
# Case Presentation

Adarsh Vangala PGY5

# Initial Presentation

59 year old woman with history of Sjogren's, htn, not previously on any medications presenting for 2 weeks of dyspnea

# Initial History

- No recent travel
- No sick contacts
- Husband, children without significant symptoms
- Afebrile
- no cough/runny nose
- No resolution with Azithromycin for CAP from outside urgent care
- Past hx of htn, controlled dm2 (a1c 6.2%)

# Initial Evaluation

Vitals WNL

No oxygen requirement

| | | |
|---|---|---|
| WBC | 10.5 | 8.6 |
| RBC | (L) 3.80 | (L) 3.43 |
| HGB | (L) 11.2 | (L) 9.7 |
| HCT | (L) 33 | (L) 30 |
| MCV | 88 | 88 |
| MCHC | 33.5 | 32.2 |
| Platelet Count | 338 | (H) 412 |
| RDWC | (H) 15.7 | (H) 15.6 |
| **Electrolytes Plus** | | |
| Sodium | (L) 134 | (L) 129 |
| Potassium | 4.6 | 4.6 |
| Chloride | 99 | (L) 95 |
| Carbon Dioxide (lab) | 19 | 24 |
| Blood Urea Nitrogen | 20 | 13 |
| Creatinine | 0.54 | (L) 0.48 |
| Glucose (lab) | * (H) 107 | * (H) 115 |
| Calcium | 9.6 | 8.6 |

# Initial Rheumatologic Labs

**Esr 86, crp 6.4,** CK/aldolase wnl

Cardiolipin IgG 11.7, beta-2-glycoprotein IgG 11.2

**ANA 1:1280 speckled**

- Smith, RNP scleroderma negative, DNA negative, C3/C4 complement wnl
- **SSA>8.0, SSB>8.0**

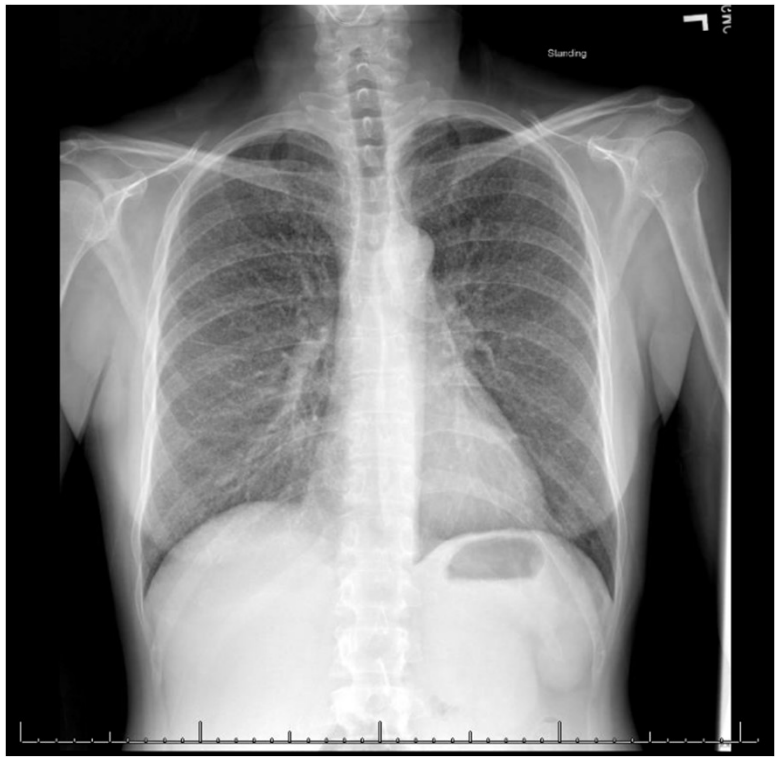
ANCA/MPO/PR3 negative

TB quant “indeterminate x2”

