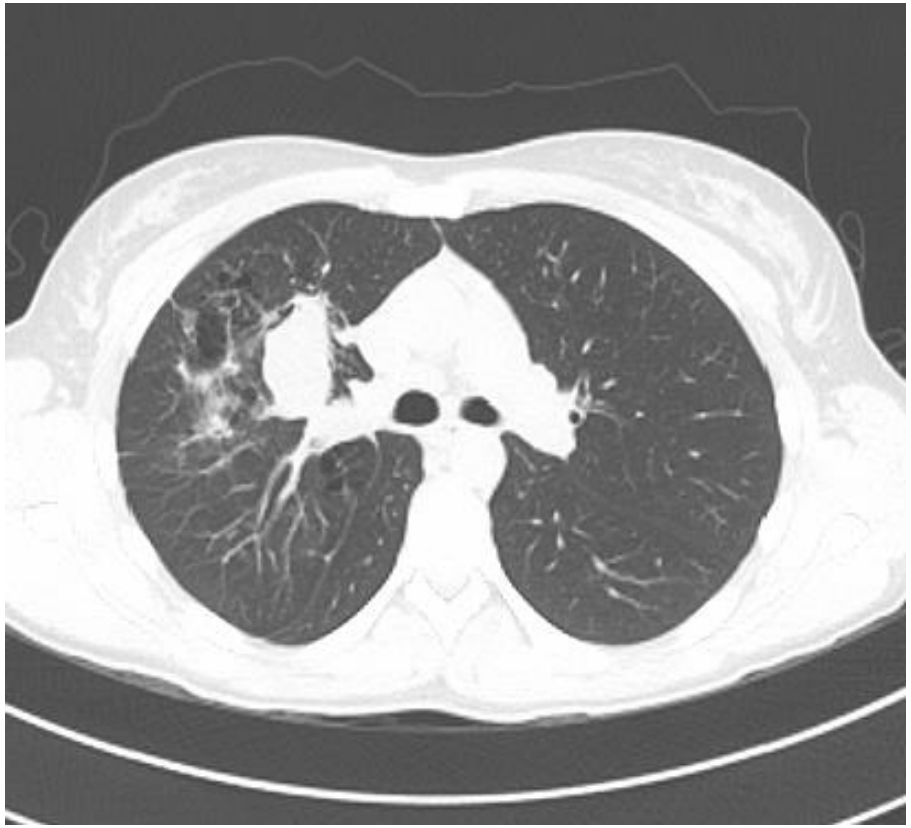
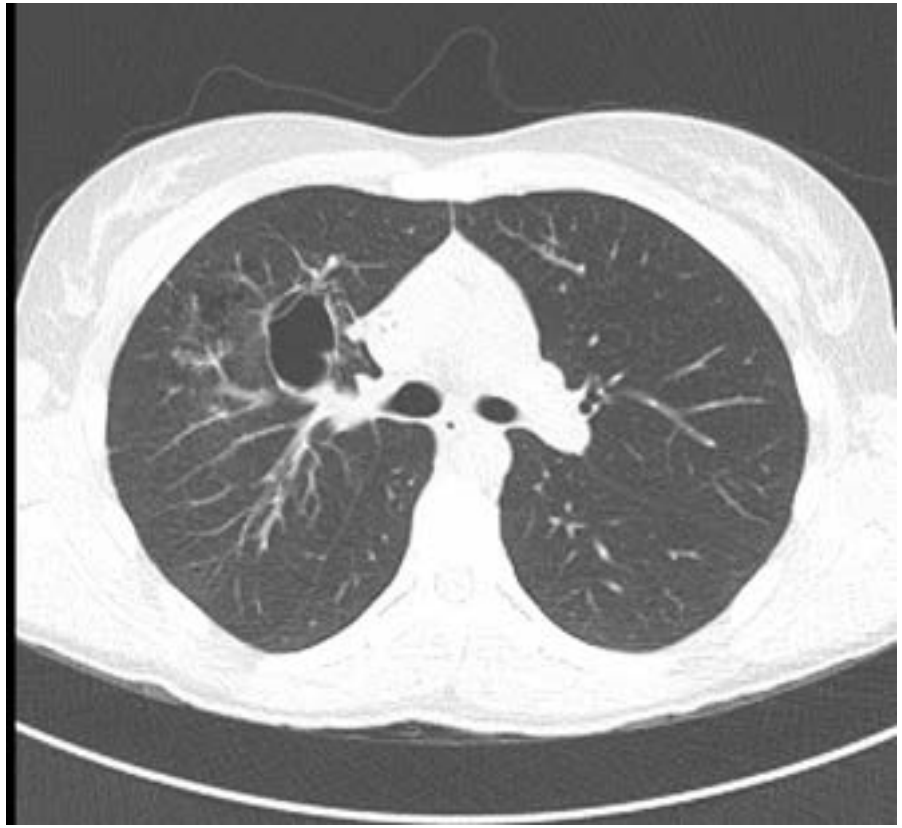
M. abscessus, subspecies *abscessus:* C28 sequevar



