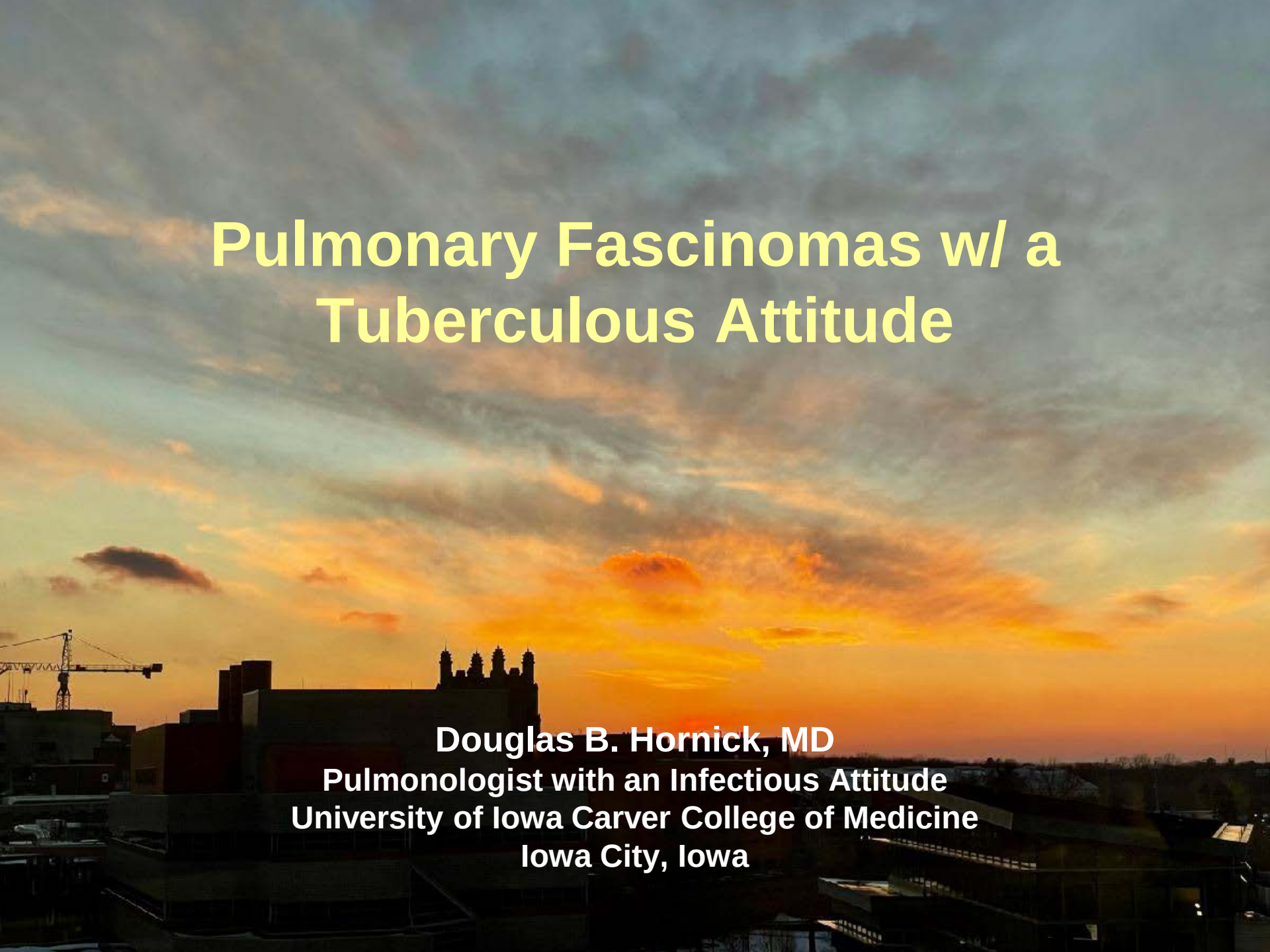

Pulmonary Fascinomas w/ a Tuberculous Attitude

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Objectives

- Review challenging and atypical presentation of pulmonary TB
- Discuss diagnostic approach and treatment that seem most appropriate
- Help me & (some) learners identify missed opportunities

Disclaimers

- I am from Iowa…More Hogs than people…& TB
- TB has remained a hobby since medical school
- Purpose: share unique cases, which I found educational
- I encourage your input…Learn from each other

Cases…

- Don’t be so negative
- Xpert by a non-Expert
- NTM dancing on the edge

Healthy but abnormal…

40 yo M referred to lung CA clinic to eval incidental RUL nodules seen on chest CT 5 months prior. No symptoms

PMH: Gallstone pancreatitis 6 mos prior; Hyperlipidemia; DM II (on insulin, HbA1C 8.3-15, I&D diabetic foot); Ruptured appy/drained 5 years prior

SH: No EtOH, Smoking, Illicit drugs; Computer Engineer; Came to US from India >20 yrs ago; HIV neg