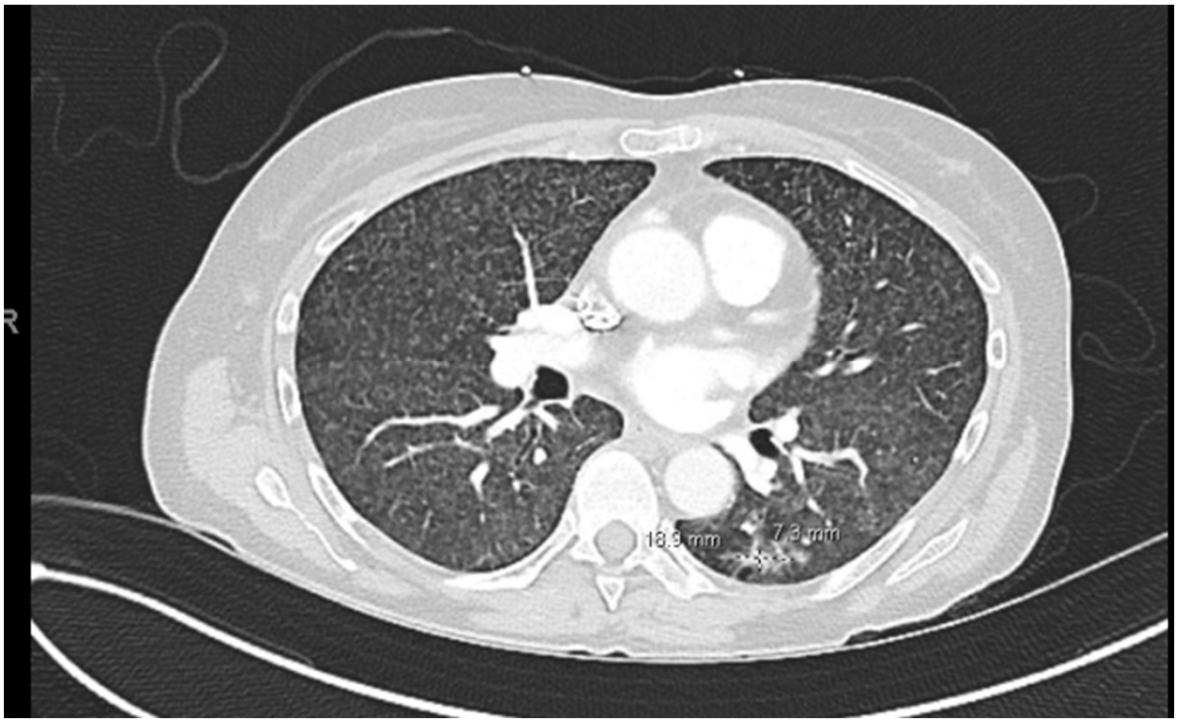
Blood cx, urine cx, viral respiratory panel negative

