Case Study #1 (Pediatric TB)

Amanda Evans, MD

June 12, 2025

TB Intensive • June 10 – 12, 2025 • Dallas, Texas

Amanda Evans, MD

Has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this activity

Consult Please!
NICU is Calling…

Amanda Evans, MD

Associate Professor • UT Southwestern Medical Center

Medical Director • Children's Health Infectious Disease Clinics

Thursday, June 12th

Objective:

- Discuss a pediatric case highlighting the complexity of pediatric care of infants/children with tuberculosis or TB exposure

Case: 23-day-old term infant, presenting with fever and abdominal distention

Presented to ED due to fever (101F) and abdominal distention. Had 3-4 diapers with bloody stools.

Parents reported his abdomen was ‘more round’ over past few days.

Mother has recently transitioned from breastmilk to exclusively formula.

ED Exam significant for:

Ill-appearing, pale infant with distended abdomen

2 L nasal cannula

Erythematous rash on face and chest

Abdomen distended with visible veins

Hypotonia, head lag noted

Case: 23 day old term infant, presenting with fever and abdominal distention

Presented to ED due to fever (101F) and abdominal distention. Had 3-4 diapers with bloody stools.

Parents reported his abdomen was 'more round' over past few days.

Mother has recently transitioned from breastmilk to exclusively formula.

ED Exam significant for:

Ill-appearing, pale infant with distended abdomen

2 L nasal cannula

Erythematous rash on face and chest

Abdomen distended with visible veins

Hypotonia, head lag noted

Differential Diagnosis?

- Late-onset Sepsis complicated with DIC
  - Group B Streptococcus
  - E coli
- Infectious gastroenteritis (viral or bacterial – e.g., Salmonella)
- Abdominal emergency (malrotation with midgut volvulus)
- Cow's milk protein-induced allergic colitis
- Swallowed Maternal Blood
- Intussusception
- Necrotizing enterocolitis (NEC)

Initial Evaluation

- **Na 131**, K 5.2, **Cl 93**, CO2 26, BUN 4, serum creatinine 0.3
- **Albumin 2.6,** ALT 29, **AST 97,** Total Bili 1.0
- **PT 15.8**, INR 1.2, **PTT 42.8**
- WBC 13.9 (54% N, 8.5% B, 30%L), H/H 12.7/36.7, **Plts 53**
- **CRP 4.02**
- CSF: WBC 4, RBC 0, Glucose 48, Protein 66

Differential Diagnosis?

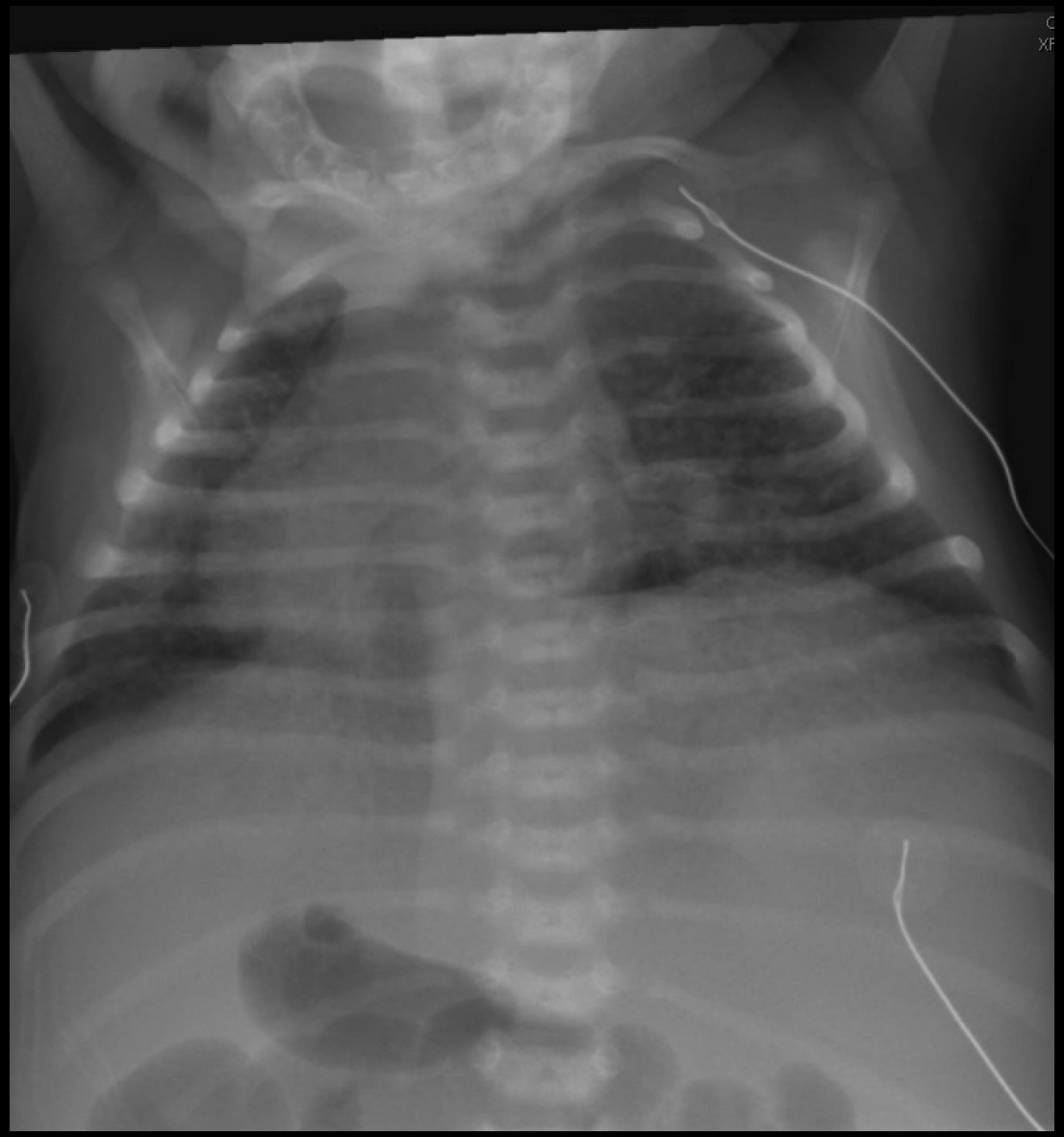
- Late-onset Sepsis complicated with DIC
  - Group B Streptococcus
  - E coli
- Cow's milk protein-induced allergic colitis
- Swallowed Maternal Blood
- Infectious gastroenteritis (viral or bacterial – e.g., Salmonella)
- Intussusception
- Abdominal emergency (malrotation with midgut volvulus)
- Necrotizing enterocolitis (NEC)

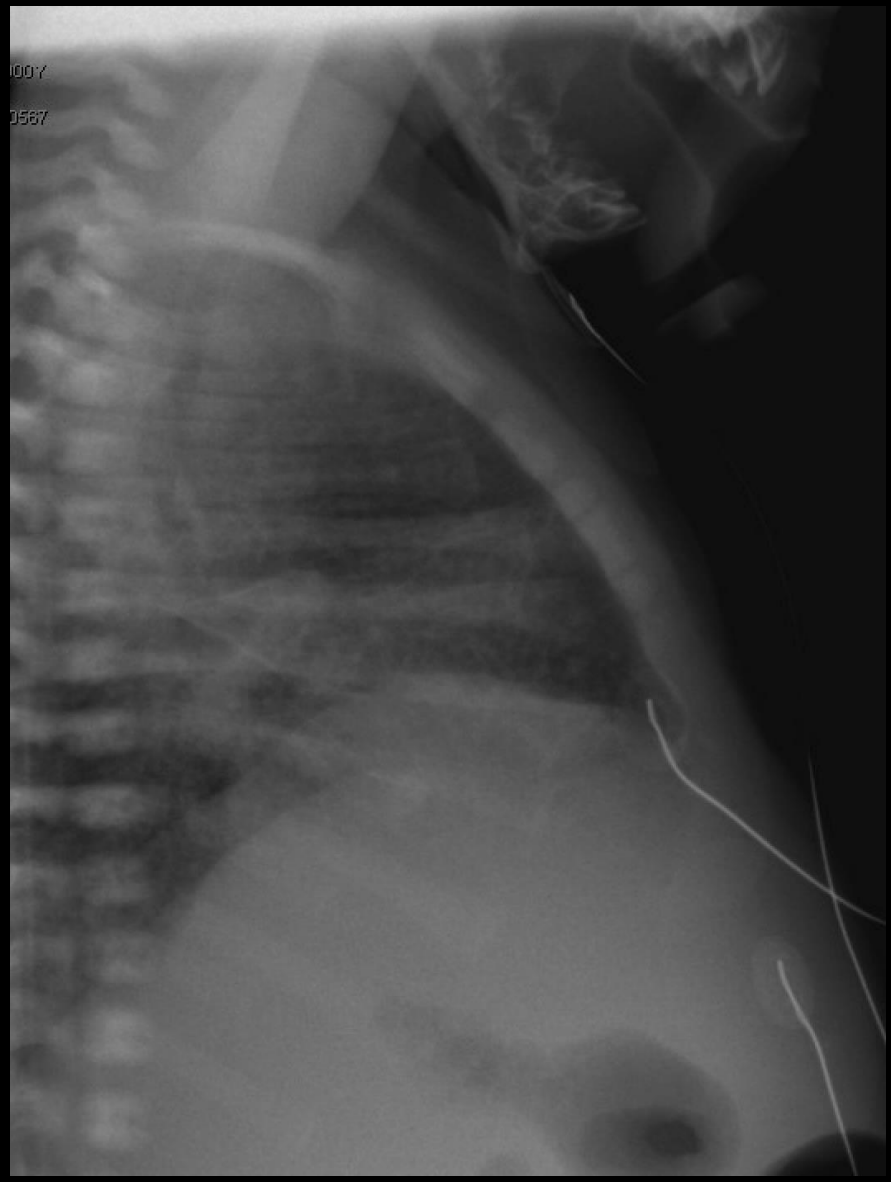
Initial Evaluation

- **Na 131**, K 5.2, **Cl 93**, CO2 26, BUN 4, serum creatinine 0.3
- **Albumin 2.6,** ALT 29, **AST 97,** Total Bili 1.0
- **PT 15.8**, INR 1.2, **PTT 42.8**
- WBC 13.9 (54% N, 8.5% B, 30%L), H/H 12.7/36.7, **Plts 53**
- **CRP 4.02**
- CSF: WBC 4, RBC 0, Glucose 48, Protein 66