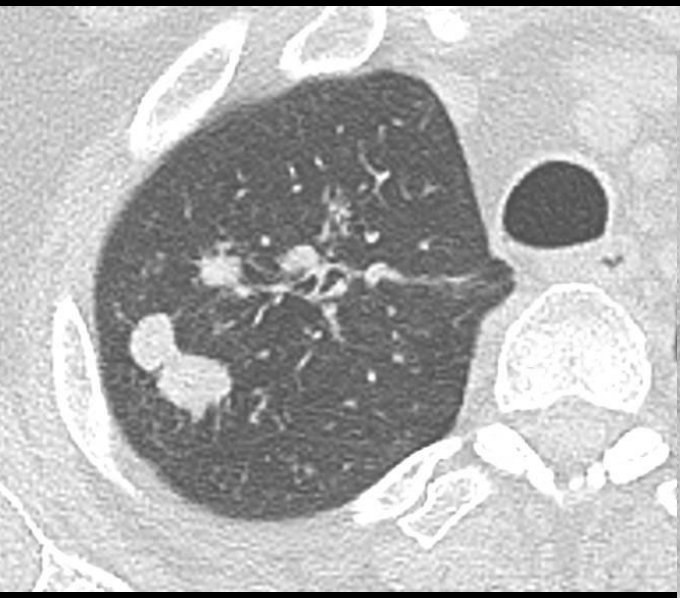
Exam unremarkable

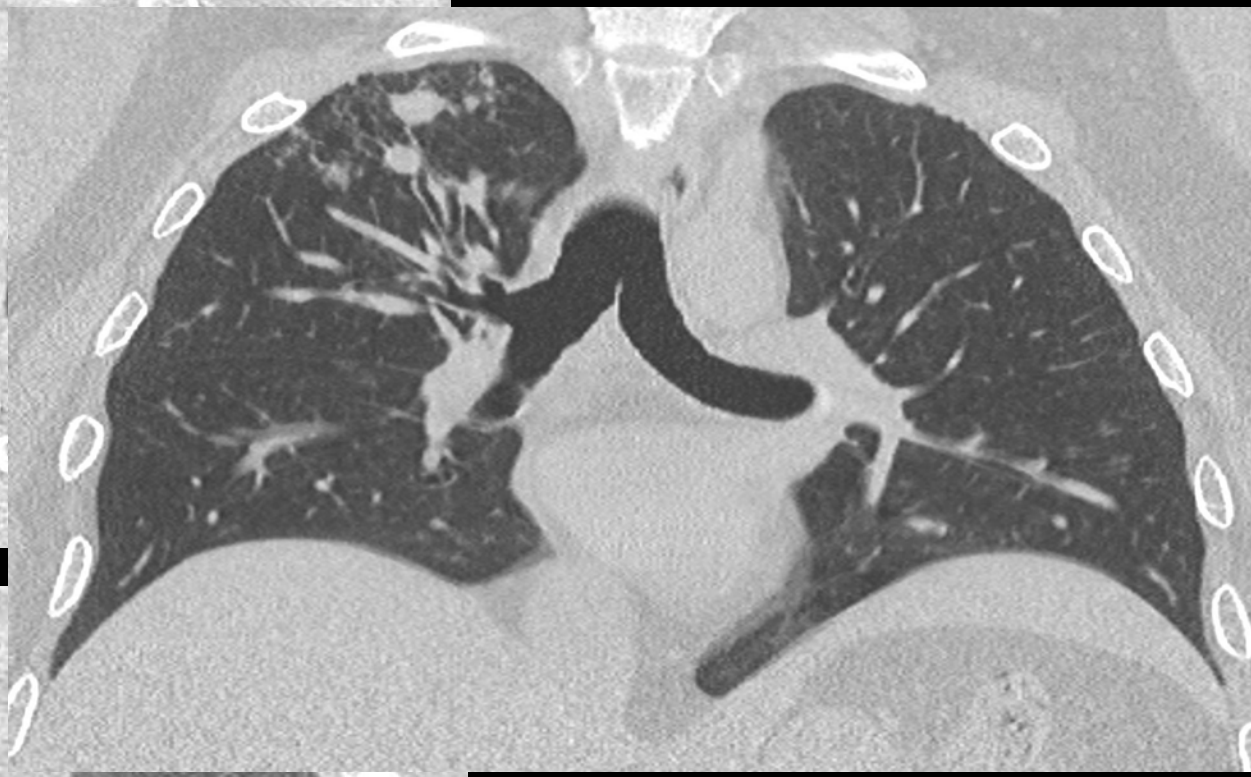
Chest CT: RUL nodules unchanged from 5 months previous, but concern for infection > malignancy