Hiv, hepb/c negative

# Initial Imaging

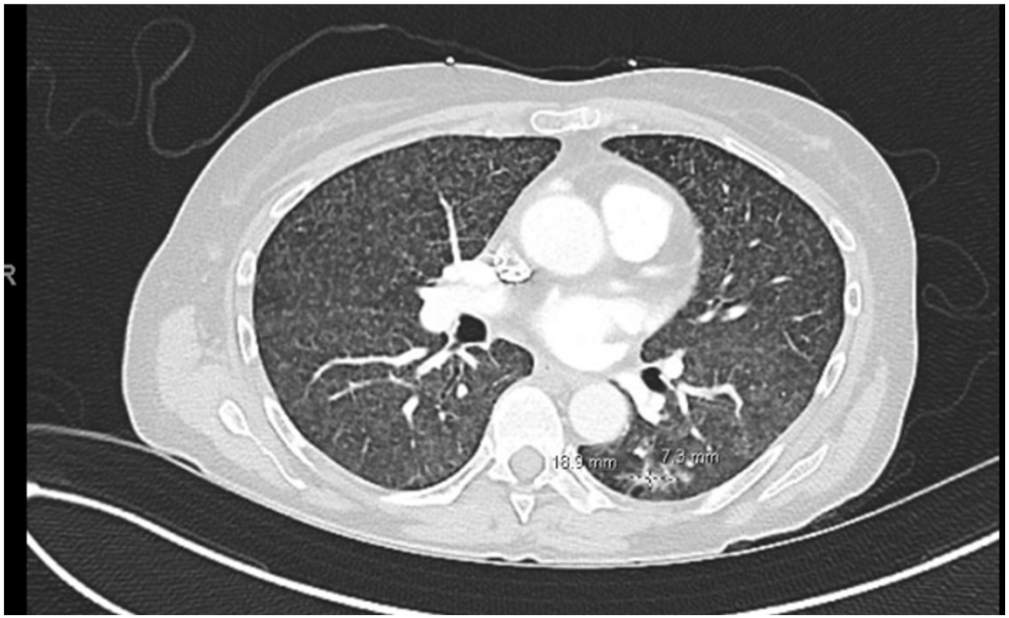


# Subsequent Imaging



# CT Scan Report

"**Miliary pattern of pulmonary nodules** which can be seen with atypical infections including TB/fungal/viral noting that additional inflammatory etiologies are within the differential and neoplastic processes are possible but less likely, particularly given the presence of fever. Consider pulmonology consultation.



# Differential Diagnosis

Fungal infection, cancer, hypersensitivity pneumonitis

# Sjogren's LIP

Lymphocytic Interstitial Pneumonia

33-50% 5 year mortality

5% B-cell lymphoma transformation

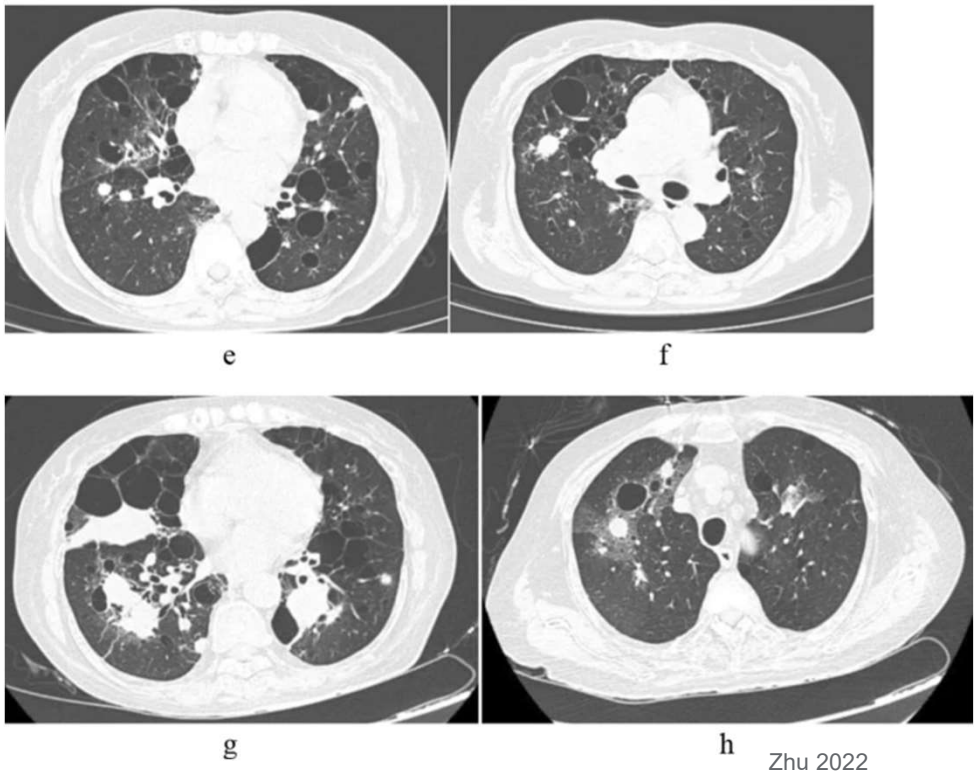
Infection (HIV, EBV), Sjogren's (25%)