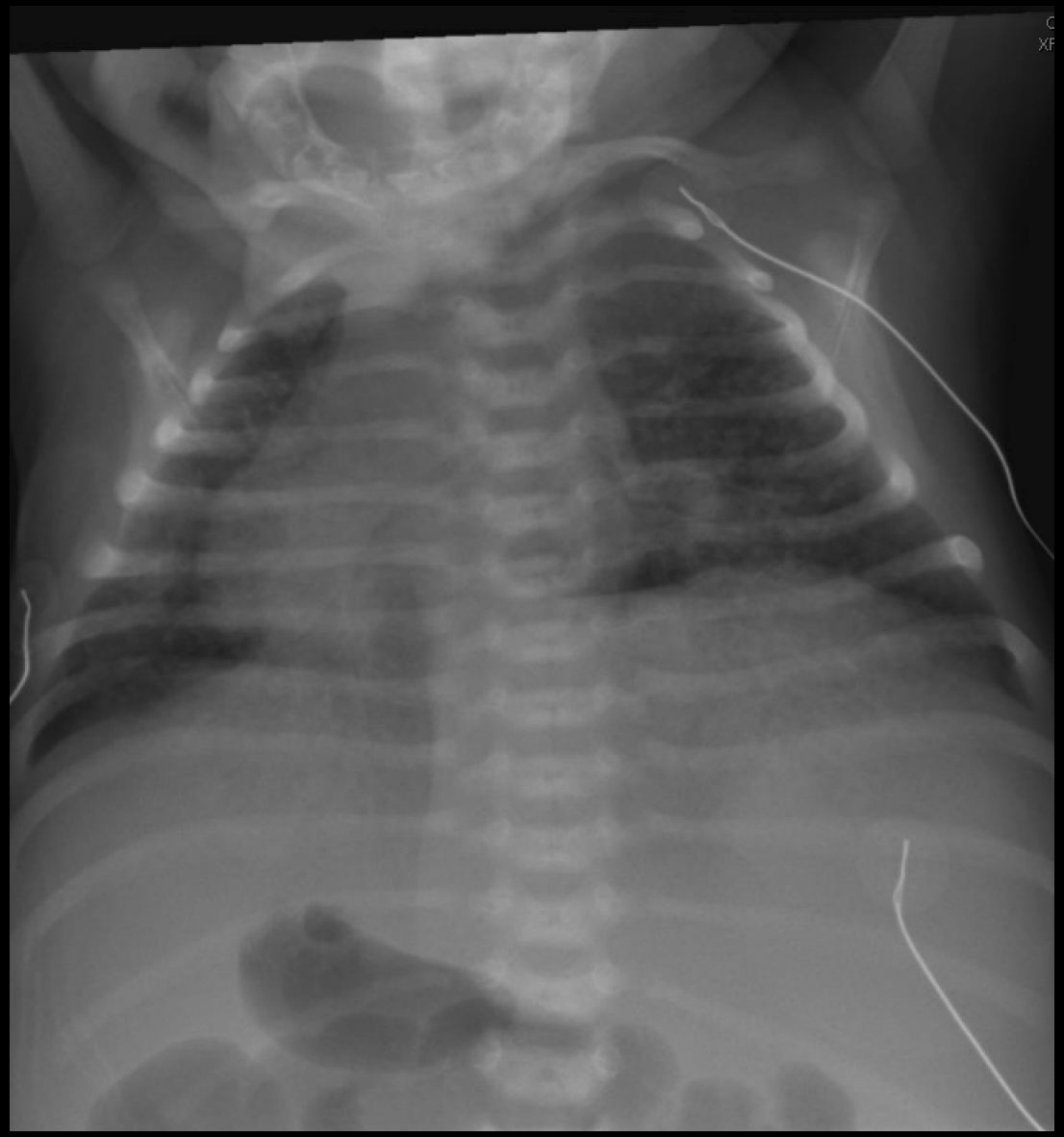
- **Blood culture – Coagulase-negative Staphylococcus**
- Repeat Blood cultures negative.
- Urine culture – negative
- CSF culture – negative

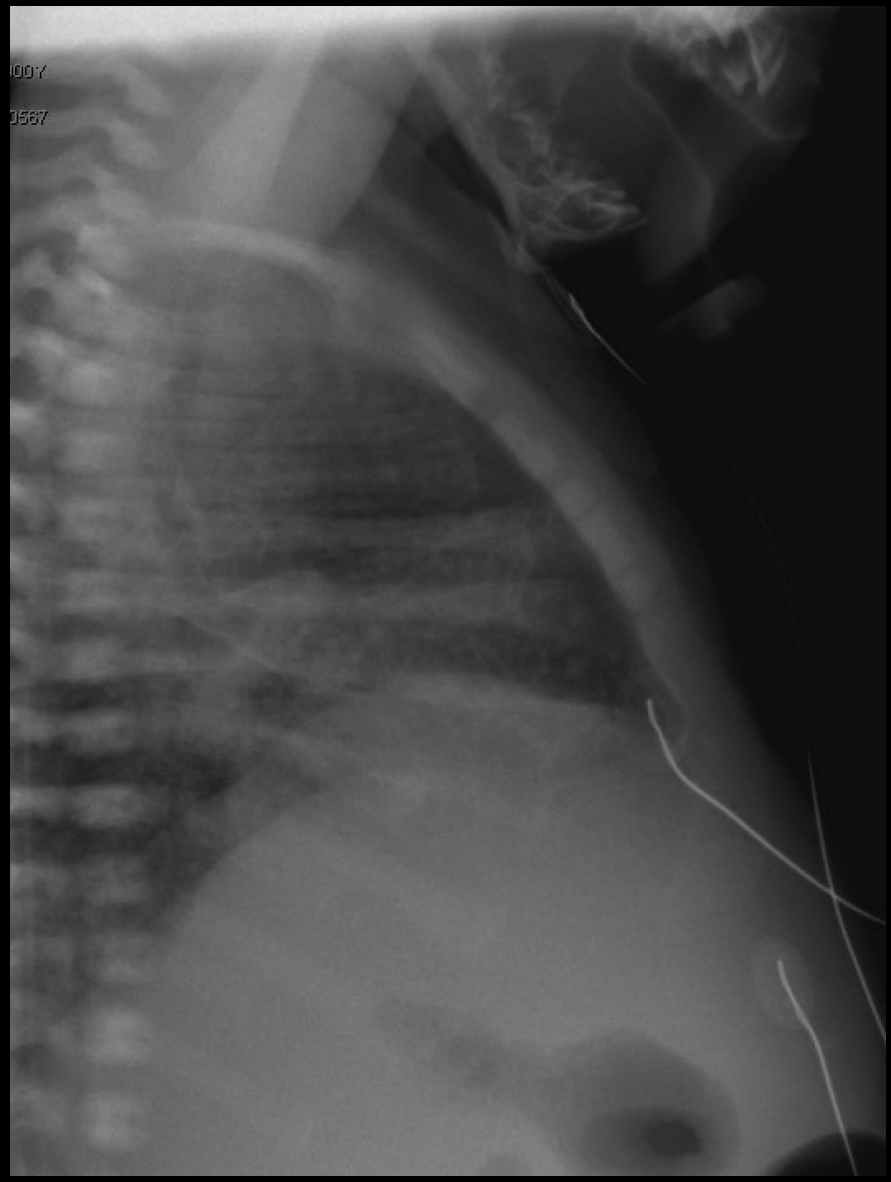
- **CMV urine PCR – detected** (viral load <2.8)
- HSV evaluation (blood, CSF, mucocutaneous sites) – not detected
- Enterovirus CSF PCR – negative
- Respiratory viral panel - negative





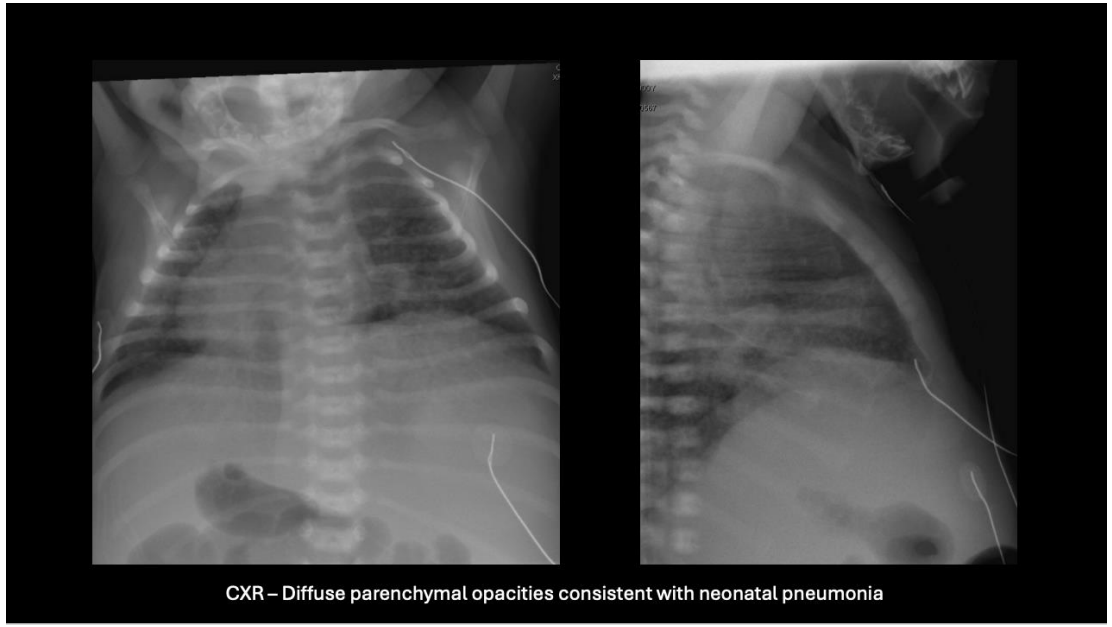
Interpretation?





