Wisconsin State Laboratory of Hygiene

UNIVERSITY OF WISCONSIN–MADISON

Case Report

Alana Sterkel, PhD, SM(ASCP)^{CM}
Assistant Director
Communicable Diseases
Wisconsin State Laboratory of Hygiene

Case History

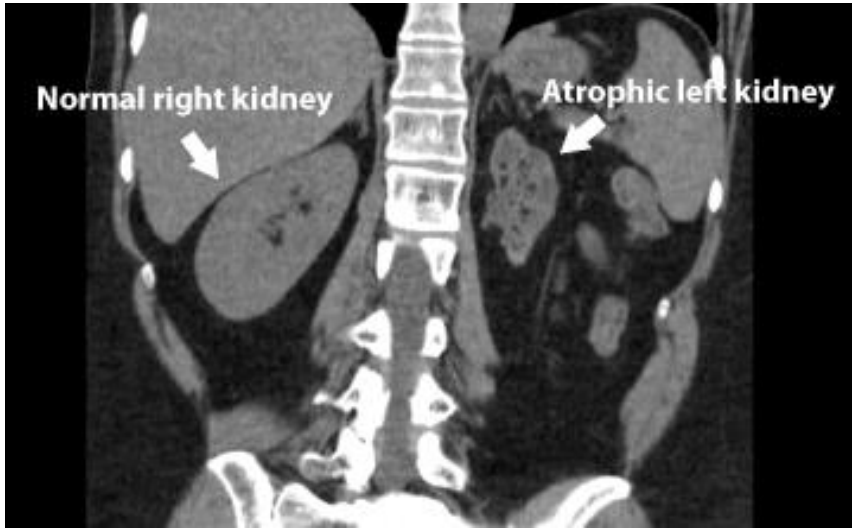
- 70 year old man presents with acute encephalopathy
  - Sudden decrease in brain function
- History epilepsy
- End Stage Renal Disease (ESRD)
  - Double Kidney transplant last year
  - Immune suppressed

Additional History

- History of Crohn's disease
  - Has undergone multiple small bowel resections
  - Suffers from short gut syndrome
  - Diarrhea, weight loss, malnutrition, and dehydration
- Reports abdominal pain

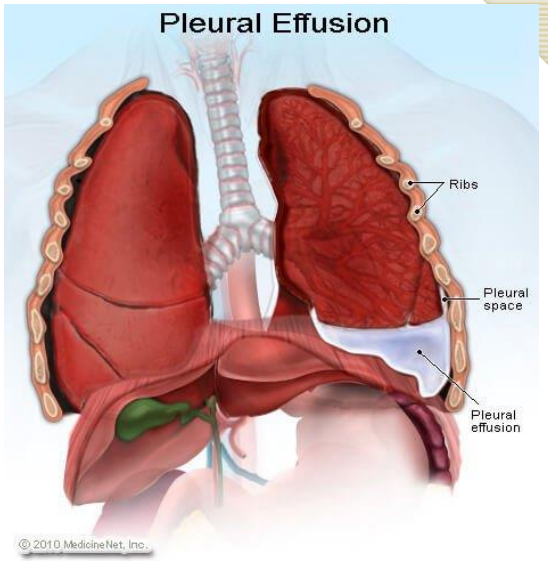
Abdominal CT Findings

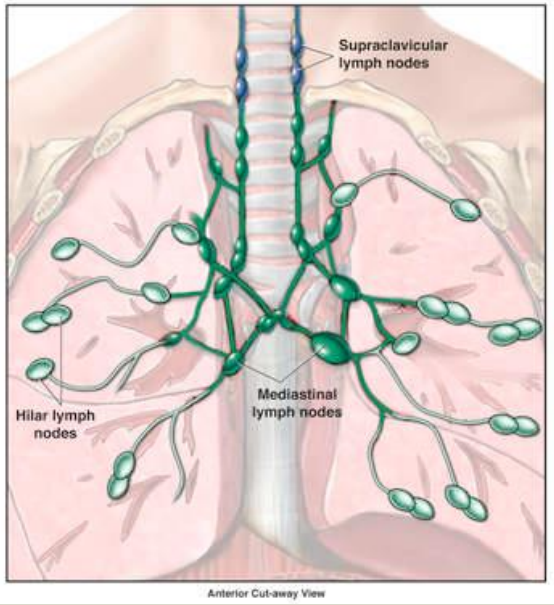
- Natural kidneys still in place and atrophied
- Numerous enlarged mesenteric lymph nodes
- Numerous surgical staples make evaluation challenging
- Pleural effusion just visible, chest CT needed



