TB Grand Rounds

Sheila Nolan, MD, W. Kemper Alston, MD, & Barbara Watson, MD

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Speaker: Sheila Nolan, MD

- Infectious disease fellow at Children’s Hospital of Philadelphia (CHOP)
- Medical degree, Temple University
- Pediatric residency, University of South Florida
A neonate with respiratory distress

Sheila M. Nolan, MD
Infectious Diseases Fellow
The Children’s Hospital of Philadelphia

Admission History

- Patient is a 36 day old ex-32 week male admitted to CHOP for worsening respiratory distress
- Baby was a 2050gm IVF product born via SVD to a 30 y/o G3P0 mom
  - RPR negative, HIV negative, HBsAg and GBS unknown
  - Pregnancy complicated by pre-term labor
  - Maternal h/o hypothyroid dx – on synthroid
Admission History

• Baby had an unremarkable NICU course until approximately 3 wks of age
  • Noted to be lethargic and began having episodes of desaturation
  • CXR showed right sided infiltrate
  • Over the next 2 weeks the baby had progressively worsening CXR and respiratory distress, eventually requiring intubation and mechanical ventilation
• Transferred to CHOP

Further history

• Upon development of respiratory distress, patient had blood cx’s drawn and an LP
  – Cx’s all negative, multiple repeat blood cx’s all negative
• He was initially started on ampicillin, gentamicin and cefotaxime
  – Tracheal aspirate cx grew Enterobacter aerogenes
  – Antibiotics changed to Vancomycin, Cefepime and amikacin
Social and Family History

- Parents originally from India, father traveled to India 6 months ago, mom has not been there in few years
- Grandparents arrived shortly after baby was delivered and have visited the NICU frequently
  - Grandmother has been coughing since arrival
- Parents deny any family history of health problems

Physical Exam

- Wt: 3340gm
- General: Lethargic, decreased tone, mildly edematous
- HEENT: AFOSF, palate intact
- Chest: coarse BS, crackles throughout
- Heart: RRR, 2+ pulses
- Abdomen: +BS, soft, NT, no HSM
- G/U: Tanner I male, testes descended b/l
- Extremities: MAEE, no hip click
- Neuro: + grasp, low tone
Laboratory Data

• WBC 14.9, Hgb 13.7, Hct 39.8, Plt 159
  – Diff: 1 myelocyte, 1 metamyelocyte, 29 bands, 41 neutrophils, 20 lymphocytes, 8 monocytes
• Na 120, K 4.8, Cl 85, Bicarb 31, BUN 5, Cr 0.3, Glu 85, Ca 8.8, Mg 1.7, Phos 4.4
• Total bili 1.1, Unconjugated bili 1.1, Total protein 4.5, Albumin 2.1, ALT 38, AST 88
• pH 7.471, CO2 46.1, O2 37, Bicarb 33.6, Base excess 9

Laboratory Data

• CSF:
  – WBC 0
  – RBC 0
  – Protein 66
  – Glucose 43
  – gram stain – rare WBC, no organisms
  – cx – neg
• Viral respiratory panel – negative
• Pertussis PCR - negative
Chest X-Ray

Diffuse bilateral parenchymal infiltrates

Microbiology Data

- Routine Blood cx: no growth
- Routine Urine cx: no growth
- Tracheal aspirate:
  - Gram stain: moderate WBC’s, few beaded gram positive rods – acid fast positive
AFB Smear of Tracheal Aspirate

http://commons.wikimedia.org/wiki/Image:Mycobacterium_tuberculosis_Ziehl-Neelsen_stain_02.jpg

AFB Smear and Culture Results

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Smear</th>
<th>Culture</th>
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<tbody>
<tr>
<td>Tracheal aspirate</td>
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<td>Gastric Aspirate</td>
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PCR and culture confirmed Mycobacterium tuberculosis
Hospital Course

• He was initially too ill to receive oral medication, so was started on a 5 drug IV regimen
  – INH
  – Rifampin
  – Amikacin
  – Linezolid
  – Ciprofloxacin

Hospital Course

• Hospital day 5, dopamine was weaned
• Within 1 week, he began NG feeds
• By the 2nd week after the initiation of therapy, the baby was extubated and tolerating full feeds. Antibiotic regimen was switched to an oral medications:
  – INH, Rifampin, Ethambutol and Pyrazinamide
Discharge X-ray

CXR prior to discharge. Baby was discharged to home 3 ½ weeks after admission

Investigation

• TST’s were administered on parents and grandparents and chest x-rays obtained
  - TST results
    • Father – 7mm
    • Mother – 10-12 mm
    • Grandparents reported as negative per PMD
  - Chest x-rays all read as negative
Investigation

- Mother reported that while she was in India being evaluated for infertility, she had an endometrial biopsy that was negative for TB.
- After Baby’s TB PCR confirmation, mother’s OB performed a D&C and the endometrium was + for AFB.
- Formalin fixed placental specimens were stained for AFB and were negative.