CXR – Diffuse parenchymal opacities consistent with neonatal pneumonia

Febrile 23- day-old infant with abdominal distention, thrombocytopenia, respiratory failure. Interstitial opacities on CXR.



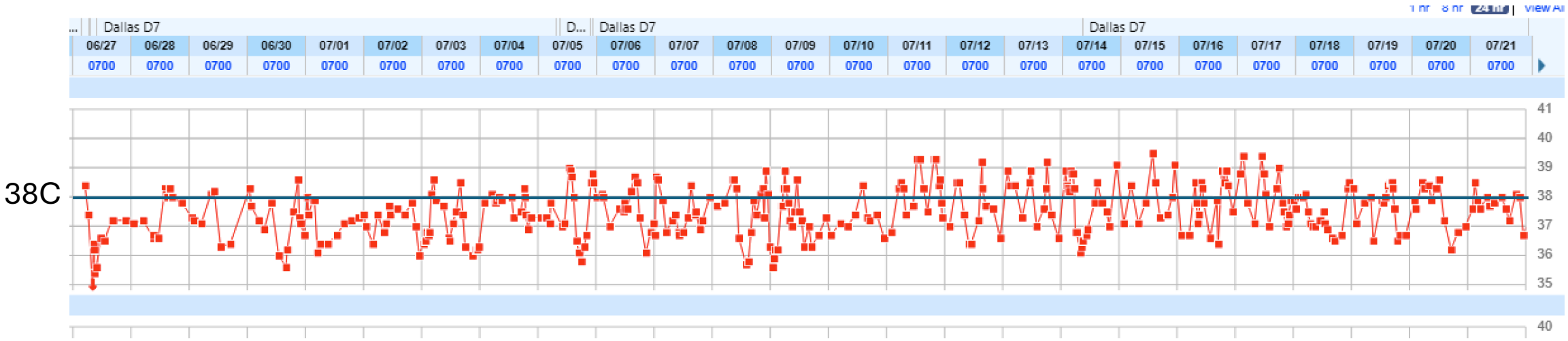
CXR – Diffuse parenchymal opacities consistent with neonatal pneumonia

Additional Evaluation?

- Lower Respiratory Cultures – Gram-negative rods
- Respiratory Viral Panel – negative
- CMV blood PCR – viral load <2.8, detected

Interventions?

- Started on valganciclovir (for symptomatic congenital CMV)
- Started on cefepime, for presumed bacterial neonatal pneumonia



Over the 1st Month of Hospitalization, with continued fever - a diagnostic test was sent…

- **AFB culture via gastric aspirate x3 – positive for Mycobacterium tuberculosis**
- AFB culture via peritoneal fluid x3 – negative
- AFB culture via CSF – negative, Mtb PCR – not detected

Infant diagnosed with:

Perinatal Tuberculosis

Tuberculosis in Infants <3 months

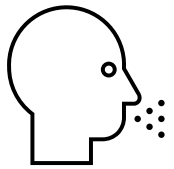
Challenging to clinically distinguish

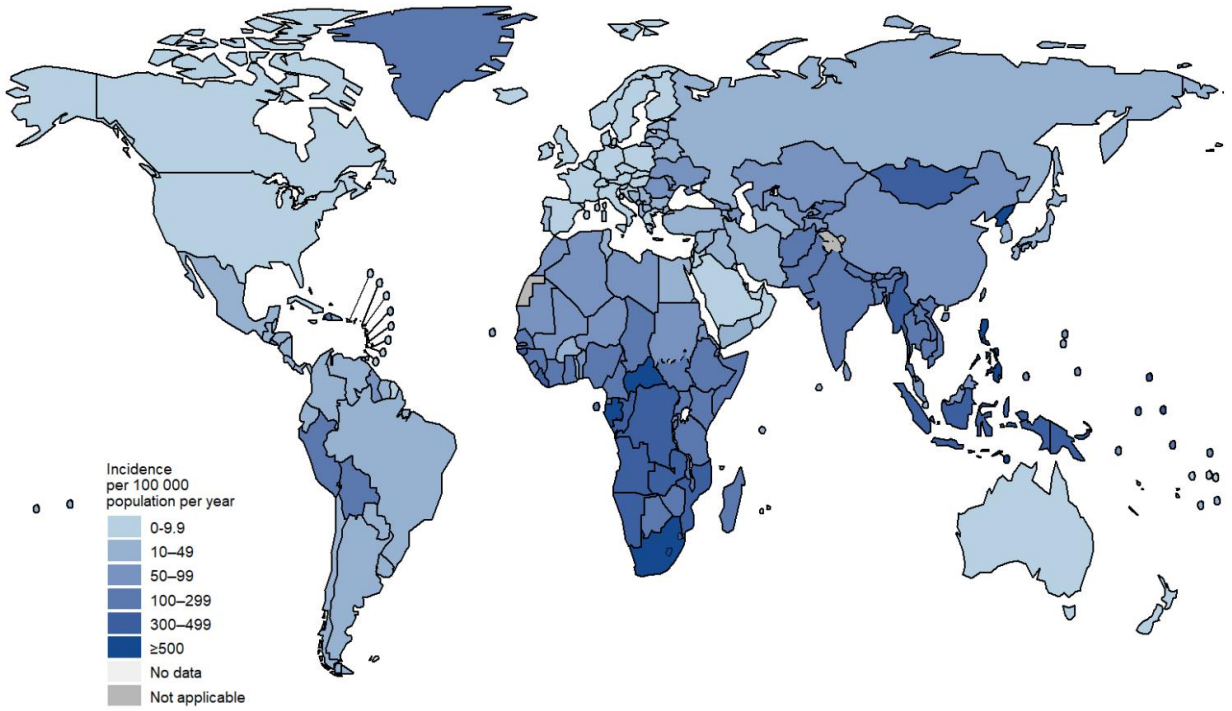
Congenital TB

In utero transmission by **hematogenous spread** through the umbilical vein or ingestion/ aspiration of TB infected **amniotic fluid** during birth.

Postnatal TB

Inhalation of M. tuberculosis bacilli spread by airborne route from mother or other close contact with infectious pulmonary tuberculosis early after birth.





Of the estimated 10.6 million new TB cases per year –
1.17 M cases occur in children.
~192,000 – 247,000 pregnant women with TB globally estimated (in 2011).
~500 cases of congenital tuberculosis reported in the literature.

Both congenital and postnatal TB in infants likely are underreported.

https://www.who.int/publications/digital/global-tuberculosis-report-2021/tb-disease-burden/incidence

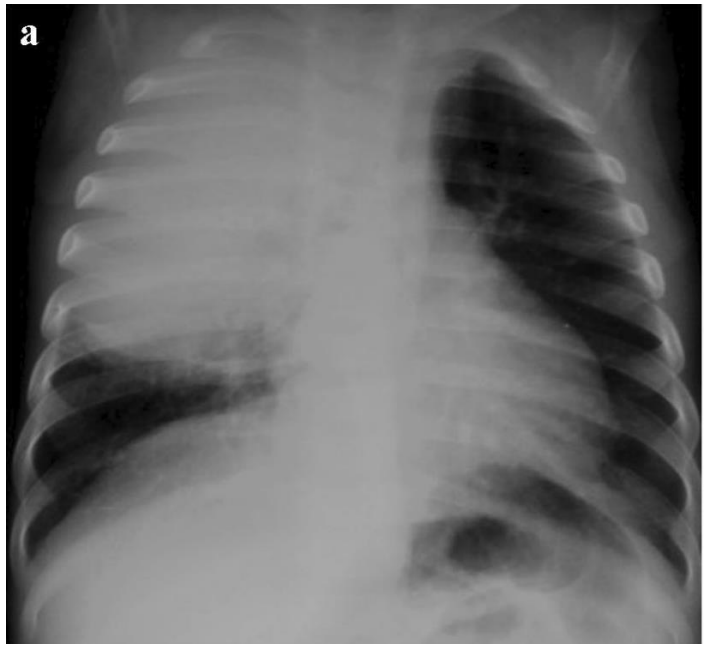
Signs and Symptoms of Congenital TB are nonspecific and overlap with other newborn infectious conditions.

Delayed diagnosis is common.

