

## A Case of Tuberculosis Congenital or Acquired?

Felicia Dworkin, MD  
NYC DOHMH Bureau TB Control  
World TB Day  
March 23, 2012



## Congenital & Neonatal TB

- Congenital TB:
  - acquired by the fetus during pregnancy of a mother with active TB disease
  - A rare disease
- Neonatal TB:
  - A more frequent form of TB in newborns
  - Acquired disease at or after birth from an infectious adult usually via airborne transmission
- The presentation, management and prognosis usually do not differ



## Congenital TB-Pathogenesis

- Tuberculous bacillemia during pregnancy may result in infection of the placenta or maternal genital tract
- 3 possible modes of infection of the fetus:
  - Hematogenous via the umbilical vein
  - Fetal aspiration of infected amniotic fluid
  - Fetal ingestion of infected amniotic fluid
- Spread of the bacilli in the fetus leads to formation of primary complexes in the liver, lungs or GI tract



## Clinical Manifestations of Congenital TB

- Infant is frequently born premature
- Delayed diagnosis is common
  - Signs of disease usually do not appear for several days or weeks
  - Often confused with other neonatal acquired infections
- Commonly presents with respiratory distress, lethargy, poor feeding, fever, irritability, abdominal distention and failure to thrive
  - Common: lymphadenopathy and hepatosplenomegaly
  - Uncommon: meningitis and jaundice
  - In some cases 1<sup>st</sup> sign is otitis media with or without mastoiditis
- Disease course is often fulminant characterized by disseminated disease



## Index Case

- Premature male born on July 21<sup>st</sup> at 31 weeks to 34 year-old Ecuadorian woman
- He developed jaundice and tachypnea believed to be due to his pre-term delivery
- Observed for 28 days in NICU
- Discharged on August 18<sup>th</sup> (29 days old) in stable condition



## Index Case-2 Months Old (September)

- Infant noted to have purulent left ear discharge
- Outpatient ENT: diagnosed with methallicin resistant staph aureus (MRSA) Otitis Externa and started on a 3 month course of Ciprodex



### Index Case-3 Months Old (October)

- Despite antibiotics, patient continued having persistent left ear discharge.
- During this time period, he also developed bilateral cervical lymphadenopathy
- Augmentin was given for 10 days by the primary physician

Differential dx: chronic otitis vs. viral illness??



### Index Case-4 Months Old (November)

- Seen by PMD for another course of high fevers and persistent lymphadenopathy
  - Large left supraclavicular lymph node
- Given a 3<sup>rd</sup> course of oral antibiotics for bronchopneumonia and chronic otitis externa



### Index Case-6 Months Old (January 6<sup>th</sup>-Hospital day 0)

- Brought and admitted to Hospital A with symptoms of:
  - 2 week fevers (104.5° at home)
  - barking non-productive cough
  - neck swelling bilaterally
  - chronic drainage from left ear
  - irritability
  - poor feeding with no weight gain during the last month



### Index Case-Physical Findings

- Physical exam significant for:
  - Acutely ill infant in mild respiratory distress, febrile (102.5 °)
  - Bilateral cervical lymphadenopathy
    - additional large left supraclavicular node
  - Enlarged spleen
  - Lungs: harsh breath sounds
  - Heart: tachycardia with normal heart sounds
  - No signs of dehydration
  - No signs of meningitis



### Index Case-Evaluation (I)

- Increased WBC (with left shift)
- Iron deficient anemia
- Blood cultures negative x3
- CXR: Bilateral infiltrates & LUL pneumonia
- Ultrasound neck: bilateral cervical nodes, (largest 1.5cm)
- Additional Lab studies:
  - Positive: respiratory and urine cultures for RSV and CMV, respectively
  - Negative tests: Toxoplasma, respiratory vial cx, EBV, influenza, parainfluenza, and Adenovirus
  - HIV test negative
  - TST: negative (0 mm induration, 10 mm erythema)

Differential diagnosis??