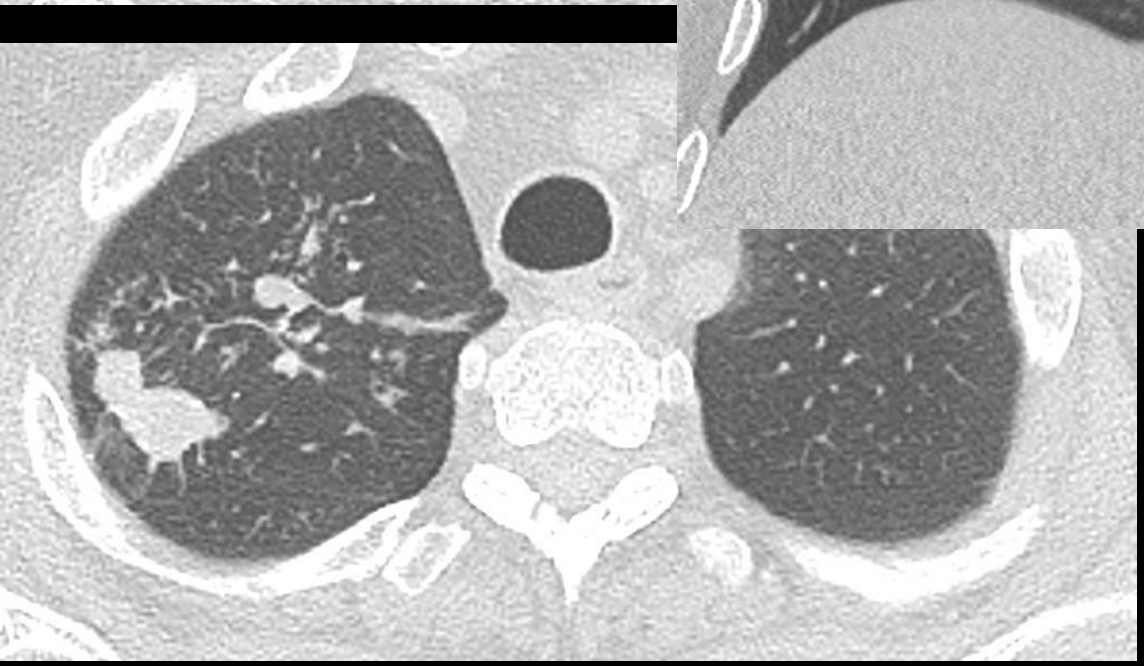
QFT-G neg; Histo & Blasto Ag/serology negative

AM sputum for AFB x3 sent…

All AFB smear neg, 1/3 grows *M. gordonae*
MD calls me: Is this NTM infection?







Non-Calcified nodules x4 RUL
Adjacent tree-in-bud nodularity
No mediastinal adenopathy
No appreciable evolution x5 mos

IGRA Negative (or Positive?)

	Ref Range & Units	1 mo ago
QuantiFERON-TB Gold Plus	Negative	Negative
The reference range for the 'TB1 Ag minus Nil ... and 'TB2 Ag minus Nil Result' is an Interferon ... level <0.35 IU/mL.		
TB1 Antigen minus Nil Result	IU/mL	0.97
TB2 Antigen minus Nil Result	IU/mL	0.97
Mitogen minus Nil result	IU/mL	0.97
Nil	IU/mL	7.20

Package Insert Interpretation

Nil (IU/ml)	TB1 minus Nil (IU/ml)	TB2 minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)*	QFT-Plus Result	Report/interpretation
≤8.0	≥0.35 and ≥25% of Nil	Any	Any	Positive†	*M. tuberculosis* infection likely
	Any	≥0.35 and ≥25% of Nil			
	<0.35 or ≥0.35 and <25% of Nil	<0.35 or ≥0.35 and <25% of Nil	≥0.50	Negative	*M. tuberculosis* infection NOT likely
	<0.35 or ≥0.35 and <25% of Nil	<0.35 or ≥0.35 and <25% of Nil	<0.50	Indeterminate‡	Likelihood of *M. tuberculosis* infection cannot be determined
>8.0§	Any				

Other Interpretations

- Nil at 7.2, much higher than norm…lymphs constitutively cranking out lots of IF-γ.
  PI: Nil >1 very uncommon across low risk, mixed risk & culture positive populations.
- Mitogen response = 8.17, minimally > nil…lymphs maxed out at baseline, minimal additional IF-γ when stimulated. PI: Healthy lymphs hit >10 IU/ml post mitogen stimulation
- Both TB1 & TB2 produced 8.17 as did mitogen control….If TB1 & TB2 tubes equal to the positive control, could test be considered positive?
- Alternatively, Lymphs little left to give under any stimulus, one can't rely results of stimulation…However PI shows mitogen-nil < 1.0 happens only in the group that has active TB…With my TB clinician hat on, this suggest it might turn out to be active TB

More Questions than Answers

- How many have seen this type of negative QFT-G result?
  How many would repeat the QFT-G?
- RUL pulmonary nodules/Tree-in-Bud…Is this a case of smoldering subclinical TB?
- What would you do next?
- Patient refused to return for Bronch/BAL
- …I think I will meet him some day

Cases…

- Don’t be so negative
- Xpert by a non-Expert
- NTM dancing on the edge

TM, TB & MUM

25 yo asymptomatic M w/positive IGRA (screening) & abnormality flagged on CXR. Denies BCG, family w active TB, exposure to anyone w/ TB