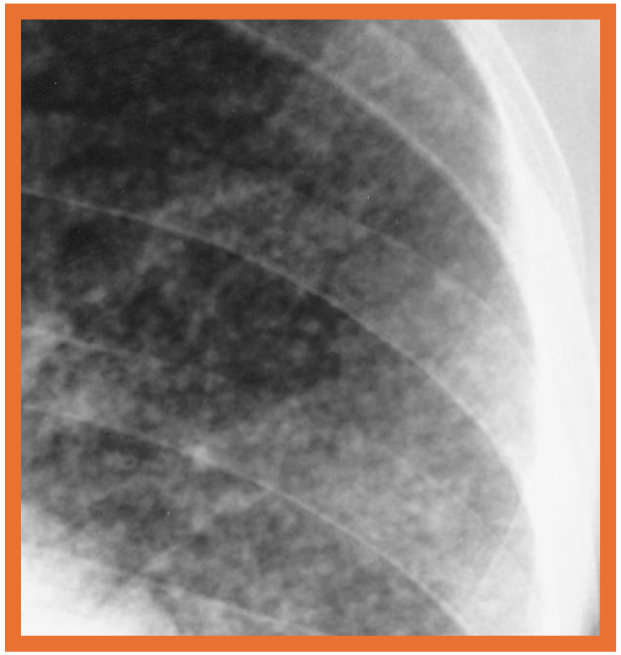
Very Common (>60%)	Common (40-60%)	Frequent (25-40%)	Infrequent (10-25%)	Rare (<10%)
Respiratory distress, tachypnea	Cough	Poor feeding	Irritability & lethargy	Skin popular/pustular or ulcerative lesions
Hepatomegaly	Prematurity/ low birth weight	Abdominal distention	Peripheral lymphadenopathy	Jaundice (obstructive)
Fever	Growth failure (Failure to thrive)	Ascites	Sepsis syndrome	Otorrhea/mastoiditis
	Splenomegaly		Seizures	Wheeze or stridor
				Apnea/cyanosis
				Vomiting
				Facial nerve palsy
				Shock
				Hemophagocytic lymphohistiocytosis

Schaaf HS, Bekker A, Rabie H. Perinatal tuberculosis-An approach to an under-recognized diagnosis. Front Public Health. 2023 Nov 7;11:1239734. doi: 10.3389/fpubh.2023.1239734. PMID: 38026389; PMCID: PMC10661895.

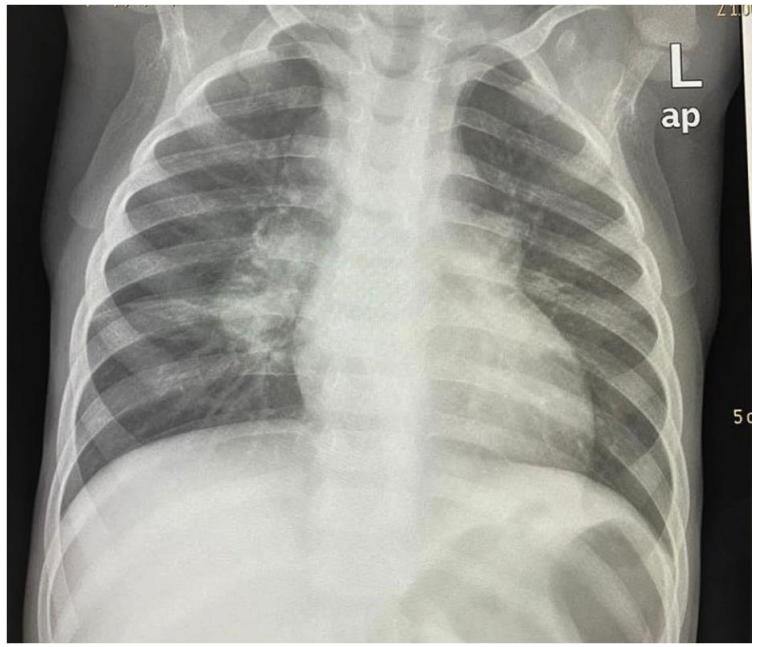
Typical Features of Chest X-rays in Congenital/Pediatric TB: more lymphadenopathy, less cavitation.



Consolidation, 30-40%



Miliary pattern, with innumerable 0.5-1.0mm nodules, 30-40%



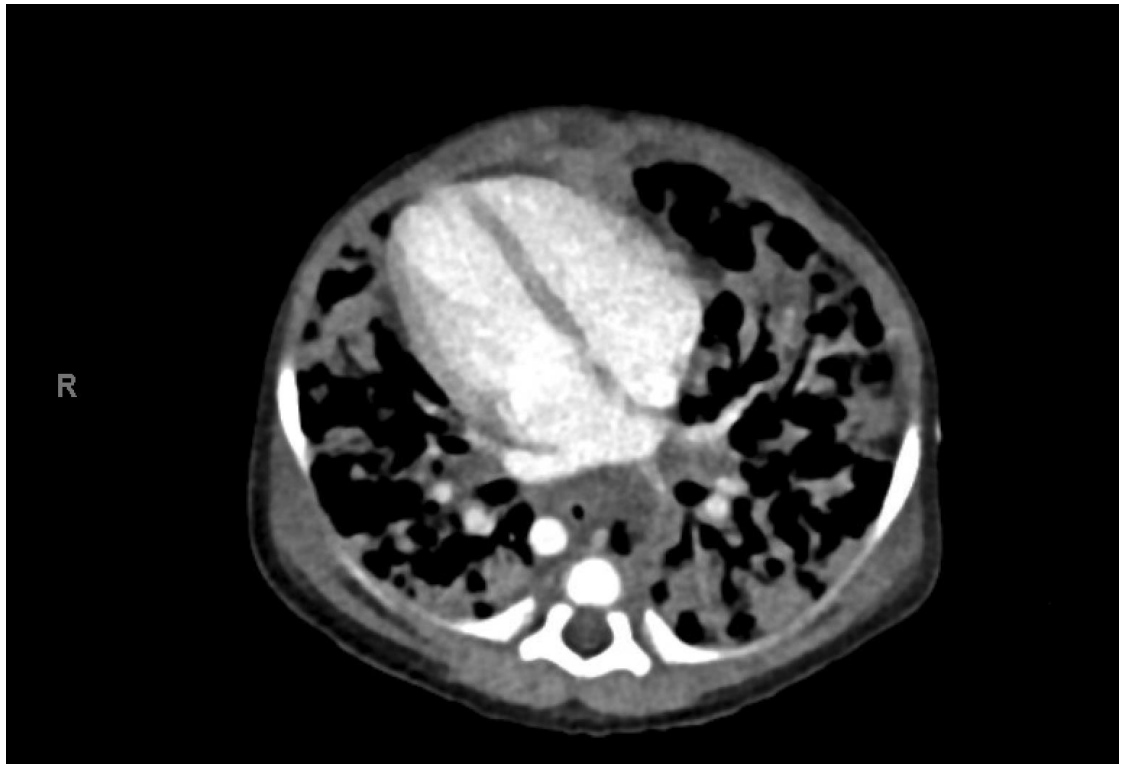
Bilateral bronchopulmonary infiltrates, 15-20%

Other findings: Intrathoracic lymphadenopathy (10-15%), pleural effusion (<5%), cavitations <5%)

Normal Chest x-ray = 5-10%

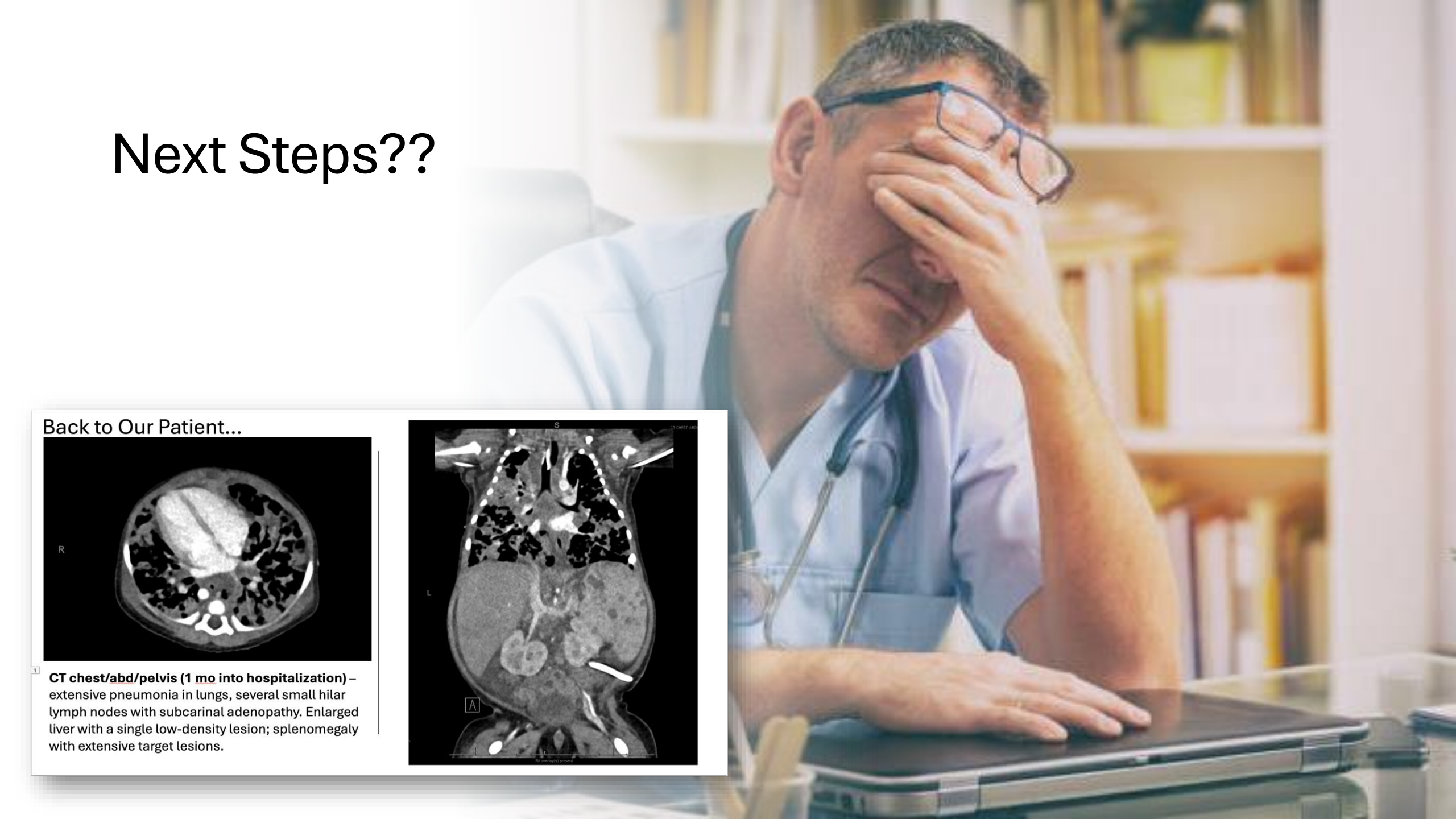
Mahomed N, Kilborn T, Smit EJ, Chu WCW, Young CYM, Koranteng N, Kasznia-Brown J, Winant AJ, Lee EY, Sodhi KS. Tuberculosis revisted: classic imaging findings in childhood. Pediatr Radiol. 2023 Aug;53(9):1799-1828. doi: 10.1007/s00247-023-05648-z. Epub 2023 May 23. PMID: 37217783; PMCID: PMC10421797.
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 249, 2985-3021.e8