- 1% prevalence in Sjogren's patients

Polyclonal IgM

BAL- increased lymphocytes

CT scan- nodules, thin walled cystic cavities




Zhu 2022

# BAL and Fluid Studies

Fluid culture negative

Flow cytometry negative

MTB PCR negative

AFB negative

Sputum AFB x3 negative

| Body Fluids | |
|---|---|
| BAL Source | Bronchial Alv |
| BAL Color | Colorless |
| BAL Appearance | HAZY |
| BAL Neutrophil % | 46 |
| BAL Lymphocyte % | 24 |
| BAL Mononuclear % | 29 |
| BAL Eosinophil % | 0 |
| BAL Other Cells % | * 1 |
| BAL NRBC % | 0 |

# Transbronchial Biopsy

SPECIMENS SUBMITTED:

A. LLL TRANSBRONCHIAL BIOPSY

DIAGNOSIS:

A. LUNG, LEFT LOWER LOBE, TRANSBRONCHIAL BIOPSY:

- SCANT BENIGN PULMONARY PARENCHYMA WITH GRANULOMATOUS INFLAMMATION, CONTAINING GIANT CELLS
- SPECIAL STAINS FOR AFB AND PAS-D ARE NEGATIVE FOR ACID-FAST AND FUNGAL ORGANISMS, RESPECTIVELY

| | |
|---|---|
| Tissue Culture + Gram Stain - | - |
| Specimen Description (SDES): | Tissue |
| Special Requests (SREQ): | NONE |
| Gram Stain (GS): | No organisms seen. |
| Gram Stain (GS): | No white blood cells seen. |
| Culture (CULT): | Actinomyces odontolyticus |
| Culture (CULT): | Isolated from liquid media only, quantity of organism is unknown. |

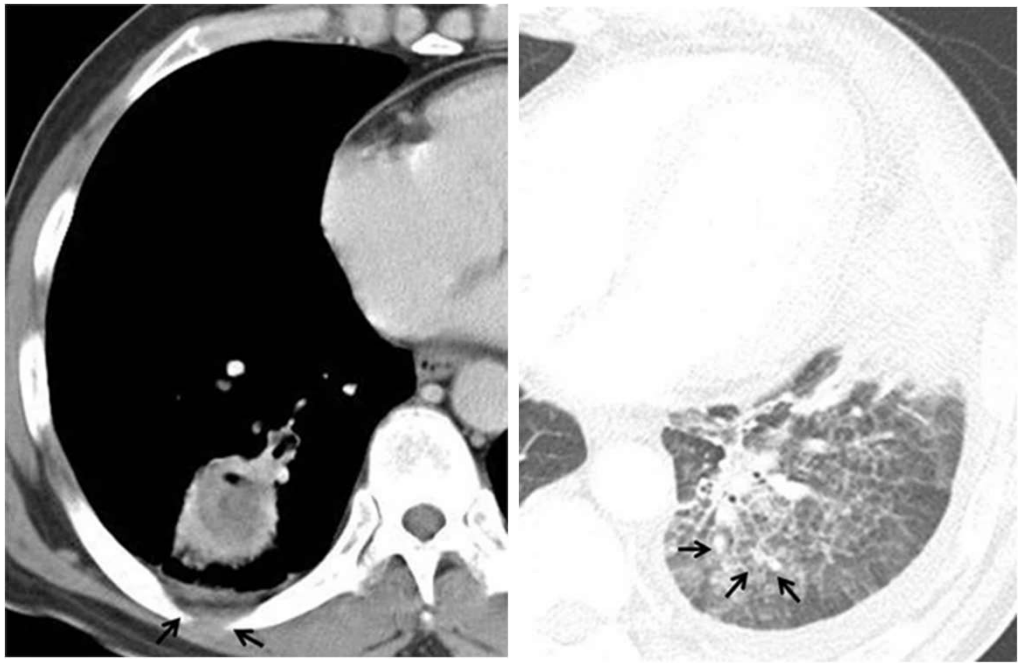
# Pulmonary Actinomycosis

Cough, low grade fever, often asymptomatic

CT- Consolidation, multifocal nodules, cavitation, pleural thickening, lymphadenopathy

2-6 weeks IV PCN followed by 6-12 months oral PCN or amoxicillin pending imaging and clinical response

