Bridging the Gap:  
Making the Connections  
When Caring for a Patient with TB

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No potential conflicts of interest to disclose!
Case Summary: History

- 44 yo male born and raised Colombia S. America
- Worked for government, (+)public contact, (+)travel
  No known contacts with active TB
- In 2004 came to Baltimore for advanced training
- Worked in several Maryland communities then Carroll County in 2015 with the public and elderly
- Ulcerative Colitis partially controlled with steroids Remicade® (infliximab) started in Jan 2016
- Patient reports TST negative by GI doc
Case Summary: Symptoms

- (May) Drenching night sweats and fever
  - 1st the day before travel to Bogota for 2 week family visit
  - Weak non-productive cough “clearing throat” (-) hemoptysis

- GI Physician moved to Texas

- (June) Ulcerative Colitis flare RUQ pain (+) Steroids

- (August) UMD ID clinic for FUO evaluation by PMP
  - (+) IGRA and CT suggested Miliary TB. HIV(-)

- (8/12) Referred to Carroll County Health Dept
  - Mask, Contact tracing, Collect sputum x3 over weekend
Screen before giving immunosuppressive therapy
• Check whether Quantiferon Gold® or TST is better

Risk with Monoclonal Antibodies against TNF-α
• esp. Infliximab (Remicade®) and Etanercept (Enbrel ®)
• 70 reports to FDA with TB with Infliximab by mid-2001
  • Ages 18-87, Mean age 57, Median onset 12 weeks (range 1-52)
  • 56% extrapulmonary and 24% disseminated (3-12 fold ↑ risk)
  • Felt to be reactivation disease and WARNING added to insert
Clinical Course

- Neg TST: 1/6
- +IGRA: 8/5, 8/19 (Bronch)
- GB Surg: 6/11
- Infliximab: Jan 15 - Aug 18 (217 days)
- Fever & Night Sweats: May 3 - Oct 10 (161 days)
- UC Flare CHC: Jun 2 - Jun 12 (11 days)
- CHC: Aug 17 - Sep 9 (24 days)
Case Summary: Hospitalization

- 8/17-9/9 Carroll Hospital admission
  - Infliximab discontinued
  - Bronchio-Alveolar lavage performed pre-treatment
  - 4 drugs daily RIF 600, INH 300, PZA 1500, EMB 1200
  - Discharged on Home O2 for dyspnea on exertion
  - Developed classic shingles treated with Acyclovir
  - Antifungal treatment started for many small hypodense areas on Abdominal CT, stopped when cultures negative

- Right sided pleural effusion 3 taps from Aug to Nov
  - Negative for AFB, TB Culture, and Cytology
Case Summary: After Discharge

- DOT 2x/wk RIF 600 INH 300 PZA 1500 EMB 1200
- Orthopnea and continued Dyspnea, Echo (-)
- Lives on 3rd floor with mother and 1-2 female family members who came to US to care for him
- NEVER had any (+) AFB so felt non-communicable
- 2x week DOT by TB Nurses
  - Facilitated specialty referrals and Family Education
- 2 House Calls
  - Meds for insomnia, but anxiety with “tincture of time”
Challenges with Making the Connections!

- It had been “years” since this health department had a case of Miliary TB or someone this complex.
- TB nurse did all post-discharge care coordination:
  - Obtaining records very difficult (ie: TST from Jan 2016)
  - Insurance company assigned home health but patient terminated due to frustration with their erratic schedule.
- Health Dept initially became his Primary Care doc:
  - Took 2-3 weeks to get an appointment with an Internist.
  - Took >4 months to get appointment with new GI doc.
  - In Jan, mother needed letter to get visa extension.
3 Family Members who provided care
  • TST (-) twice, each 3 months apart

TST = 15 mm in contact born in S Korea IGRA (+)
  • Maybe had BCG as child
  • CXR (-), HIV (-)
  • Determined LTBI and put on 9 months INH

Co-worker claims (-) TST but won’t bring report
Making the Connections: Is this MDR?