Back to Our Patient…



CT chest/abd/pelvis (1 mo into hospitalization) – extensive pneumonia in lungs, several small hilar lymph nodes with subcarinal adenopathy. Enlarged liver with a single low-density lesion; splenomegaly with extensive target lesions.

Next Steps??



Back to Our Patient…

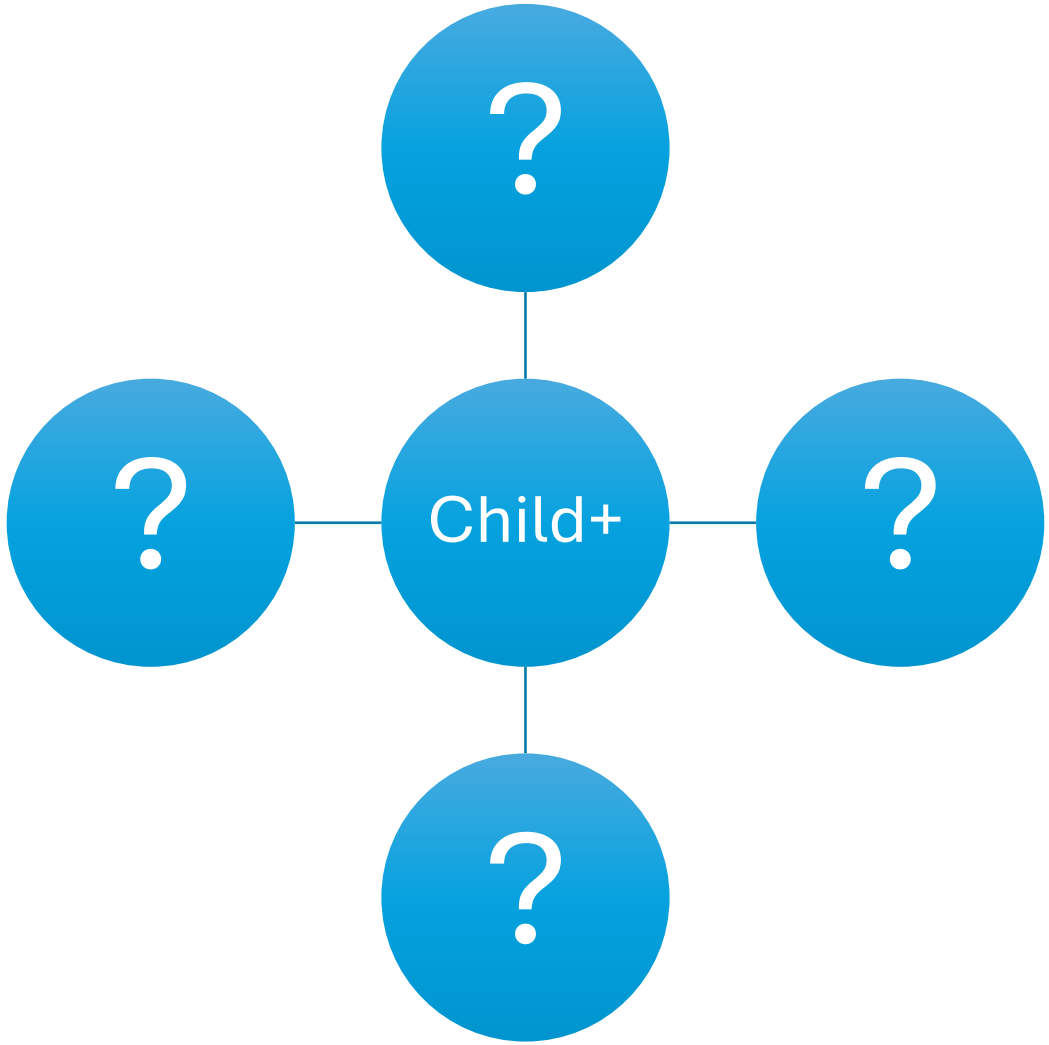
CT chest/abd/pelvis (1 mo into hospitalization) – extensive pneumonia in lungs, several small hilar lymph nodes with subcarinal adenopathy. Enlarged liver with a single low-density lesion; splenomegaly with extensive target lesions.

Obtained Further History & Exposures:

- Born at 40 weeks gestation, to G2P1 mother, normal prenatal course, good prenatal care. Negative HIV, syphilis, HepB labs.
- Mother – traveled to Mexico on a cruise at 20 wks gestation
- Paternal grandmother visiting from China 3 wks prior to delivery was previously staying at parent's house

- On further evaluation – Mother had positive PPD 3 years prior. No symptoms consistent with active TB. CXR repeated at time of hospitalization – showed calcification as well as left pleural thickening vs effusion; ultimately diagnosed with and treated for pulmonary tuberculosis.

Epidemiologic Investigation of close contacts around child with TB disease



Notified Infection Prevention & Control 

- What would be your recommendations for Infant in NICU?
- Would you separate the mother from the Infant?
- Any other recommendations?

TB Transmission can occur in the NICU from both Congenital and Nosocomial Exposures, but is rare.

65-day-old preterm infant with poor weight gain, respiratory failure with pneumonia, diagnosed postmortem with fulminant tuberculosis with disseminated miliary disease

Intubated/ventilated on oscillator; Open bed for last 20 days of life

Placenta – focal subchorionic acute inflammation, no granulomatous disease; No Acid-fast bacilli seen.

FAMILY – both parents and 4yr sib +TST. 2yo sib newly positive TST. 4yr sib +hilar adenopathy on CXR. Everyone asymptomatic.
Father = sputum negative
Mother = endometrial biopsy +*M tuberculosis*

NICU Exposure = Same Room as Index Case >=24hrs

14 Infants

Baseline TST and Gastric aspirates for TB culture all negative
INH prophylaxis x 6 mo
Follow up TST at 3 mo – all negative

NICU Exposure = Any NICU contact when pt present

260 Health Care Workers

Annual TST - all negative

Follow up TST at 3 mo – 2 RNs +TST, Negative CXR, Dx LTBI

Persons exposed to infant	Tuberculin skin testing: no. of persons	
	Tested	Positive
NICU infants	14	0
Visitors	27	4*
Health care workers	260	2† (0.8%)

NOTE. NICU = neonatal intensive care unit.
* Positive for unknown duration.
† Tuberculin skin test conversion.

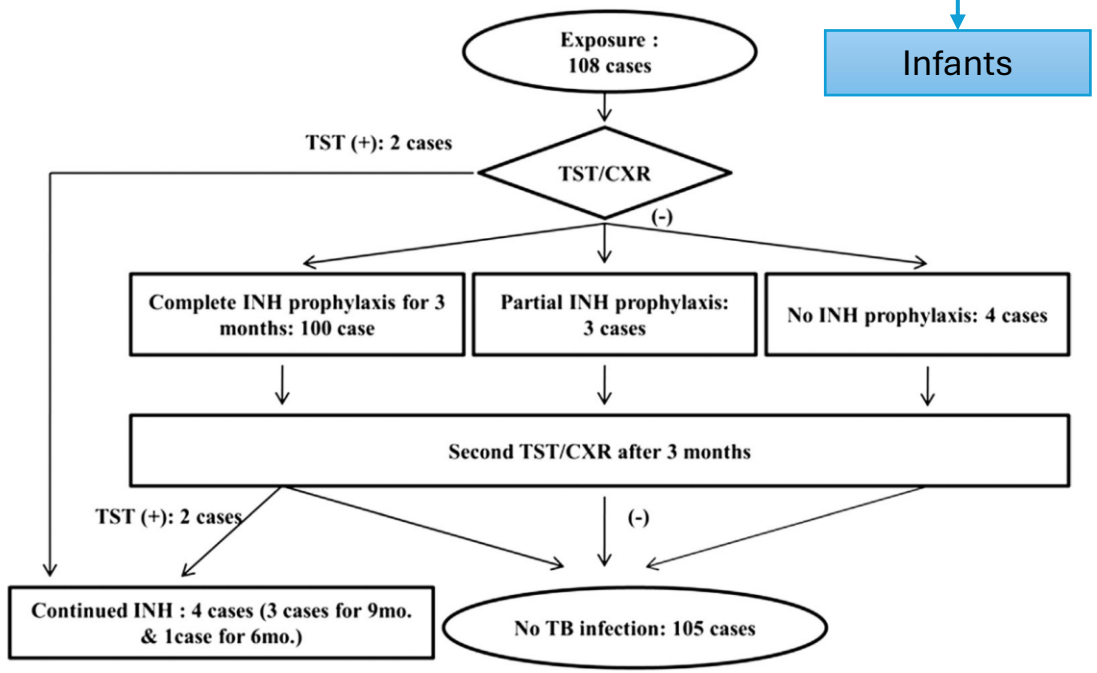
Lee LH, LeVea CM, Graman PS. Congenital tuberculosis in a neonatal intensive care unit: case report, epidemiological investigation, and management of exposures. Clin Infect Dis. 1998 Sep;27(3):474-7. doi: 10.1086/514690. PMID: 9770143.