Surgical resection for abscess, life-threatening hemoptysis



Mabeza 2003

Han 2013

# Readmission- AHRF

Worsened Dyspnea

2L O2 requirement

Cbc, cmp, lactate wnl

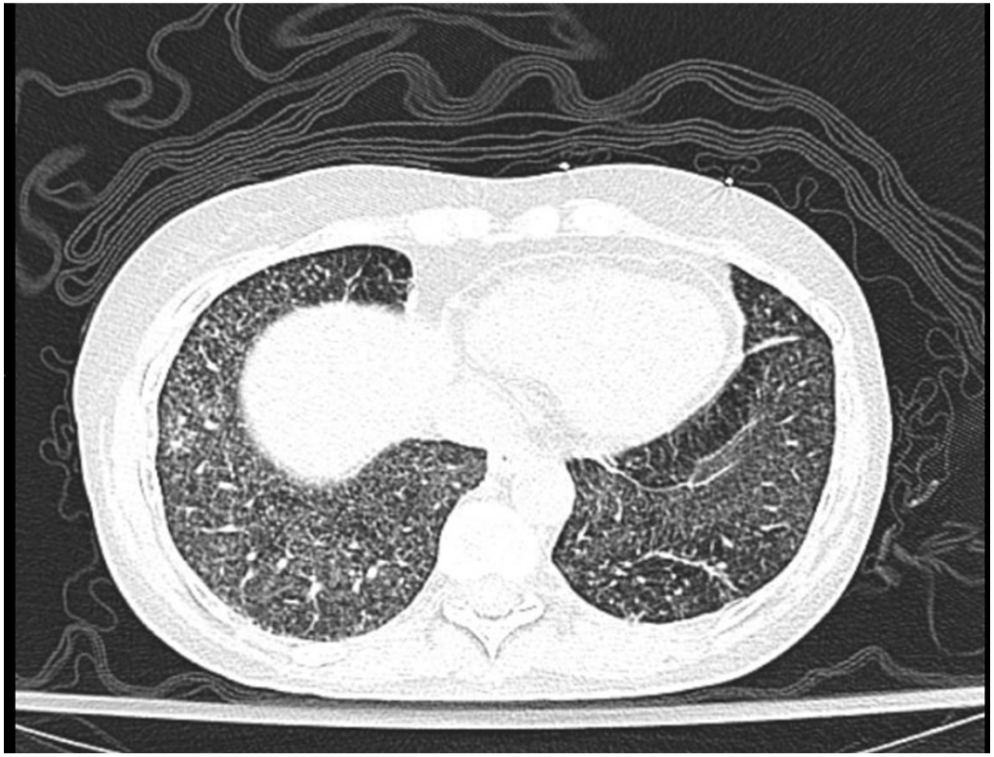
# Clinical Course

Increased O2 requirement from 2L to 6L

Afebrile

Cbc, cmp unchanged, wnl

CT scan showing progression of of miliary nodules



# Open Lung Biopsy - CT Surgery

A. RIGHT UPPER LOBE WEDGE (LUNG BIOPSY)
B. RIGHT MIDDLE LOBE WEDGE (LUNG BIOPSY)

DIAGNOSIS:
A. LUNG, RIGHT UPPER LOBE; WEDGE:
- PENDING MAYO CLINIC CONSULTATION
- PRELIMINARY DIAGNOSIS:
  - ABUNDANT CASEATING GRANULOMAS
  - GRANULOMAS PRESENT AT INKED PARENCHYMAL RESECTION MARGIN
  - SEE COMMENT

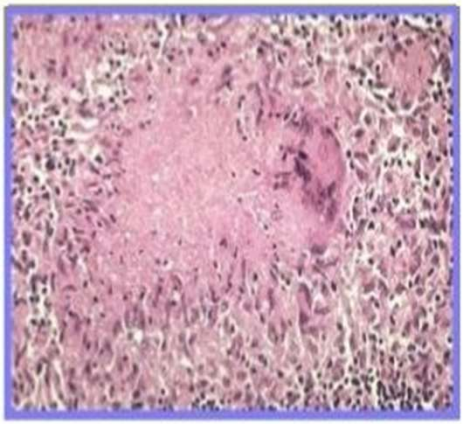
B. LUNG, RIGHT MIDDLE LOBE; WEDGE:
- PENDING MAYO CLINIC CONSULTATION
- PRELIMINARY DIAGNOSIS:
  - ABUNDANT CASEATING GRANULOMAS
  - GRANULOMAS PRESENT AT INKED PARENCHYMAL RESECTION MARGIN
  - SEE COMMENT