11/2017



1/2018

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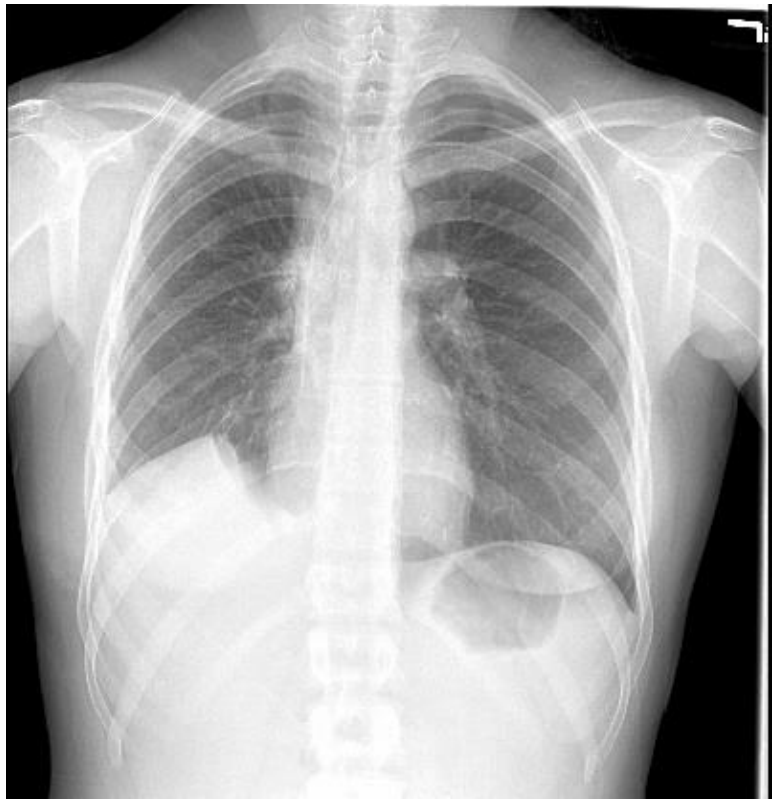
Follow up



- Aggressive IV + PO therapy
- Right upper lobectomy
- Completion of 12 months of negative cultures
- 3.5 years later, no evidence of recurrence

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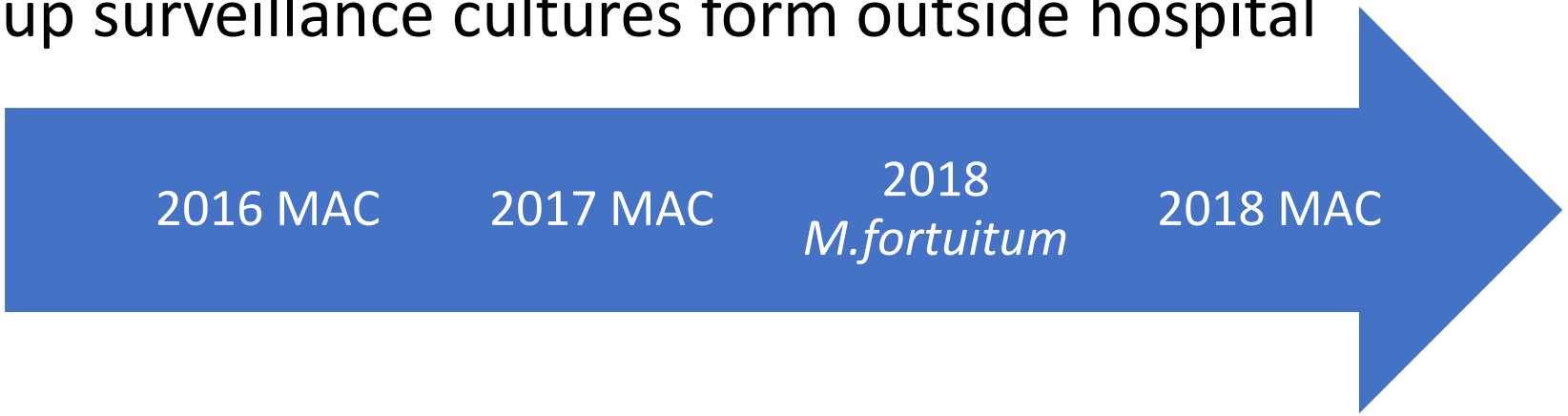
Case Four

- 64 year old female with chronic cough of 4 years
- Repeated courses of azithromycin for bronchitis
- 2014 AFB cultures +M. intracellulare, macrolide resistant
- Treatment at NJH with ethambutol/rifampin/moxifloxacin + IV amikacin
- RML, lingulectomy

Case Four

- 1/2016, she achieves 12 months of negative cultures and d/c therapy

- Intermittent cough, mild and stable
- Follow up surveillance cultures form outside hospital



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With these follow up cultures would you

1. Restart prior 4 drug NTM therapy
2. Start Azithromycin, ethambutol, rifampin (A/E/R) while waiting for susceptibility results
3. Order repeat imaging and start A/E/R therapy if her CT scan shows progression

Follow up

KEY POINTS

- Flares in symptoms over the years were attributed to pseudomonas aeruginosa infections and symptoms abate with antipseudomonal therapy.
- CT scan has remained stable now 5 years off therapy despite intermittent growth of different NTM species.
- Underlying bronchiectasis increases her risk of NTM-LD in the future
- Counseling includes: continued airway clearance, avoidance of immunosuppressive agents including ICS, environmental avoidance

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