Exposure to an infected adult (health care worker) within the NICU can lead to TB infection.

24 yr old Health Care Worker, Pulm TB

NICU - Seoul, Korea

Infants



3.7% nosocomial transmission rate to hospitalized neonates

Ahn JG, Kim DS, Kim KH. Nosocomial exposure to active pulmonary tuberculosis in a neonatal intensive care unit. Am J Infect Control. 2015 Dec 1;43(12):1292-5. doi: 10.1016/j.ajic.2015.07.020. Epub 2015 Aug 22. PMID: 26307044.

Notified Infection Prevention & Control

IP&C guidance:

- *Infant:*
  - *Risk of transmission from infants who cannot cough forcefully is very low, but not zero.*
  - *Maintain on airborne isolation precautions.*

Mother :

- *Had no symptoms concerning for active pulmonary disease; CXR not consistent with active pulmonary disease. Risk of transmission from mother low. She was referred to a provider for treatment and limited on her movement within the unit.*
- *She was not separated from the infant.*
- *OK to breastfeed if desired, unless mother has drug-resistant TB or is too ill.*

What further investigation would you complete for the infant?

Risk of Progression from *M. tuberculosis* infection to disease is age-dependent.

Infants <12 months experience the highest risk of developing TB disease after TB infection.
Also at high risk for developing disseminated disease or meningitis.

Age at Initial Infection or When Close Contact with Known Tuberculosis Case (yr)	Review of Pre-Chemotherapy Literature		Meta-Analysis of Recent Cohort Studies
	Percentage (%) of Children Who Develop Pulmonary Disease	Percentage (%) of Children Who Develop Meningitis or Disseminated Disease	Percentage (%) of Children Who Develop Any Tuberculosis Disease Within 2 Years of Initial Infection
<1	30–40	10–20	7.6
1	10	2–5	
2–4	5	0.5	
5–9	2	<0.5	5.2
10-14	10–20	<0.5	5.6
15–19	Not given	Not given	6.7

Int J Tuberc Lung Dis . 2004;8:392–402
Lancet . 2020;395:973–984

SPINAL FLUID		
Appearance, CSF	Clear	Bloody
Nucleated Cells, CSF	4	3
RBC, CSF	0	8,000 ▲
Bands CSF		12 ▲
Polys, CSF		12 ▲
Lymphs, CSF	42	46
Mono/Macrophage, CSF	58	20
Metamyelocytes CSF		10
nRBC, CSF		3
Number of Cells, CSF	150	59
Glucose, CSF	48 ▼	43 ▼
Protein CSF	66 ▲	59 ▲

AFB culture negative
M tuberculosis PCR (CSF) negative

MRI Brain –

- IMPRESSION:

1. No abnormal leptomeningeal and enhancement.

2. Small foci of increased T1 signal within the left posterior corona radiata as well as a small focus of restricted diffusion within the posterior limb of the internal capsule on the left. These findings may relate to subtle ischemic injury.

Mycobacterial therapy was started.

- What medications would you start?

1-month-old male infant with respiratory failure & pneumonia, in critical/severe condition, slight abnormality on MRI brain

- CSF studies pending.
- Does not qualify for a ‘shorten’ regimen; minimum 6 months for pulmonary disease.

- In children with tuberculosis meningitis – AAP recommends initial phase: 4-drug regimen = INH, Rifampin, Pyrazinamide, ethionamide or aminoglycoside, followed by INH + Rifampin for additional 7-10 months.
  - Adjunctive therapy = corticosteroid therapy with dexamethasone or prednisone tapered over 6-8 weeks.

Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, Chaisson LH, Chaisson RE, Daley CL, Grzemska M, Higashi JM, Ho CS, Hopewell PC, Keshavjee SA, Lienhardt C, Menzies R, Merrifield C, Narita M, O'Brien R, Peloquin CA, Raftery A, Saukkonen J, Schaaf HS, Sotgiu G, Starke JR, Migliori GB, Vernon A. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016 Oct 1;63(7):e147-e195. doi: 10.1093/cid/ciw376. Epub 2016 Aug 10. PMID: 27516382; PMCID: PMC6590850.

Amikacin IV

Pyrazinamide suspension

Rifampin suspension

Isoniazid suspension

Steroids were considered, but since CSF Mtb PCR was not detected, were initially deferred.

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

1 wk into therapy:

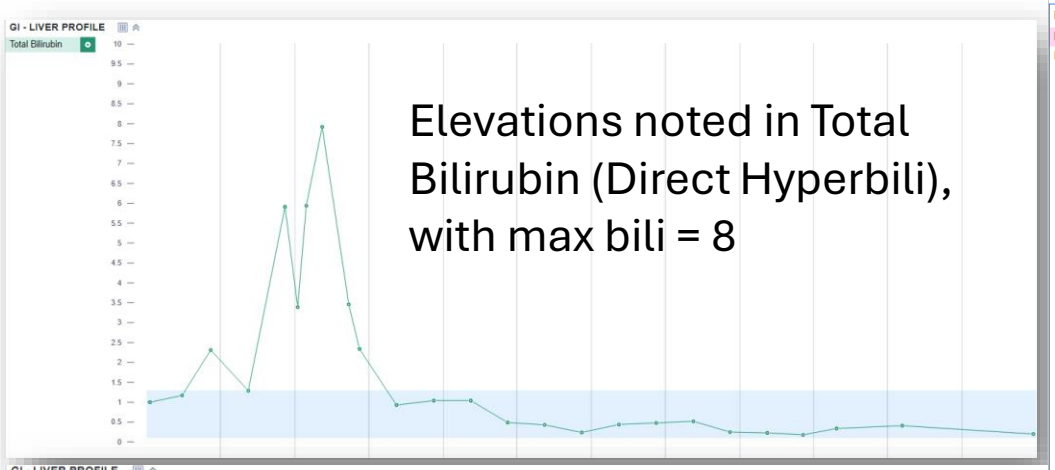
Amikacin IV

Pyrazinamide suspension

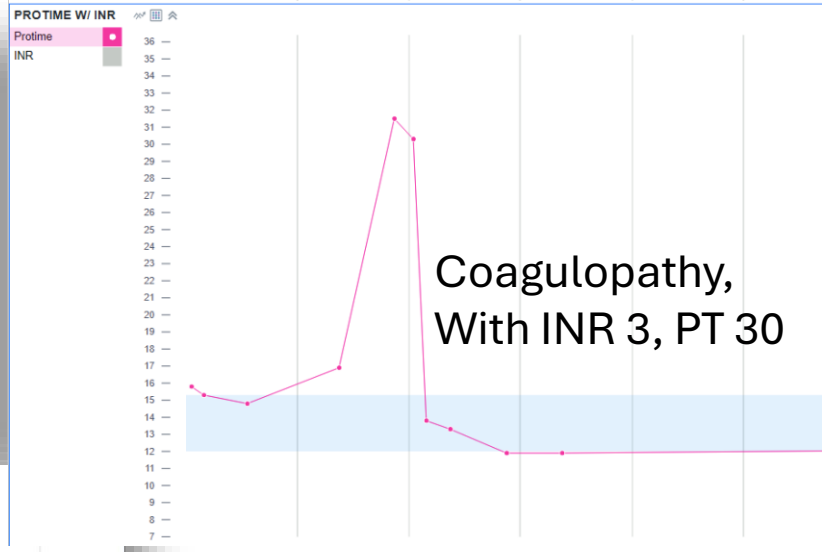
Rifampin suspension

Isoniazid suspension

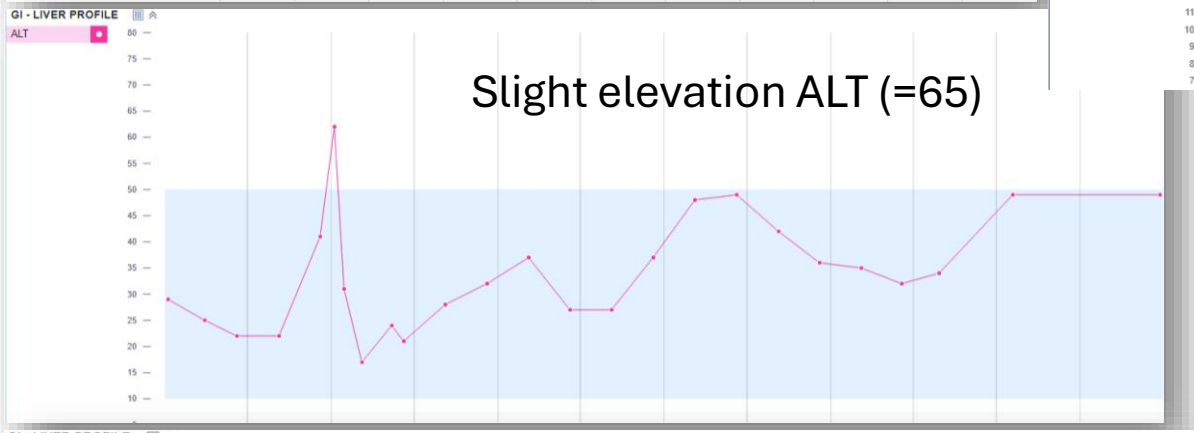
Steroids were considered, but since CSF Mtb PCR was not detected, were deferred.