# Caseating Granulomas

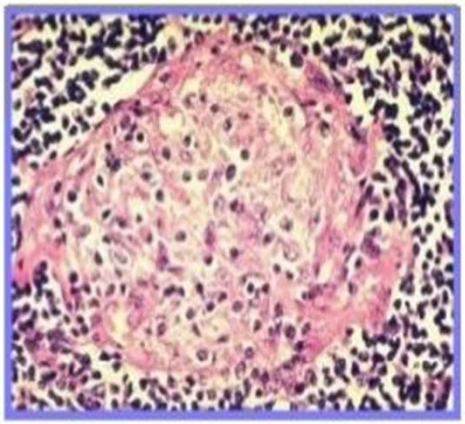
Caseating granulomas have areas of central necrosis

Differential diagnosis for caseating granuloma

- Infection:
  - TB, non-TB mycobacterium
  - nocardia, yersinia, bartonella,
  - Coccidioides, histoplasma, blastomyces, Aspergillus
- Non-infectious
  - Rheumatoid nodule, granuloma annulare, GPA, necrobiosis lipoidica



Caseating granulomas
**TB**



Non caseating granulomas
**Sarcoidosis**

Epomedicine 2017

# Worsening Acute Hypoxic Respiratory Failure

Afebrile but hypotensive and requiring mechanical ventilation in ICU

Treat for Presumed Sarcoidosis or Sjogren's LIP?

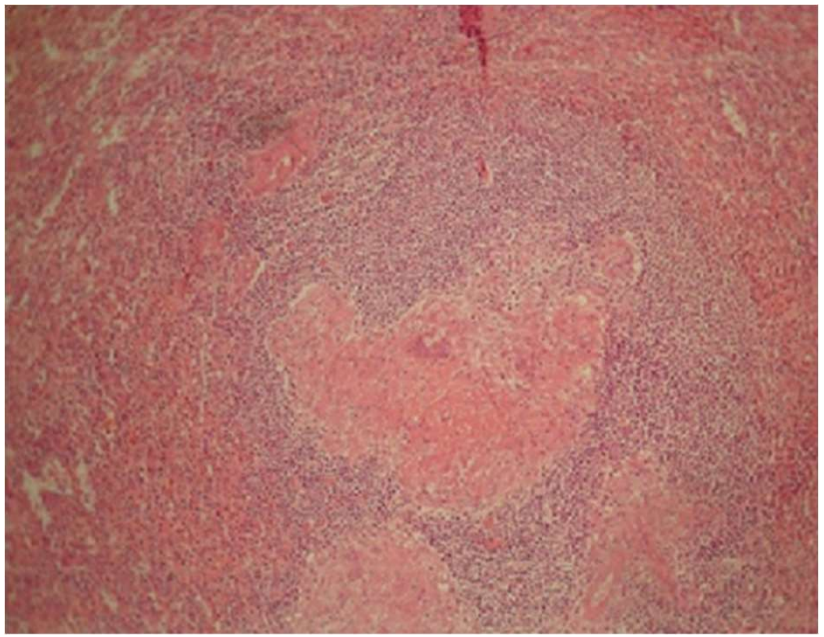
- Empiric methylpred 1g given by ICU team overnight
- Broad spectrum ABX, acyclovir, antifungal coverage

# Sarcoidosis and Caseating Granuloma

Sarcoidosis traditionally forms noncaseating granuloma

Case reports of necrotizing sarcoid granuloma (NSG)

- Generally defined by lack of response to RIPE therapy



Splenic Biopsy of Patient with NSG

Binesh 2012

# Immunosuppression?

Continued mechanical ventilation

ID feels actinomyces is likely contaminant after review of slides with pathology

# Immunosuppression?

Continued mechanical ventilation

Infectious workup remains negative

Worsening hypotension requiring multiple pressors

- TTE LVEF 25-30%
- Started by MICU on stress dose hydrocortisone

# Immunosuppression?

Infectious workup remains negative

Worsening respiratory status on ventilator despite broad spectrum antibiotic coverage

