

Case Study: TB-HIV co-infection

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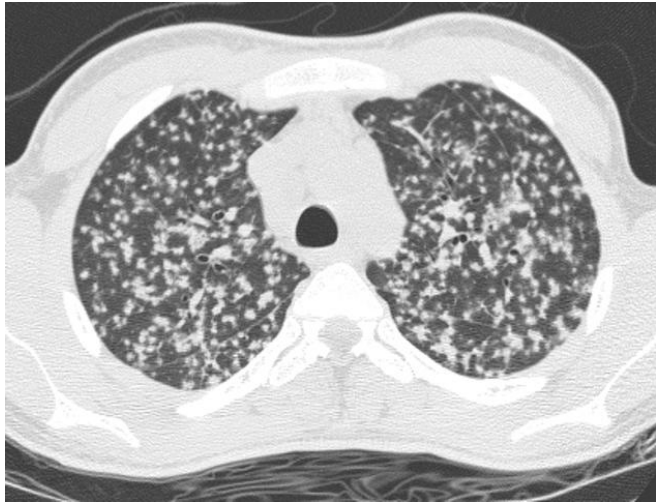
- **33 year-old female from Liberia**
- **Arrived USA December 2015**
- **Seeking asylum**
- **Symptoms April 2016**
- **Hospitalized June 2016**

Hospitalized 6/28/16

- 6/28 CXR Hilar adenopathy
- 6/29 QFT +
- 6/29 Chest CT: miliary pattern
- 7/1 & 7/7 lymph node biopsies; AFB smear+
- No known TB exposure

Incidence of TB in Liberia
308/100,000 (USA = 3.2)





Miliary TB

Characterized by large amounts of TB bacilli, with seeding of bacilli in the lungs & hemotogenous spread throughout the body



6/30/16

- HIV reactive
- Viral load: 720,000
- CD4 = 22 [Normal range: 500 – 1500]
- No other apparent opportunistic infections
- Exposure unknown

HIV TB

Incidence in Liberia:

TB-HIV = 40 (USA = .18)

2014: 9.6 million new cases
active TB, with 12% co-infected

Medical plan:

- Continue isolation
- RIPE daily x 2 wks before starting HAART → initiated 7/13
- Prophylactic Bactrim (PCP & toxoplasmosis) & azithromycin (MAC)
- DC home after 3 weeks

Challenges:

- No cough → no sputums
- Lymph node biopsy processing
- Nausea & low-grade fevers
- Anticipating IRIS
- Immigrant status → confers no health insurance
- Transportation, food, housing, living expenses

Addressing challenges:

- Patience (specimen processing)
- Symptom management
- ABC for Health
- ARCW case mgmt only
- Postpone biometric screening
- ALA incentives:
probiotics, pizza, magazines,
groceries, thermometer, gift cards,
birthday gifts, bus passes



After one week home:

- “I feel terrible”
- Next evening text messages 5:30pm – 10:30pm
- Fever uncontrolled by Naproxen & reaches 103.3° F
- ER
- Re-hospitalized

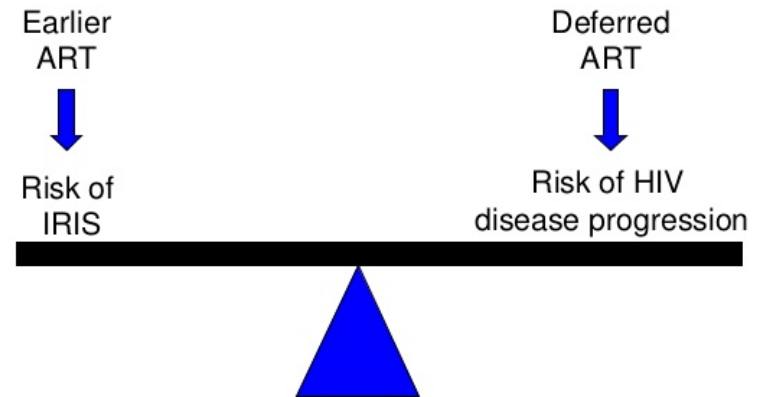
What’s going on?



Immune Reconstitution Inflammation Syndrome (IRIS)

- Body becomes flooded with white cells → proinflammatory cytokine cascade followed by reinforcements
- And...body may respond to dead TB with inflammatory effect
- This is good (appropriately fighting opportunistic infections) & bad (inflammation, fever, tissue damage)
- Occurs in about 20% starting HAART; usually spontaneous recovery

When to start ART in TB?



Fortunately, IRIS seemed to be pretty short-lived...