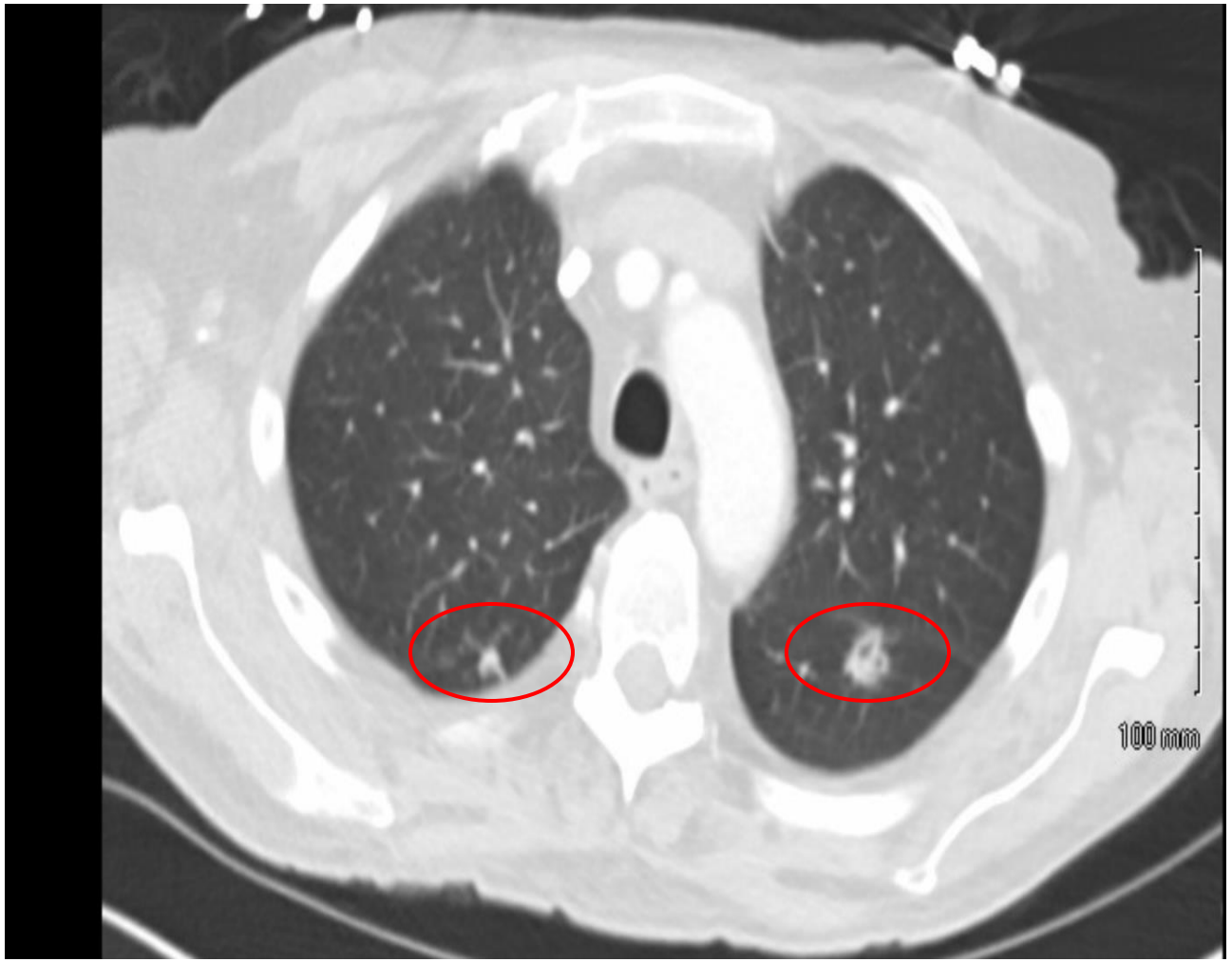
Chest CT

- Small bilateral pleural effusions
- Atelectasis in both lower lobes
- Single enlarged right hilar lymph node
- Multiple soft tissue nodules