Repeat CT scan unchanged from previous

# TB Quant Results

| Quantiferon TB Gold Plus Interpretation | (A) (c) Quantit |
|---|---|
| NIL | 2.91 |
| TB1 minus Nil | (H) 1.54 |
| TB2 minus Nil | (H) 1.89 |
| MITO minus Nil | 0.41 |
| Blastom Ab Result | |

# Positive TB IGRA Testing

TB1 tube- MTB complex antigens ESAT-6, CFP-10

- Assay measures IFN-gamma secretion from CD4+ T cells

TB2 tube- ESAT-6, CFP-10, additional antigens to elicit CD8+ response

- Assay measures IGN-gamma from CD4+ and CD8+ T cells

Active or Latent TB- both TB1 Nil and TB2 Nil

- < =0.35 IU/mL = Negative
- > 0.35 IU/mL = Positive

# Indeterminate IGRA testing

Low Mitogen Response (positive control)

- Mitogen (less than 0.5 IU/mL) = Indeterminate
- Can’t adequately generate immune response
- Low lymphocytes, immunosuppression, specimen handling

Elevated Nil Value

- Nil values greater than 8.0 IU/mL = Indeterminate
- Measures baseline circulating IFN-gamma and subtracted from values for other tubes (-Nil)
- Autoimmune disease, chronic inflammation, specimen handling

# Final Hospital Course and Post-Hospital Discharge

Started on RIPE therapy empirically for likely TB

Open lung biopsy tissue culture positive for AFB staining organism, likely mycobacterium

Extubated and down to 1.5L with exertion O2 at 2 month hospital follow-up

Sendout Mycobacterial culture from open lung biopsy positive for AFB likely MTB after discharge

# Sputum TB testing

One study from Pakistan of 156 patients with known pulmonary TB - TB endemic region

- 7.8% yield AFB smear, 21.6% AFB culture, 34.3% Molecular assay

Meta Analysis suggests 2-5% incremental yield with serial AFB smears

Mase 2007

Sumalani 2019

# BAL for TB testing

Table 1

Diagnostic validity of sputum smear-negative TB for BAL examination

| | BAL Examination (%) | Confidence Intervals (95%) |
|---|---|---|
| Sensitivity | 60 | 53 to 68 |
| Specificity | 91 | 86 to 96 |
| Positive Predictive Value(PPV) | 89 | 83 to 95 |
| Negative Predictive Value(NPV) | 64 | 57 to 71 |
| $LR^+$ | 64.6 | 3.71 to 11.22 |
| $LR^-$ | 0.44 | 0.36 to 0.53 |

Nikbash 2015

# Biopsy For TB testing

Study of 84 patients

93% overall yield from biopsy
- 78% yield biopsy histology
- 62% yield biopsy tissue culture

12% yield fluid culture

15% yield Sputum AFB with cxr opacities

**TABLE 1. Yield of diagnostic methods in 84 cases of tuberculous pleural effusions**

| Method of Diagnosis | Total (*n* = 84) | HIV Seronegative (*n* = 71) | HIV Seropositive (*n* = 13) | p Value* |
|---|---|---|---|---|
| Presumptive diagnosis | 5 (6) | 5 (7) | 0 | 1.0 |
| Pleural biopsy tissue | 78 (93) | 65 (91) | 13 (100) | 0.58 |
| Bacteriologic diagnosis | 52 (62) | 42 (59) | 10 (77) | 0.36 |
| AFB smear positive | 14 (17) | 9 (13) | 5 (38) | 0.06 |
| Culture for *M.tb* positive | 52 (62) | 42 (59) | 10 (77) | 0.36 |
| Histologic diagnosis | 66 (78) | 54 (76) | 12 (92) | 0.28 |
| Pleural fluid | 10 (12) | 7 (10) | 3 (23) | 0.18 |
| AFB smear positive | 2 (2) | 1 (1) | 1 (8) | 0.28 |
| Culture for *M.tb* positive | 9 (11) | 7 (10) | 2 (15) | 0.62 |
| Sputum induction | 44 (52) | 34 (48) | 10 (77) | 0.10 |
| AFB smear positive | 10 (12) | 7 (10) | 3 (23) | 0.18 |
| Culture for *M.tb* positive | 44 (52) | 34 (48) | 10 (77) | 0.10 |

* p Value of the yield of diagnostic methods between HIV seronegative and HIV seropositive tuberculous pleural patients.

n = number of cases (%).