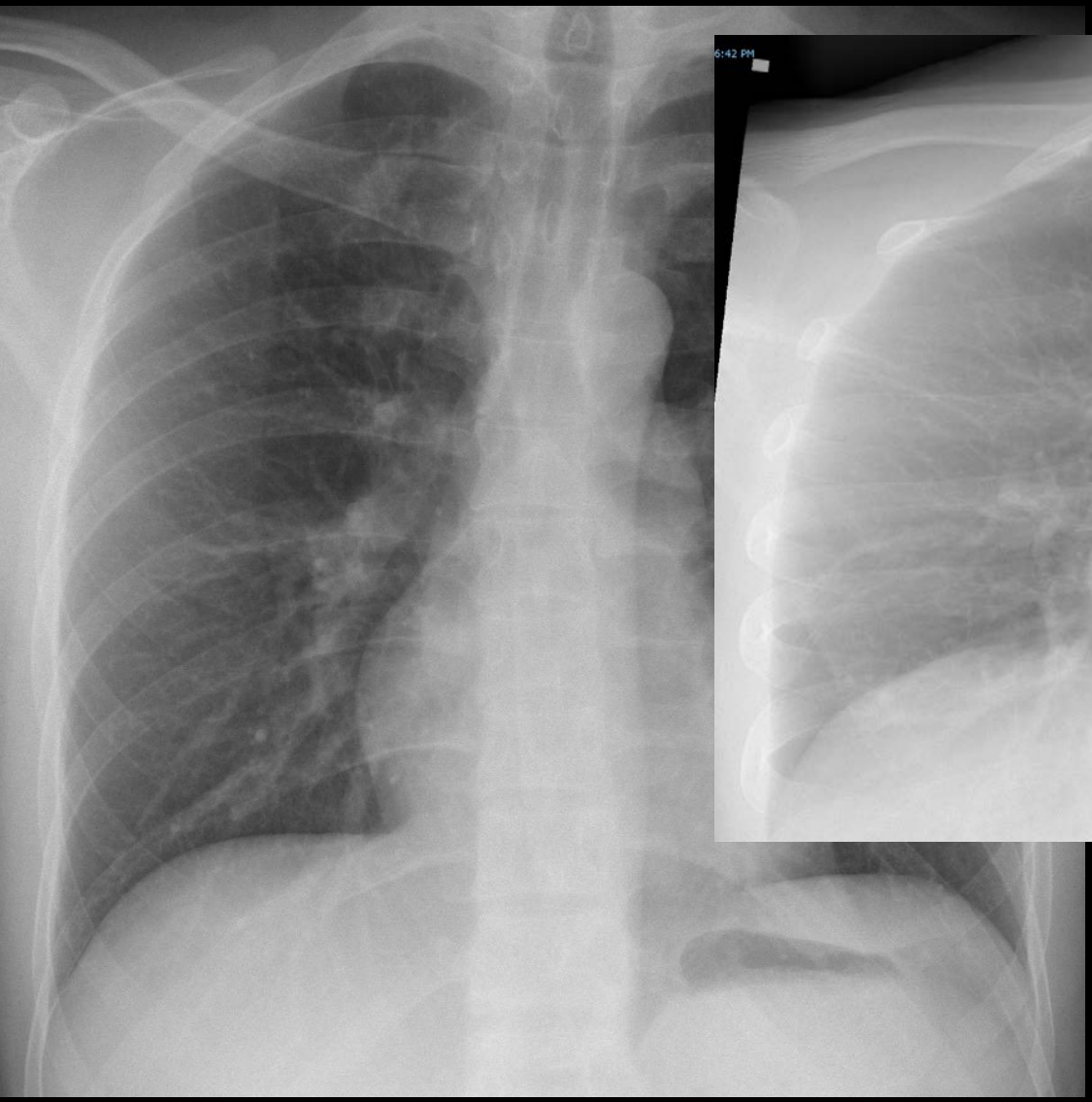
PMH: COVID19 6 mos prior, no residual. Fully immunized