Elevations noted in Total Bilirubin (Direct Hyperbili), with max bili = 8

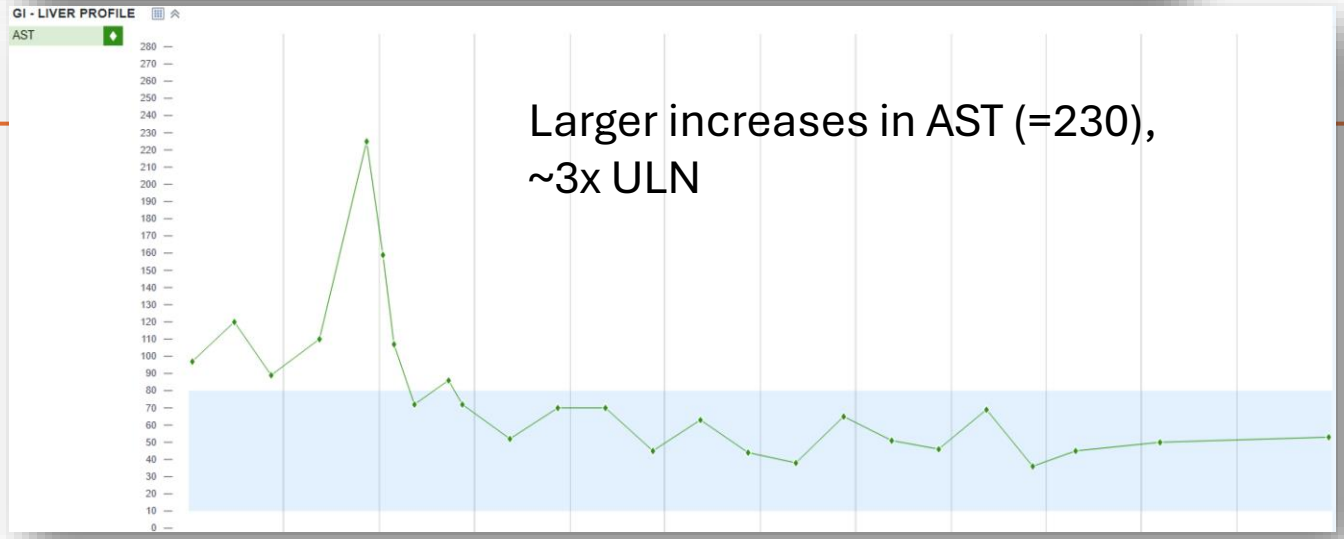


Coagulopathy, With INR 3, PT 30



Slight elevation ALT (=65)

Continued Thrombocytopenia, With Plts = 20s



Larger increases in AST (=230), ~3x ULN

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

TB Drug-Induced Liver Injury is not common in pediatric patients (0.2%-8%).
- Associated with younger age (<5yrs), extrapulmonary TB, and use of PZA

Amikacin IV

Pyrazinamide suspension

Rifampin suspension

Isoniazid suspension

Isoniazid, Rifampin, Pyrazinamide all can cause drug-induced liver injury.

If ALT >= 3x upper limit of normal with hepatic dysfunction or >=5x ULN, then stop medications immediately.

Steroids were considered, but since CSF Mtb PCR was not detected, were initially deferred.

Table 7. Other Causes of Abnormal Liver Function Tests That Should Be Excluded

Viral hepatitis (hepatitis A, B, and C in all patients; Epstein-Barr virus, cytomegalovirus, and herpes simplex in immunosuppressed patients)
Biliary tract disease
Alcohol
Other hepatotoxic drugs (eg, acetaminophen, acetaminophen-containing multiagent preparations, lipid-lowering agents, other drugs)
Select herbal and dietary supplements

Source: American Thoracic Society [56].

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, Chaisson LH, Chaisson RE, Daley CL, Grzemska M, Higashi JM, Ho CS, Hopewell PC, Keshavjee SA, Lienhardt C, Menzies R, Merrifield C, Narita M, O'Brien R, Peloquin CA, Raftery A, Saukkonen J, Schaaf HS, Sotgiu G, Starke JR, Migliori GB, Vernon A. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016 Oct 1;63(7):e147-e195. doi: 10.1093/cid/ciw376. Epub 2016 Aug 10. PMID: 27516382; PMCID: PMC6590850.

Amikacin IV 

~~Pyrazinamide suspension~~ → Levofloxacin suspension

~~Rifampin suspension~~ → Ethambutol suspension

Isoniazid suspension 

Steroids were considered, but since CSF Mtb PCR was not detected, were deferred.

Imaging showed no signs of biliary dilatation.
Completed 3 doses of Vitamin K
CMV infection playing role?

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

Amikacin IV

~~Pyrazinamide suspension~~ → Levofloxacin suspension

~~Rifampin suspension~~ → Ethambutol suspension + Rifampin suspension

Isoniazid suspension

Liver function was monitored/stable

Steroids (2mg/kg/day prednisone) were started due to extensive ascites.

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

Amikacin IV

~~Pyrazinamide suspension~~ → Levofloxacin suspension

~~Rifampin suspension~~ → Ethambutol suspension + Rifampin suspension

Isoniazid suspension

Steroids (2mg/kg/day prednisone) were started due to extensive ascites.

Antimicrobial susceptibility resulted:

Comment: Culture POSITIVE for Mycobacterium tuberculosis Identified by DNA probe and PCR. Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS	
TBMIC	
ORGANISM	Mycobacterium tuberculosis
Isoniazid 0.1 ug/mL	Suscept
Rifampin 1.0 ug/mL	Suscept
Ethambutol 5.0 ug/mL	Suscept
Pyrazinamide 100 ug/mL	Suscept

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

1 mo

Adjustments made to regimen based on susceptibility

Amikacin IV

~~Pyrazinamide suspension~~ → Levofloxacin suspension

~~Rifampin suspension~~ → ~~Ethambutol suspension~~ + Rifampin suspension

Isoniazid suspension

Steroids (2mg/kg/day prednisone) continued due to extensive ascites, plan 4-6 wks, with taper

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

1 mo

Antimicrobial susceptibility resulted:

Comment: Culture POSITIVE for
Mycobacterium tuberculosis
Identified by DNA probe and PCR.
Test developed and characteristics determined by
ARUP Laboratories. See Compliance Statement B:
aruplab.com/CS
TBMIC

ORGANISM	Mycobacterium tuberculosis
Isoniazid 0.1 ug/mL	Suscept
Rifampin 1.0 ug/mL	Suscept
Ethambutol 5.0 ug/mL	Suscept
Pyrazinamide 100 ug/mL	Suscept

2 mo into therapy:

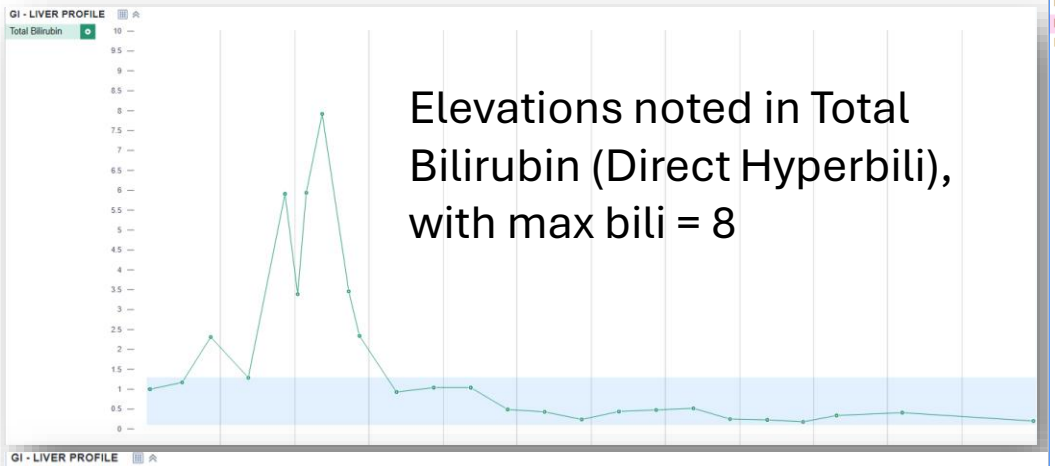
Amikacin IV

Levofloxacin suspension

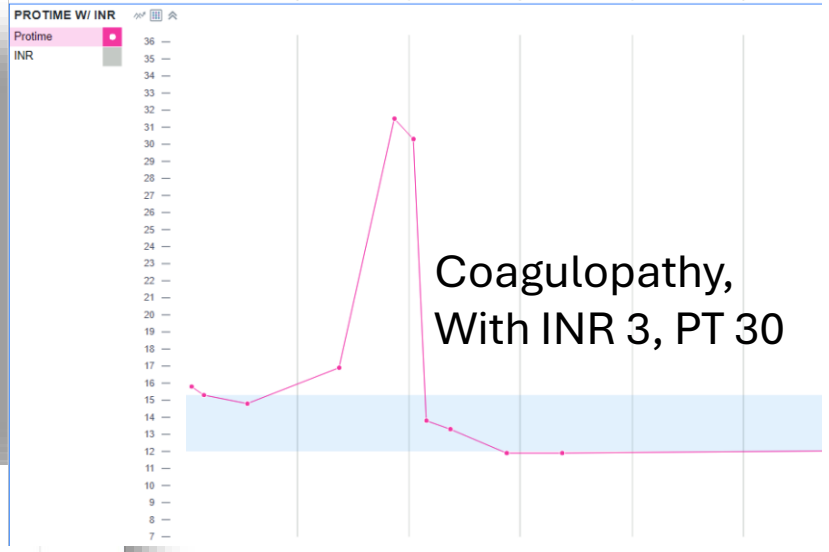
Rifampin suspension

Isoniazid suspension

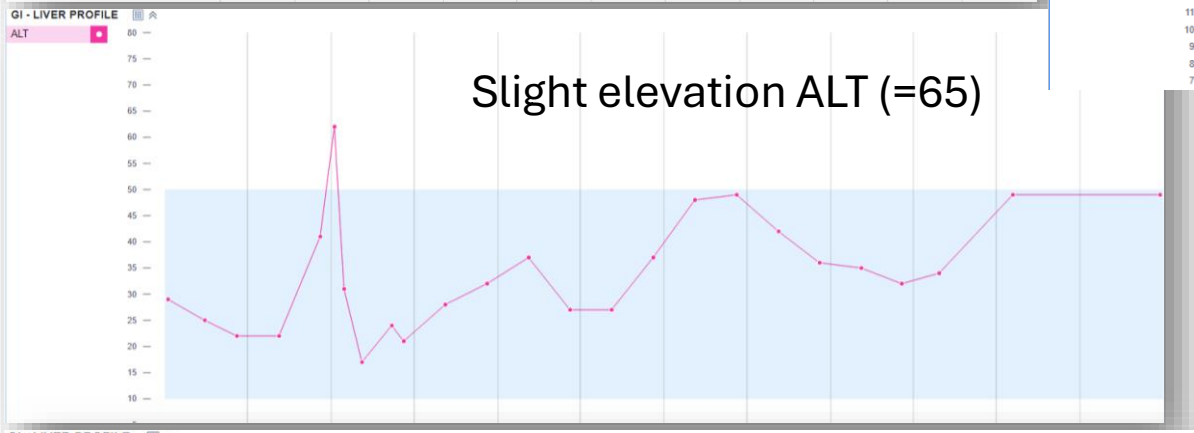
+Steroids



Elevations noted in Total Bilirubin (Direct Hyperbili), with max bili = 8

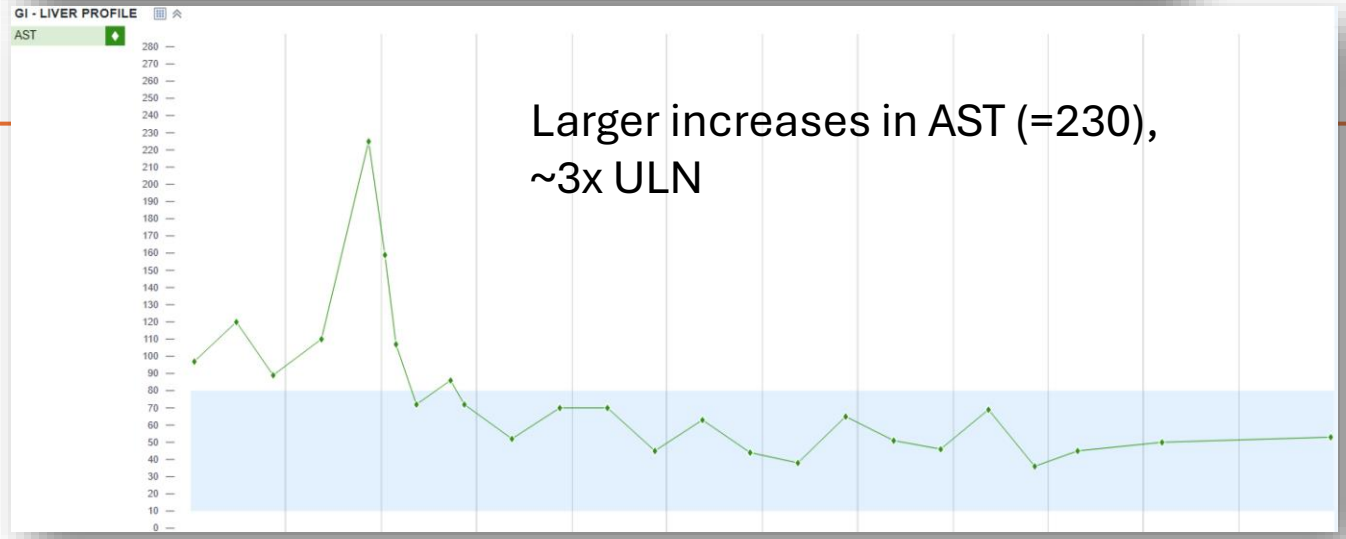


Coagulopathy, With INR 3, PT 30



Slight elevation ALT (=65)

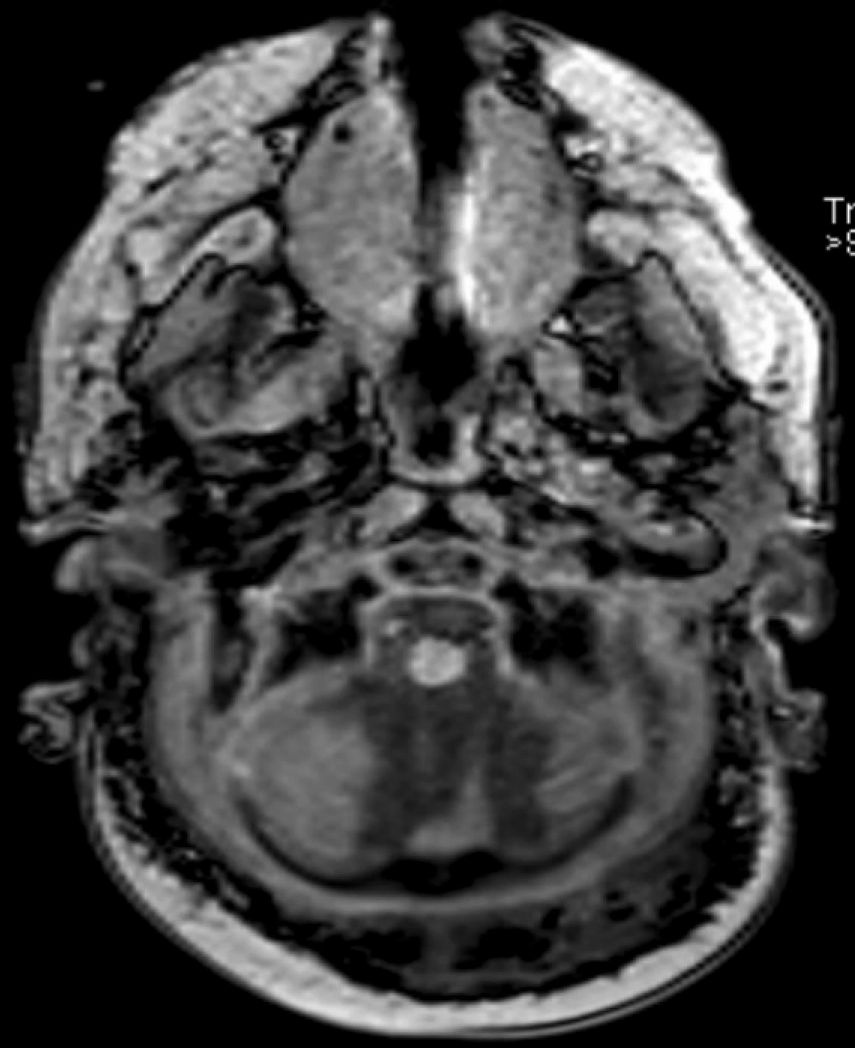
LFTs and liver function normalized



Larger increases in AST (=230), ~3x ULN

Diagnosis: Miliary TB, with pulmonary, CNS, abdominal involvement

2 mo into treatment:
Noted to have cushingoid appearance, still on ventilator;
Repeated MRI Brain



CNS involvement

MRI Brain –
IMPRESSION:
1. Multifocal foci of T1 shortening and T2 hypointense signal, some of which have enhancement as described above consistent with **tuberculomas from miliary TB**. No abscess or empyema. No basal diffuse leptomeningeal enhancement. No evidence of hydrocephalus.
2. There is periventricular white matter volume loss.

Summary: 1-month-old male infant with miliary / CNS Tuberculosis (Congenital vs Postnatal)

- Hospitalized for 4 months

- Course was complicated with:
  - Respiratory failure, developed chronic lung disease (went home with home oxygen therapy)
  - Severe ascites, s/p peritoneal drain
  - Hepatotoxicity due to presumed TB drug induced liver injury
  - Documented CNS involvement on brain imaging
  - Feeding intolerance, with g-tube placement
  - Delayed milestones, with PT/OT//ST

- Medications, completed:
  - 13 months of combination TB medication
  - 5 months of steroids, which including a very, very long taper