*Definition of abbreviations*: AFB = acid fast bacilli; *M.tb* = *Mycobacterium tuberculosis*.

Conde 2003

# Conclusions

TB can be hard to diagnose

TB shouldn’t be treated with immunosuppressive medications

# References


Binesh, F., et al. “Systemic Sarcoidosis with Caseating Granuloma.” *Case Reports*, vol. 2012, no. jan23 1, Jan. 2012, pp. bcr0520114278–bcr0520114278. *DOI.org (Crossref)*, https://doi.org/10.1136/bcr.05.2011.4278.

Conde, Marcus B., et al. “Yield of Sputum Induction in the Diagnosis of Pleural Tuberculosis.” *American Journal of Respiratory and Critical Care Medicine*, vol. 167, no. 5, Mar. 2003, pp. 723–25. *DOI.org (Crossref)*, https://doi.org/10.1164/rccm.2111019.

Epomedicine. “Difference between Sarcoidosis and Tuberculosis.” *Epomedicine*, 13 Jan. 2017, https://epomedicine.com/medical-students/difference-sarcoidosis-tuberculosis/.

Han, Ji-Yeon, et al. “An Overview of Thoracic Actinomycosis: CT Features.” *Insights into Imaging*, vol. 4, no. 2, Apr. 2013, pp. 245–52. *insightsimaging.springeropen.com*, https://doi.org/10.1007/s13244-012-0205-9.

Mabeza, G. F., and J. Macfarlane. “Pulmonary Actinomycosis.” *European Respiratory Journal*, vol. 21, no. 3, Mar. 2003, pp. 545–51. *erj.ersjournals.com*, https://doi.org/10.1183/09031936.03.00089103.

Mase, S. R., et al. “Yield of Serial Sputum Specimen Examinations in the Diagnosis of Pulmonary Tuberculosis: A Systematic Review.” *Database of Abstracts of Reviews of Effects (DARE): Quality-Assessed Reviews [Internet]*, Centre for Reviews and Dissemination (UK), 2007. *www.ncbi.nlm.nih.gov*, https://www.ncbi.nlm.nih.gov/books/NBK73472/.

Nikbakhsh, Novin, et al. “The Value of Bronchoalveolar Lavage in the Diagnosis of Sputum Smear-NegativePulmonary Tuberculosis.” *Iranian Journal of Pathology*, vol. 10, no. 1, 2015, pp. 35–40. *PubMed Central*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539783/.

*Quantiferon Gold*. https://jdos.nicholsinstitute.com/dos/cmclab/test/370093. Accessed 27 Sept. 2024.

*Quest Diagnostics: Test Directory*. https://testdirectory.questdiagnostics.com/test/test-detail/36970/quantiferon-tb-gold-plus-1-tube?cc=MASTER. Accessed 27 Sept. 2024.

Sumalani, K. K., et al. “Diagnostic Yield of Sputum Induction in Patients with Pleural Tuberculosis at a Tertiary Care Hospital in Karachi.” *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease*, vol. 23, no. 11, Nov. 2019, pp. 1213–16. *PubMed*, https://doi.org/10.5588/ijtld.18.0830.

Zhu, Chengyuan, et al. “Transformation of Lymphoid Interstitial Pneumonia (LIP) into Malignant Lymphoma in Patients with Sjogren’s Syndrome: A Case Report and Literature Review.” *Journal of Cardiothoracic Surgery*, vol. 17, no. 1, Apr. 2022, p. 79. *BioMed Central*, https://doi.org/10.1186/s13019-022-01826-6.