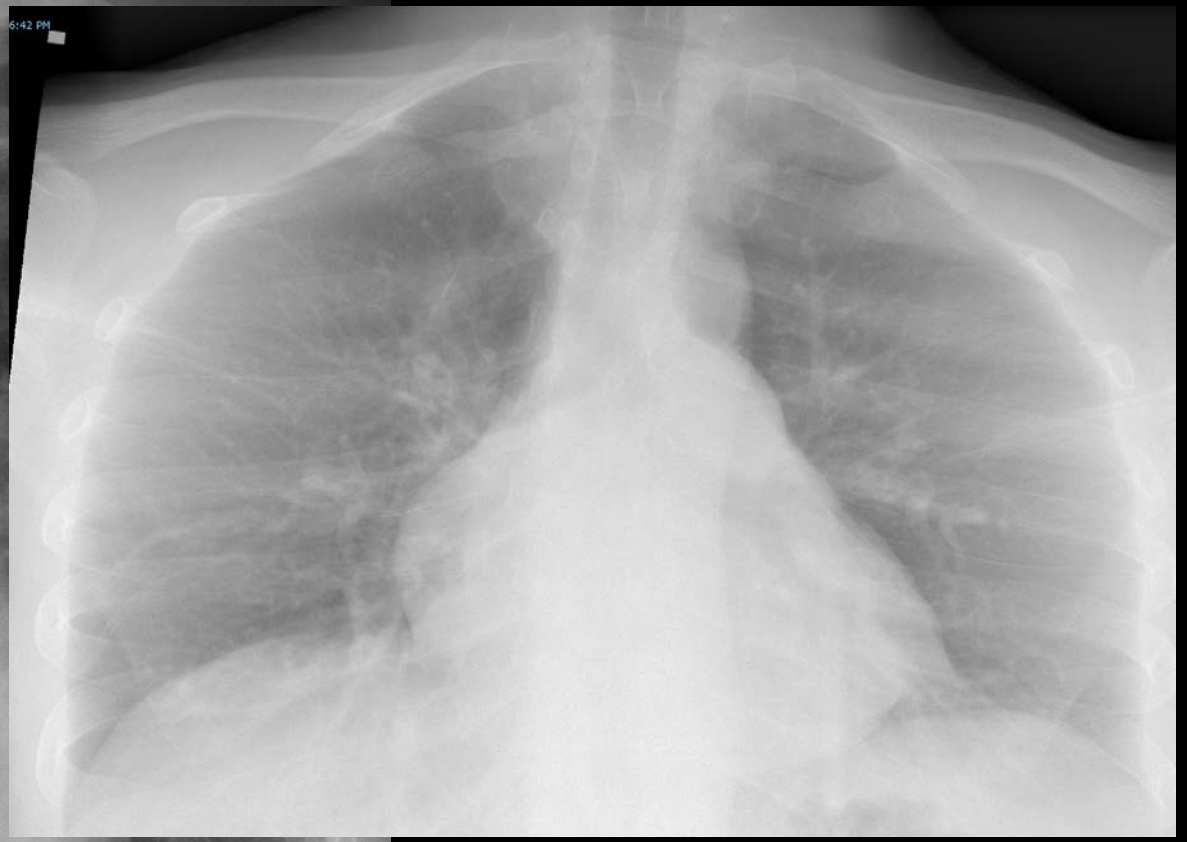
SH: No EtOH, Smoking, illicit drugs; Business graduate student; Came to US from Myanmar fall 2021; HIV neg

Exam unremarkable

3 AM sputa submitted: AFB smear neg, 2 Xpert neg (ultimately 1 culture grew *M. arupense*)

Chest x-ray…





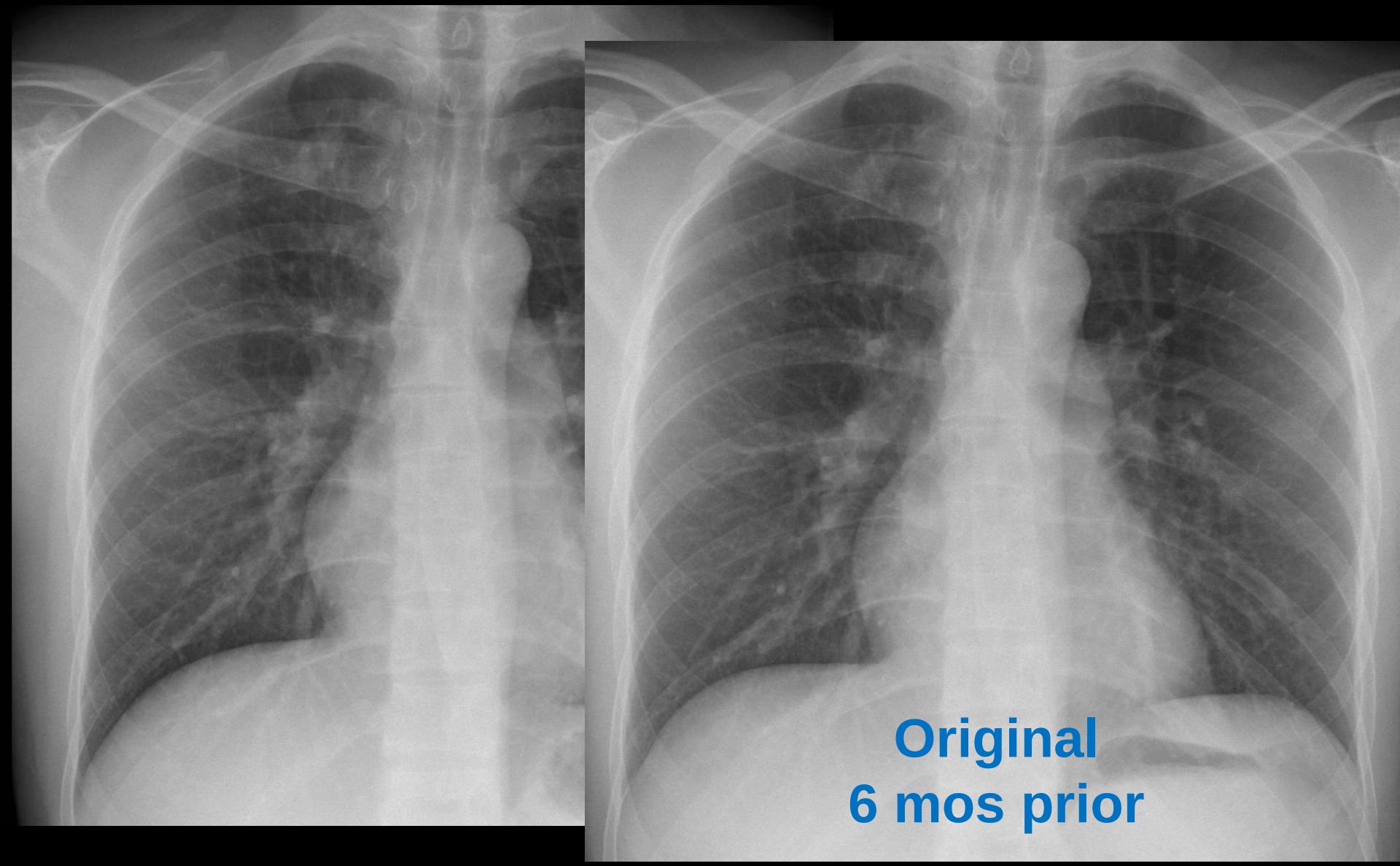
Non-Calcified RUL 3.5 x 2 cm mass a/w tip of 1st rib (?)
Apical Lordotic view, no longer visible…vascular asymmetry (?)
No mediastinal adenopathy