- (8/19) bronchial lavage 100-200 colonies TB
- (8/18) sputum AFB negative but culture (+) TB
  - 9/16 reported as (S)RIF only, (R) to other first line drugs
  - MDR is usually (R) to both RIF & INH
  - 10/14 Lab suggests mixed sample; trying to separate
  - 10/21 Probes confirmed mixed growth with M. avium

- (9/15) sputum (+) others negative from 9/13 & 9/14
  - (R) Streptomycin, but (S) RIF, INH, EMB, & PZA
  - Secondary: (S) Ofloxacin, Kanamycin, Ethionamide, Para Aminosalicylic Acid
Case Summary: Slow Improvement in Oct Nov

- (Fall) feels better with sweats decreasing by 5th wk
- (10/11) Last fever after 2 mo 4 drug therapy
- Continued afebrile with periodic flushing (T <99°F)

- (10/6) Add daily MOXI 400mg self-administered to DOT 2x/wk RIF 600 INH 300 PZA 1500 EMB 1200
(10/18) 4 Hour Post-Dose levels
  - Difficult to coordinate with Home Health and Courier
  - Route via DHMH Lab or Quest then to LI Jewish Lab
  - RIF 5.93 ug/ml at 4 hours (2 hour range is 8-24ug/ml)
  - INH sub-therapeutic

(11/3) INH order was inpatient dose for 19 doses

(11/17) DOT 2x/wk RIF 600 INH 900 PZA 1500 EMB 1200
Later Clinical Course

- Afebrile: Oct 11 - Nov 30 (51 days)
- Univ MD: Feb 3 - Mar 9 (35 days)

- Swelling: Jan 24
- Pleurisy: Dec 1
- Malaise: Dec 15
- Chest CT R/O PE: Dec 3
- 101.7: Dec 1
- 102: Dec 25
- 101.4-102.4: Dec 30
- 102: Jan 24
- Afebrile: Jan 23

- 51 days: Oct 11 - Nov 30
- 35 days: Feb 3 - Mar 9
Making the Connections: Diagnostic Challenges

- (1/17-19/2017) 3 Sputa (-) as of 2/17
- Patient noted swelling on L supraclavicular fossa
- (2/3) Internist called
  - Arranged UMD Admission
  - Patient went to Mid-Town Campus!
- Surgery for bilateral empyema postponed so there could be two thoracic surgeons at the surgery
- (2/23) Node (+) TB-DNA Probe but RIF resistant
  - (+) mutation in rpoB gene referred CDC for further testing
Miliary TB is hard to diagnose (took 3 ½ months)

Clinical deterioration after initial response to treatment is known as a “paradoxical reaction”

- Vidal 2005: retrospective review from 3 centers in Spain
- 1999-2003 active TB in 6/284 (2.1%) infliximab patients
- Of these 4 (67%) had a paradoxical reaction 1 month later, consistent with persistence of infliximab for 3-4 wks
- Suggestion that steroids may regulate immune response
Making the Connections: With the TB Lab

Bronchio-Alveolar Lavage
Aug 19
TB
Aug 18
TB
Sep 15

Serum RIF OK, INH Low
Nov 30
(R) STM, (S) other 1st & 2nd line
Dec 5
(S) INH RIF EMB
Nov 3

Mixed avium + TB
Oct 21
(R) RIF only, (S) others by probe
Mar 3

2016
Aug
Sep
Oct
Nov
Dec

2017
Feb
Mar

Aug 18
2 Neg
Sep 13
Oct 30
gordoniae
Oct 29
fortuitum
Oct 22
Neg

Nov 27
Neg
Nov 26
gordoniae
Nov 25
Neg
Jan 19
Neg
Jan 18
Neg
Jan 17
Neg

2017
Feb 24
TB Empyema

Aug 20
Neg

Is this MDR??
Sep 10 - Sep 21

(+)Probe
Aug 18 - Oct 21
(+)TB 100-200 col
Aug 19 - Sep 14
(+)Probe
Sep 15 - Nov 3
Making the Connections: With the TB Lab

**Serum RIF OK, INH Low**

- Nov 30
  - (R) STM, (S) other 1st & 2nd line

- Dec 5
  - (R) RIF only, (S) others by probe

- Mar 3
  - Neg

**TB Empyema**

- Feb 24

**Is this MDR??**

- Sep 10 - Sep 21

**(+)-Probes**

- Aug 18 - Oct 21

**(+)-TB 100-200 col**

- Aug 19 - Sep 14

**(+)-Probes**

- Sep 15 - Nov 3