### Index Case-Hospital A, Day 2

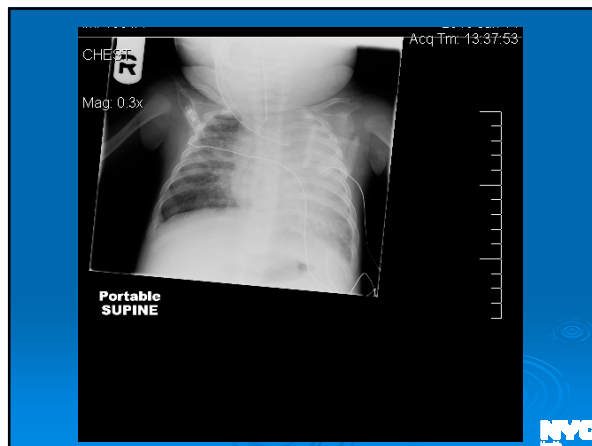
- Initial working diagnosis of bacterial pneumonia with sepsis and MRSA chronic otitis
  - Placed in single room on contact precautions due to MRSA
  - Given IV antibiotics
- January 7<sup>th</sup> (Hospital day 2)- ENT performs a needle aspiration of Lt. supraclavicular lymph node which was non-diagnostic
- January 10<sup>th</sup> (Hospital day 5): Patient transferred to Hospital B, as condition is not improving
  - Differential: viral/bacterial process vs. immunologic deficient disease vs. malignancy

How about Tuberculosis?



## Hospital B (January 10<sup>th</sup>-Hospital Day 5)

- Chest x-ray: bilateral interstitial disease and left sided consolidation
- Continued on antibiotics for bacterial, viral infections (RSV) and caspofungin added for possible fungal disease
- Consultations by hematology, ENT and ID requested
- Jan 13<sup>th</sup> (hosp. day 8): additional imaging studies obtained
  - CT of neck, chest, abdomen, head



**CT neck (Jan 13<sup>th</sup>)**

- Extensive bilateral cervical adenopathy
- suspicious for thymic infiltration

**CT chest (Jan 13<sup>th</sup>):**

- multiple pulmonary lesions with large mass in the right lung; possible mass in the left lung
- Extensive mediastinal & hilar adenopathy

**CT abdomen/pelvis (Jan 13<sup>th</sup>):**

- Massive lymphadenopathy with a conglomerate of nodes in the mesentery.

(Appearance favors lymphoproliferative disease.)

**CT Head (Jan 13<sup>th</sup>):**

- Focal ring enhancing lesions in left cerebellar hemisphere (8 mm) and right frontal lobe (1x5 mm). No surrounding edema.
- Left otitis externa changes with destruction of the mastoids and complete opacification of the mastoids and middle ear spaces.

(The differential diagnosis includes focal meningitis vs. brain abscess)

## Diagnostic Test-Jan 14<sup>th</sup>-17<sup>th</sup> (Hospital B-Day 9-12)

- Lymph node Biopsy :
  - large areas of necrosis, non-caseating and caseating granulomas with giant cells. AFB stain is positive with numerous micro-organisms
- LP : unremarkable
- Remained intubated after the biopsy for the next 10 days (1/14-24)
- Jan 17<sup>th</sup>: Sputum obtained from the ET-tube :
  - +3 AFB smear

Diagnosis of TB is finally made!!



## Therapy Begun for TB-Jan 18<sup>th</sup> (Hospital B-Day 13)

- Started daily INH 80mg, Rifampin 110mg, PZA 220mg, and Ethambutol 110mg
  - Steroids are given because of disseminated disease
  - Susceptible to all first line drugs
- Additional sputum/gastric aspirates done: smear positive; culture positive *M. tuberculosis*
- Discharged on February 4<sup>th</sup> (hosp. day 29) to follow up with hospital & DOHMH chest center
  - Weight at almost 7 months age: 5.15kg (11.3 lbs.)
  - Growth curve is below the 5<sup>th</sup> percentile for age & weight



## Source Case Investigation

- Immediate family: mother, estranged father, 3 year old sibling
  - 3 year old: TST negative twice & x-ray negative
  - Father: TST positive, x-ray negative; refused LTBI therapy
- Mother seen at Hospital B; admitted on Jan. 17<sup>th</sup> with an abnormal x-ray



## Source Case-Mother Evaluation

- She denied any current respiratory symptoms, but complained of fatigue and weight loss post-delivery back in July
- During this pregnancy, she said the TST test was negative, and she didn't recall doing a chest x-ray
- History obtained from records during 1<sup>st</sup> pregnancy in 2007
  - Claimed she was TST positive
  - Chest x-ray was negative
  - Was supposed to return post-partum for LTBI therapy but did not