Subsequently…

- Dx: LTBI
- Rx: RIF x 4 months
- Month 4: asymptomatic random bloody cough (neg COVID-19/ RVP PCR)

What now?

- Isolation, sputum AFB smear, Xpert & culture x 3
- Bleeding leading to cough once every few days
- Chest X-ray…


Original
6 mos prior

More data…

- All 3 sputa AFB smear negative
- 2nd Xpert specimen: TB pos & RIF resistant (others neg)

What now?

- MDDR (CDC): Insufficient DNA in sample
- 2nd week: No symptoms, rare bleeding & 3 AFB smear, Xperts negative; Nothing growing in early cultures
- Low bacterial load…could this be false RIF resistance?

Xpert by a Non-Expert

- Ct = Cycle Threshold
  - # PCR cycles to amplify MTB DNA to detectable level
  - Semi-quantitative cycle # (eg, Hi Ct<16, Vy Low >28)
- Overlapping PCR probes (A-E) target 81 bp Rifampin Resistance Determining Region (RRDR) of *rpoB* gene
  - Ct variation <2 for all 5 probes: TB detected
  - Ct diff hi & low probes >4: *rpoB* mutation, RIF resistant
- This patient's probes:
  - A 31.4, B 30.6, C 30.6; Valid if Ct not >39
  - D 31.3, E 0.0 (no threshold crossing…); Valid if Ct not >36
  - MTB pos: Ct w/in valid range & smallest delta Ct any probes <2
  - Delta hi and low (30.6 – 0) > 4…RIF resistant
  - Does E 0.0 count? Meets only one of 2 criteria to be called Indeterminate