Questions & Comments
Genital Tuberculosis

- Reportedly causes 7-56% of infertility in developing countries
- Endometrial aspirates and biopsies often negative for AFB smear and culture, PCR may be more useful
- PPD often negative, 55% sensitivity, 80% specificity
- Organs most frequently affected
  - Fallopian tubes 95-100%
  - Endometrium 50-60%
  - Ovaries 20-30%

Hysterosalpingogram of a patient with tuberculosis of the fallopian tubes shows right-sided hydrosalpinx with an occluded left fallopian tube

http://www.gfmer.ch/selected_images_v2/detail_list.php?cat1=7&cat3=592&stype=d
Tuberculosis Salpingitis

http://www.gfmer.ch/selected_images_v2/detail_list.php?cat1=7&cat3=592&stype=d

Congenital Tuberculosis

• Rare, post-natal acquired TB is much more common
• Acquired via hematogenous spread through umbilical vein from an infected placenta or aspiration or ingestion of infected amniotic fluid
Congenital Tuberculosis

- Usually presents in first 2-4 weeks of life
  - Can range from first few days up to 4 months
- Clinical manifestations include fever, respiratory distress, abdominal distension, lethargy, irritability, hepatosplenomegaly, lymphadenopathy, jaundice, ear discharge and skin papules

Discussion

- TB diagnosis and evaluation in neonates and infants
- Treatment of neonatal TB
- Other questions & comments?
DNA Fingerprinting Results

References

Discharge & Follow-up

Speaker: W. Kemper Alston, MD, MPH

- TB Medical Consultant for Vermont Department of Health
- Associate Professor of Medicine at University of Vermont- College of Medicine
- Attending Physician of ID Unit, Hospital Epidemiologist, Chairman of Infection Control Committee, & Employee Health Service Consultant at Fletcher Allen Health Care
“Empyema Necessitatis”

W. Kemper Alston, MD, MPH
Fletcher Allen Health Care
University of Vermont
Burlington, Vermont

Patient History

- 77 year-old male referred to ID Clinic on 8/24/05 by his primary care because of a large, painful, fluctuant, left posterior chest wall mass
- Complained of pain over his left chest (anterior, lateral, and posterior) for 2 months
- Treated with azithromycin in early 8/05, then was seen in a local ER
Past Medical History

- Severe, oxygen-dependent, chronic lung disease. Followed by Pulmonary. Described at times as obstructive, restrictive, bronchiectatic, fibrotic, & hypercapneic
- Diabetes, hyperlipidemia, PUD, CHF, and anemia
- Review of systems: Sweats, weight loss, SOB, cough, & difficulty urinating (all chronic). No fever, GI complaints, rash, or neurological complaints

Medications & Social History

- Simvastatin, glyburide, tamsulosin, metformin, lansoprazole, furosemide, fluticasone/salmeterol, & albuterol/ipratropium
- Had a steroid taper in 5/05
- Allergic to sulfa
- Lives at home with his wife
- Former smoker. No alcohol
Physical Examination

- Chronically ill-appearing, in a wheelchair, on supplemental oxygen with labored respirations.
- Afebrile, 77.5 kg, BP 130/58, pulse 110/min., respirations 22/min., 93% saturation on 4 liters/min.
- Decreased breath sounds throughout, with bronchial breath sounds at left apex. Exam of chest wall...
Laboratory Data

- ER 8/8/05: WBC 13.8
- 8/18/05: WBC 11.4, HCT 34%, Plat 349K, ESR 96
- CXR & CT scan...
Diagnostic Work-up

- Sono-guided aspirate of the lesion was performed on 8/11/05:
  - Cytology: Inflammatory; no malignancy
  - Gram stain: Polys, no organisms
  - Bacterial culture: Negative
  - AFB smear negative, culture pending
  - Fungal stain negative, culture pending
OK, there is more history...

- Mother and brother had tuberculosis
- Diagnosed with TB as a teenager, in the 1940s. Presumably pulmonary and pleural disease
- He was in and out of the Pittsford Sanatorium in Pittsford, VT between 1941 and 1945, where he was treated with arsenic drops
- He had empyema, draining thru the chest wall, and chest tubes...
Pittsford Sanatorium

- Built in 1907. The site was chosen because it was believed to receive the most sunshine in Vermont. The first patient was admitted 12/16/1907
- In 1917 the mean LOS was 141 days
- In May, 1971 it was turned over to the VT State Police as a training facility
- The building is said to be haunted by one of its former nurses
More History

- In approximately 1971 he was treated with 1 year of INH alone by Pulmonary
- Sputum AFB was negative at that time
- His wife is TST negative