## Source Case-Mother

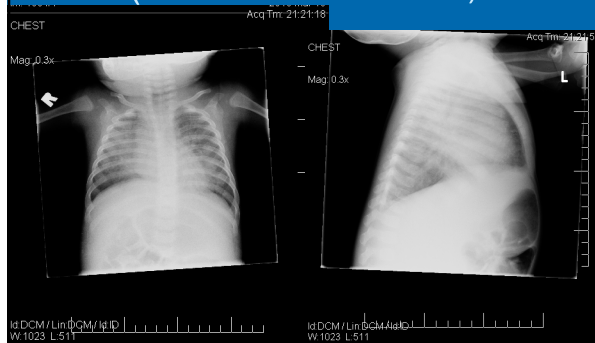


## Source Case-Mother

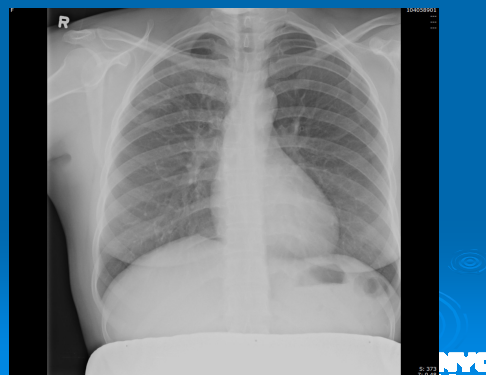
- Sputum x3 AFB smear negative, culture positive for *M. tuberculosis*
  - Drug susceptible
  - Genotype matches infant
- Started IRPE on January 18<sup>th</sup>, same day as infant



## Infant Follow up: March 16<sup>th</sup> (2 months on medications)



## Mother After 7 months Therapy



## Evaluation & Treatment

### Clinical Manifestations of Congenital TB

- Infant is frequently born premature
- Delayed diagnosis is common
  - Signs of disease usually do not appear for several days or weeks
  - Often confused with other neonatal acquired infections
- Commonly presents with respiratory distress, lethargy, poor feeding, fever, irritability, abdominal distention and failure to thrive
  - Common: lymphadenopathy and hepatosplenomegaly
  - Uncommon: meningitis and jaundice
  - In some cases 1<sup>st</sup> sign is otitis media with or without mastoiditis
- Disease course is often fulminant characterized by disseminated disease

### Congenital & Neonatal TB- Evaluation

- If TB disease is suspected in the newborn perform:
  - TST: is usually negative
  - Chest x-ray, lumbar puncture, appropriate cultures including gastric aspirates
  - Placental examination by histology for granuloma & AFB and culture for TB
- If TB disease is highly suspected, regardless of the newborn's TST result:
  - Begin INH, Rifampin, PZA and an injectable (amikacin, streptomycin, kanamycin)

### Congenital & Neonatal TB- Evaluation(2)

- Evaluate the mother for presence of pulmonary or extrapulmonary disease, including uterine tuberculosis disease
  - TST, chest x-ray, sputum
  - Evaluate other household contacts as indicated
- If meningitis of the newborn is confirmed, steroids should be added

## Congenital & Neonatal TB LTBI Therapy

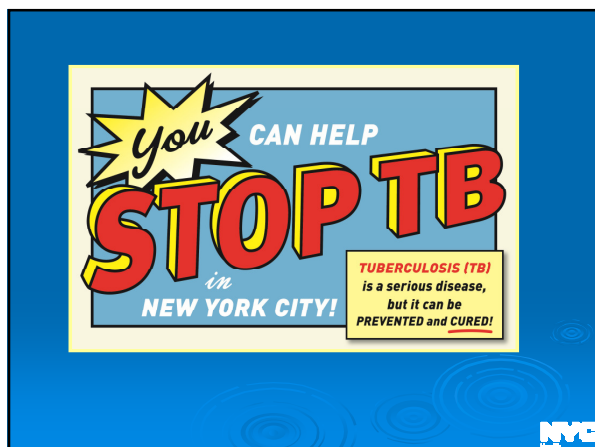
- If TB ruled out and mother has active disease, place the newborn on INH for 3 months or until the mother is culture negative.
- Repeat the TST at age 3 months:
  - Infant TST +: reassess for TB disease and if ruled out continue INH for 9 months total
  - Infant TST -: repeat the TST again at 6 months, continue INH
    - If TST positive at 6 months, reassess for TB disease, and if ruled out continue INH for a total of 9 months.

NYC

## Congenital & Neonatal TB Conclusions

- Need to consider tuberculosis as part of the differential diagnosis in newborns or infants who:
  - Are born premature without another etiology
  - Are not feeding, not gaining weight normally or who have failure to thrive
  - Have frequent illness or non-resolving infections (especially otitis or mastoiditis)
  - Have abnormal findings on chest x-ray or adenopathy
  - Mother found to have active TB during pregnancy or at the time of delivery

NYC



NYC