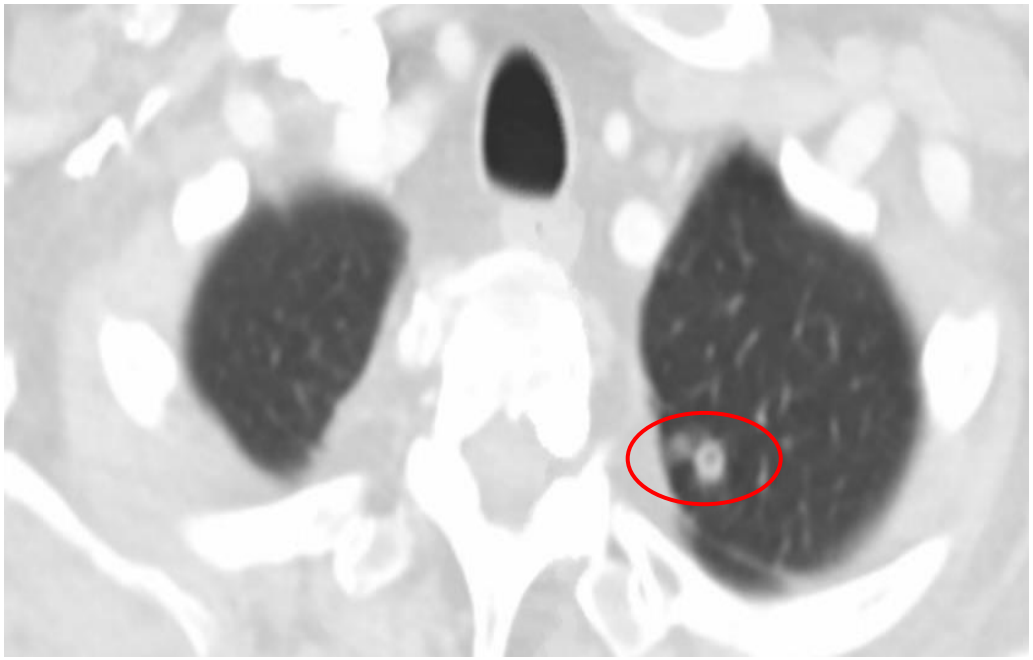


Chest CT Findings



Chest CT Findings

- Multiple bilateral lung nodules not seen in previous CT (2-15 mm)
  - "central cavitation"
  - "This may represent metastatic disease"



Biopsy of the Lymph Node

- Sent for mycobacterial smear and culture
- **Smear AFB positive (4+)**
- Patient placed in isolation for TB
- Reflexed to TB/MAC PCR
  - Negative for both
- Culture set up in MGIT broth and 7H11 agar
  - MGIT negative at 42 days

NTM Cheat Sheet

Species	Lung disease	Lymphadenitis	Disseminated disease	Culture requires
M. kansasi	yes	?	yes	
M. xenopi	yes	not really	bone/joint	growth at 45 deg
M. haemophilum	yes, rare	yes skin lesions common	yes, rare	add ferric ammon citrate or hemin; 28-30 deg C
M. szulgai	yes, often cavitary	yes, rare	yes, rare	
M. genavense	yes, rare	yes, rare	yes, rare	add Mycobactin J
M. malmoense	yes, rare in U.S.	yes, rare in U.S.	yes, rare in U.S.	
M. marinum	not likely	not likely	not likely	need to grow at 30-33 C
M. simiae	unlikely, reported	?	unlikely, reported	

Then…

- Small colonies on primary 7H11
  - Does not subculture
- Call from clinician suspecting a certain NTM
- Subculture to 7H11 supplemented with Mycobactin J
- Culture for 2 weeks at 37 C
  - Kinyoun Stain = medium AFB
  - MALDI = No peaks
  - 16S sequencing =

    M. genavense (100%)

What do you think?

A) *M. avium*

B) *M. haemophilum*

C) *M. genevense*

D) *M. szulgai*

Based on Dr. suspicion

- Subculture to 7H11 supplemented with Mycobactin J

- Tiny smooth colonies after 2 weeks at 37 C
- Kinyoun Stain = medium AFB
- MALDI = No peaks
- 16S sequencing =

What do you think?