Clinical Course

- The fluid culture from 8/05 grew *M. tuberculosis*
- Seen in follow-up 9/29/05 and begun on INH, rifampin, PZA & B6
- Baseline LFTs normal
- On 10/20/05 sensitivities returned resistant to INH, sensitive to rifampin, ethambutol, and PZA
- INH was changed to ethambutol
Clinical Course

- Tolerated meds well, with normal LFTs, but a large, fluctuant collection persisted
- Aspirated again for relief of symptoms in 10/05, 12/05, and 3/06 (1st two not cultured, the last was culture negative)
- CT scan 7/27/06 with 7 x 3 cm. fluid collection
- Treated until 9/30/06
- Seen 11/17/06 and was doing well
Clinical Course

- Admitted to local hospital 4/18-25/07 with presumed COPD exacerbation (fatigue, cough, and dyspnea)
- CXR was unchanged
- Sonogram revealed no drainable fluid collection
- Sputum x3 smear and culture negative
- Persistent monocytosis (50%)
- Seen 5/1/07 and doing well...

Empyema Necessitatis

The accumulation of pus in the pleural cavity, with subsequent rupture into the surrounding soft tissue. Drainage may occur into the breast, bronchus, mediastinum, esophagus, diaphragm, pericardium or retroperitoneum. Pus may even reach the flank, groin or thigh. Before antibiotics became available, empyema necessitatis was a complication of tuberculosis, fungal infections and various forms of pneumonia.
Empyema Necessitatis

The spontaneous extension of pus through the parietal pleura and chest wall from an empyema with the formation of a subcutaneous abscess. In most circumstances this occurs secondary to a tuberculous empyema. There may be an associated bronchopleural fistula.
Discussion

- Reactivation disease 60 years after treatment in a sanatorium
- The impact of INH monotherapy in the setting of untreated TB disease
- Management of INH resistance
- Management of “empyema necessitatis” in someone who is clearly not a surgical candidate
- The association of monocytosis with TB

Speaker: Barbara Watson, MD

- Medical Director for the Immunization Program & Associate Director of TB Control Program at Philadelphia Department of Public Health
- Responsible for all issues related to pediatric TB
- Associate Professor of Pediatrics at Jefferson Medical College
Is this Rassmussen’s aneurysm?

Barbara Watson, MD
Pediatric Consultant
TB Control Program
Philadelphia Department of Public Health

Patient History

- 16 year old US born Hispanic male
- Presents with 7 month history of cough, night sweats, fever, including hemoptysis 1 month prior to admission
- Admitting diagnosis – hemoptysis – unknown cause
- Tuberculin skin test – “positive”
- Discharge diagnosis – sinusitis
- Patient referred to TB clinic
- TST repeated at TB clinic and read as negative
- On 2-12-07, CHOP reported to TB Control that sputum smear AFB positive
- Patient continued to have hemoptysis
Social History

- Substance abuse
  - Marijuana cigarettes 5-7 daily
- 5 sexual partners
- History of juvenile detention

Physical Exam

- Vitals – Temp 37.4, Pulse 68, RR=20, BP 107/70, Pulse ox 98% on room air
- Pertinent physical findings – no nasal congestion, adenopathy
- Normal PE
**Laboratory Results**

- CBC – Hb 16.4, Hct 44.5, WCC 9.9 - segs 70, lymphs 20, plt - 280
- HIV – negative
- LFTs - ALT 26, AST 31
- RPR negative

**Radiographic Findings**

- CXR – nodule RUL
- CT scan revealed RUL nodular densities and ground glass opacities, not visualized on CXR
- Angiography with no evidence of aneurysm
- Normal pulmonary function tests
**Bacteriology**

- Specimens obtained at CHOP
  - Sputum x3 – AFB negative, culture grew MAI
  - Bronchoscopy – BAL – many WCC, no orgs, CMV and RSV, AFB negative
- Specimens obtained at TB clinic
  - Induced specimens x3 – AFB positive, culture pending

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**Treatment Course**

- Treatment regimen -RIPE
- Start- 2-9-06
  - Directly observed therapy (DOT)
Treatment Course Cont’d

- Cough severity improved
- Continuing to complain of hemoptysis
  - Small amounts blood witnessed by DSI and at clinic visit
- Cough, night sweats, and chills eventually resolved

Rassmussen’s Aneurysm

- van den Heuvel and van Rensburg
  October 2006 NEJM 355 (16): e17
- Images in clinical medicine
- 54 male with past history of TB and hemoptysis
**Rasmussen’s Aneurysm**

![Images of medical scans]

**NEJM 2006**

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**Ongoing problem list in 3-07**

- Issue with court date for car theft
- Police call re contagiousness
- AFB – culture - ? MAI only
- On 4-10-07, MRI showed normal pulmonary arteries, aorta
- Above procedure delayed court issues
Discussion

- Lessons learned
  - Need timely discharge records from hospitals especially in patients with social risk factors who play games

- Questions for the audience - TB or not TB?

Thank you!!