Presumed TB, Possibly MDRTB

Treatment initiated based on MDRTB guidelines

- Linezolid
- Moxifloxacin
- Cycloserine
- Bedaquiline
- Clofazimine

Awaiting culture & subsequent MDDR

Cases…

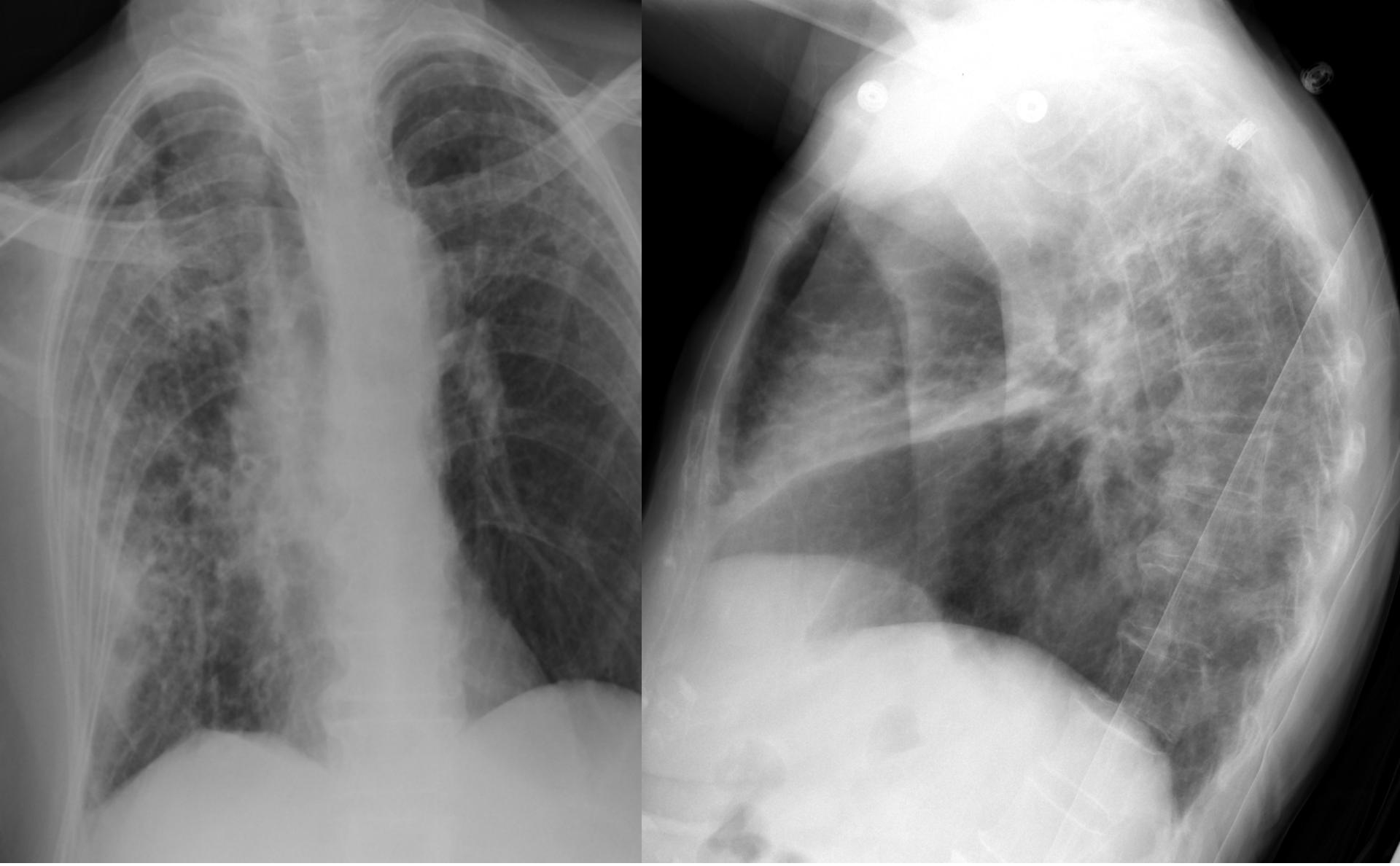
- Don’t be so negative
- Xpert by a non-Expert
- NTM dancing on the edge

Lady doth protest…

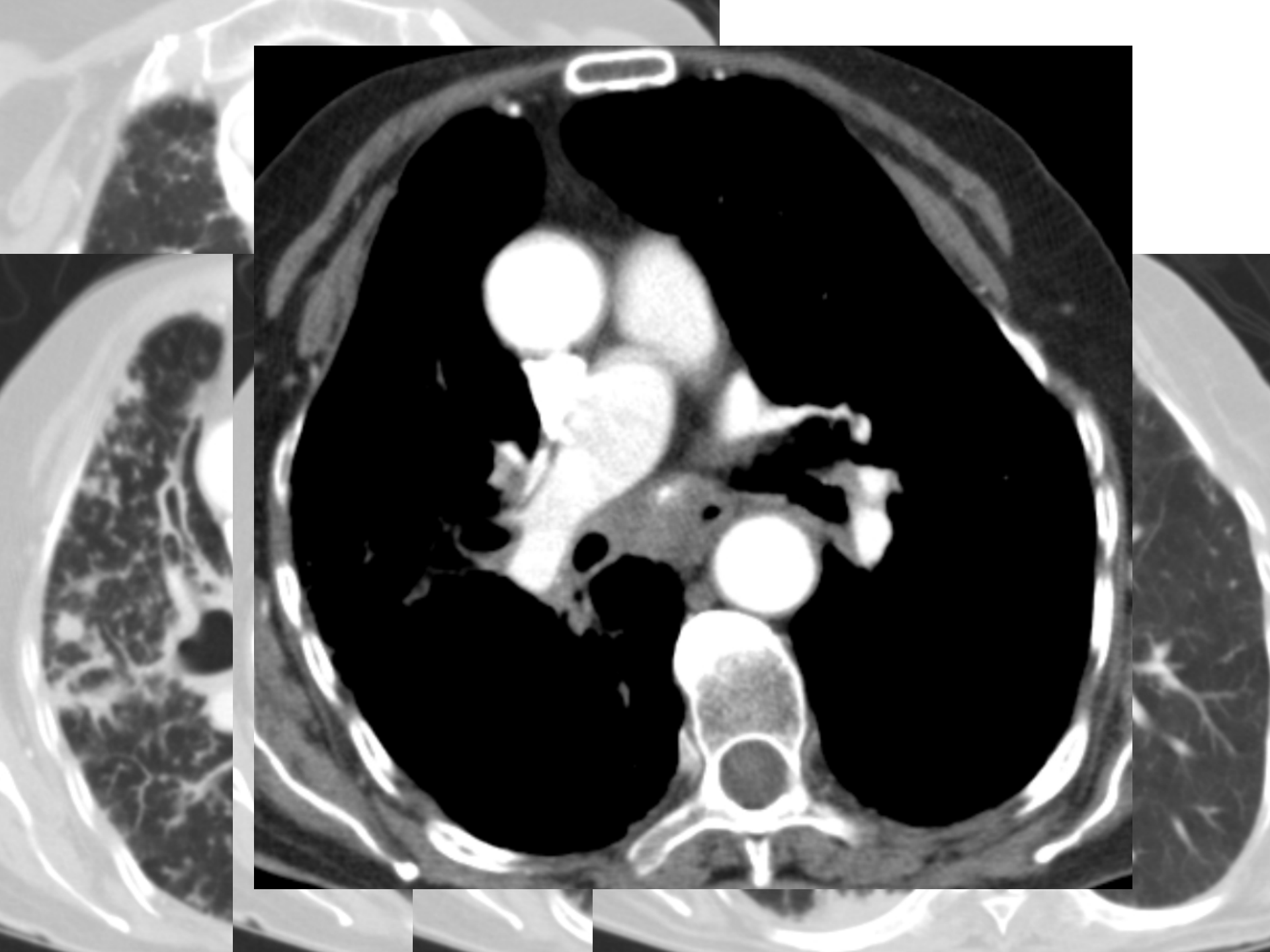
81 yo woman with gradual deterioration over 6 months since prior hospitalization for R sided pneumonia