A) *M. avium*

B) *M. haemophilum*

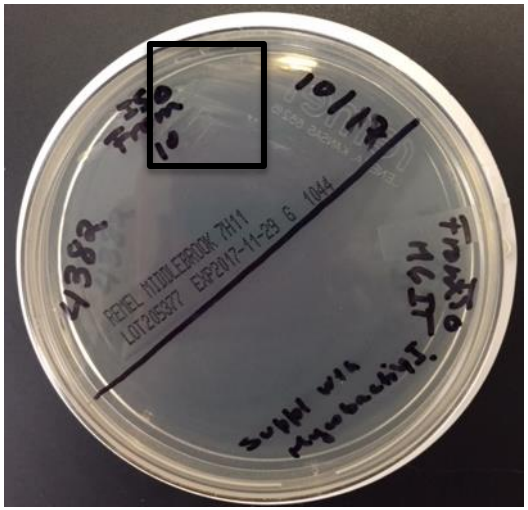
C) *M. genevense*

D) *M. szulgai*

M. genavense

M. genavense

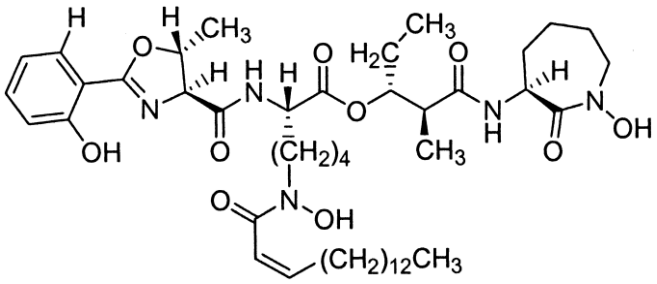
- Tiny, transparent, smooth, non-photochromogenic colonies
- Slow growth within 3–12 weeks at 31 -42˚ C
- Fails to grow on L-J and 7H11 medium unless supplemented



How we got it to grow

- 7H11 supplemented with 2 ug **Mycobactin J**
  - Siderophore (Iron chelator)
  - Purified from *Mycobacterium avium* subsp. *Paratuberculosis*

Vs. *M. haemophilum* requires iron (hemin)



Schwartz BD, De Voss JJ. *Tetrahedron Letters*. 2001

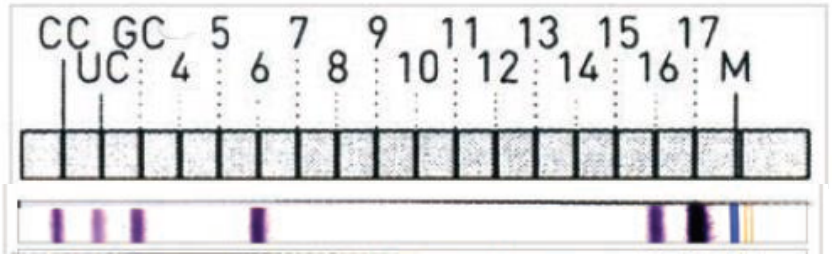
Bottger E, Hirschel B, Coyle M. *Inter J Sys Bact*. 1993

Identification

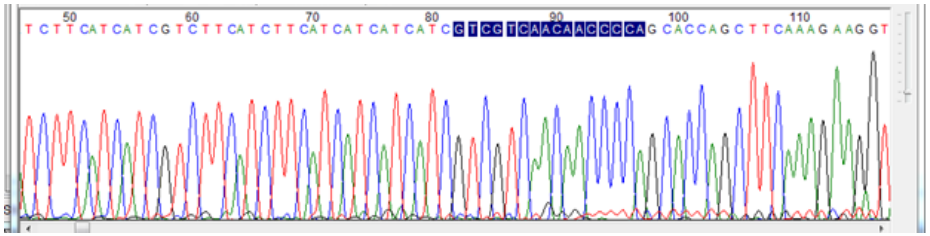
- Niacin and Nitrate reduction negative
- MALDI TOF

- Line Probe Assay

Line Probe Assay



- Unique 16S rDNA sequence



M. genavense

- Presents very similar to MAC
- Associated with enteritis, genital infections, soft tissue infections, and lymphadenopathy
- In HIV positive and other immune compromised individuals
- Causes up to 12.8% of all NTM infections in AIDS patients
- Susceptible to streptomycin and rifampicin
- Resistant to isoniazid and ethambutol

M. genavense

- Isolate in 1991 from the blood of an AIDS patient in Geneva, Switzerland
- Officially recognized in 1993
- Most common cause of mycobacterial disease in parrots and parakeets

Summary

For immune compromised patients with samples that are smear positive, MGIT negative, and have colonies that don't sub to 7H11,

Consider *M. genavense* and try supplementing with Mycobactin J

Communicate with the lab!