- Persistent, non-productive cough, poor appetite, weight loss ~ 10#, fatigue, no fevers or night sweats…Primary MD started Prednisone 20 mg daily 2 weeks previous
- Admitted from ER again for RML CAP: moxifloxacin IV
- PMH: Hypertension; Meds: Metoprolol
- SHx: Life long nonsmoker, No EtOH/substance abuse/HIV RF
- FHx: Sibling died from Pancreatic Ca
- Exam: Cachectic, frail, elderly woman w/ no other remarkable findings
- Labs: WBC 12.6

- X-rays…



Radiologist comment besides RML disease, stable findings compared to Chest x-ray 6 months earlier…



Summary of Radiographs

- Chest x-ray stable abnormal, other than progressive RML changes
- Chest CT:
  - No cavity in upper lobes (or anywhere)… however evidence for nodular bronchiectasis
  - RML & RLL nodular & atelectatic bronchiectasis w/ compensatory hyperinflation of L lung
  - Mediastinal LN enlarged…1.5 x 1.5 cm sub-carinal LN (not calcified, contrast enhancing vessel w/in)

…More Data

TST negative & sputum AFB smear positive

Most likely diagnosis?

Nodular Bronchiectasis in elderly female…

Scenario 1: Bronchiectasis (nodular), no cavity, AFB smear positive, PCR pending

- Isolate in home and initiate TB treatment, OR
- Await PCR result, then treat accordingly, OR
- Initiate MAC treatment, OR
- Call pulmonary for bronchoscopy, OR…

What about?...

TST negative & sputum AFB smear positive

Most likely diagnosis?

Nodular Bronchiectasis in elderly female…

Scenario 2: Bronchiectasis (nodular), no cavity, AFB smear positive, PCR negative

- Isolate in home, initiate TB treatment, await more data, OR
- Anticipate MAC, expand bronchial clearance, improve nutrition, initiate guideline based treatment for MAC, OR
- Call pulmonary for bronchoscopy, OR…

Actual story: Hispanic female (IA x 9 yrs), PCR & culture pan-susceptible *M tuberculosis,* started HRZE plus Enhanced nutrition & Bronchial Clearance Improving…

…More Data

1st & 2nd month AFB sputum smear/culture neg, then

3rd month AFB smear neg, culture positive, PCR neg:

- Patient doing well, culture grows MAC
  - Continue TB Rx & ignore MAC, OR
  - Continue TB Rx & expand bronchial clearance (ie, add neb 7% NaCl), OR
  - As above & add macrolide, OR
  - Call pulmonary for bronchoscopy, OR…

- Patient doing well, culture grows *M abscessus* subsp *abscessus*
  - Continue TB Rx & ignore NTM, OR
  - Continue TB Rx & expand bronchial clearance, OR
  - As above & add guideline based Rx for M abscessus, OR
  - Call pulmonary for bronchoscopy, OR…

On the Edge: TB <--> NTM

- Few references…Most are laboratory analysis of co-cultures TB w NTM & minimal clinical detail
- Differentiating TB from NTM cavitary disease utilizing CT image analysis tools promising (Yan et al *BMC Pulm Med* 22(4) 2022)
- How common is non-cavitary TB among patients with bronchiectasis (nodular)?
  - A/w regions where TB more highly endemic?
  - Consider lab cross-contamination
  - Other factors?
- Active TB on treatment & NTM isolated from sputum
  - Few references…Most are laboratory analyses of co-cultures TB & NTM with minimal clinical detail
  - Cavitary cases, TB Rx not altered. Afterward f/u recommended, progression rare…
  - In bronchiectasis, is this more likely co-infection? Manage differently than cavitary?