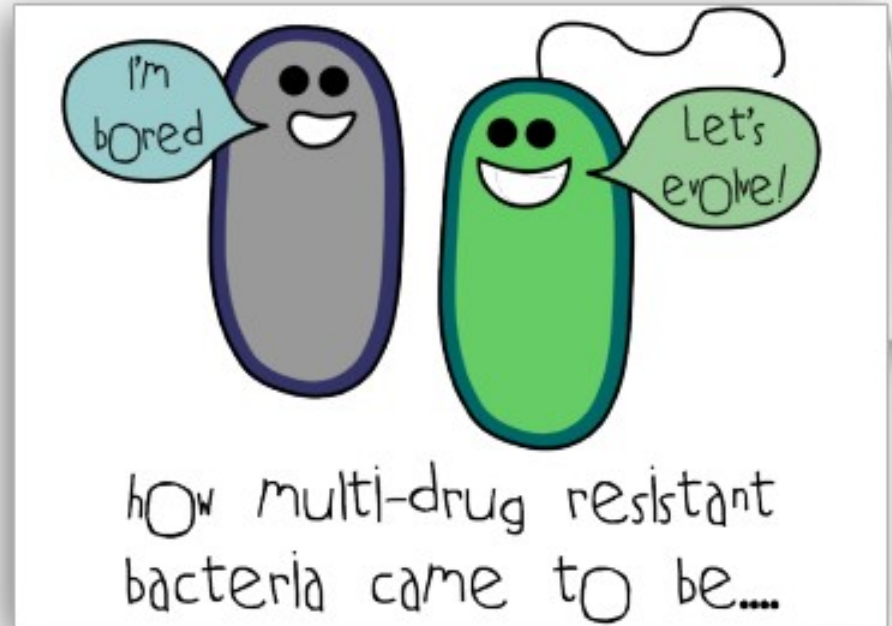
- Fever controlled & client home after 5 days
- IBP prn at home
- Continue RIPE
- Tentatively transfer care to ARCW
- Med changes: d/c rifampin, atripla, & bactrim; start rifabutin, truvada, & tivicay
- Complete initiation phase
- Moving forward:
 - Viral load ↓
 - CD4 ↑
 - Immigration
 - 1st round of contacts all negative...

1-year old son living with relatives in Liberia

- 25% chance of maternal-child HIV transmission
- In apparent good health aside from brief respiratory illness a month ago
- Email contact with Liberian public health who confirmed ability to test
- Delay in contact information from client
- Lack of response from Liberia once referral sent

Unexpected set-backs

- INH resistance
- Discordant drug susceptibility tests
- MGIT: PZA resistance
- MDDR: no indication of mutation that confers PZA resistance
- Culture-based DSTs likely low PZA resistance
- Mayo consult and med changes



Diagnostic Testing

| Specimen Collection Date | Specimen Type | Results |
|-------------------------------------|--------------------------|---|
| 6/28 | Blood | HIV test: reactive (positive) |
| 6/29 | Chest CT | “Innumerable tiny pulmonary nodules seen throughout all lung zones bilaterally in military pattern. Above pattern can be seen in the setting of tuberculosis or other mycobacterial infection.” |
| 6/29 | Blood | AFB smear negative, mycobacteria culture negative |
| 6/30 | Blood | QuantiFERON positive, abnormal |
| 7/1 | Urine, stool | AFB smear negative, mycobacteria culture negative |
| 7/1 | Axillary lymph node | Pathology report: AFB seen using Ziehl–Neelsen stain |

Diagnostic Testing

| Specimen Collection Date | Specimen Type | Results |
|--------------------------|-------------------|---|
| 7/7 | Lymph node biopsy | <ul style="list-style-type: none">• Smear positive at St. Mary's• specimen sent to WSLH for PCR• 7/8 MAC PCR negative• 7/8 TB PCR positive• 7/14 GeneXpert (Milwaukee): TB DNA detected, no rpoB mutation, predicted rifampin susceptible• 8/23 (48 days): culture positive at St. Mary's• 8/24 (49 days): ID as MTBC at WSLH• 9/6 (61 days): PRELIM results: INH and PZA resistant• MDDR results CDC |

CDC MDDR Results

Results for Molecular Detection of Drug Resistance (Sanger Sequencing, complete panel); Conventional Drug Susceptibility Test in progress.

| Locus (Region) | Mutation | Interpretation (Based on our in-house evaluation of 550 clinical isolates) |
|--------------------------------|---|---|
| rpoB (RRDR) | Mutation: TCG>TTG; Ser469Leu | Probably Rifampin susceptible. (97% of RIF-R isolates in our in-house evaluation of 550 clinical isolates have a mutation in the 81 bp RRDR at this locus) The Ser469Leu mutation occurs outside the 81bp RRDR; the effect of the Ser469Leu mutation on RMP resistance is unknown. |
| inhA (promoter) | No mutation | Isoniazid resistant. (100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are INH-R.) |
| katG (Ser315 codon) | Mutation: AGC>ACC; Ser315Thr | |
| embB (Met306, Gly406) | Neutral mutation: GAG>GCG; Glu378Ala | Cannot rule out ethambutol resistance. (79% of EMB-R isolates in our in-house evaluation of 550 clinical isolates have a mutation other than the ones detected at this locus.) The Glu378Ala mutation is likely a neutral mutation and is not associated with resistance |
| prnA (promoter, coding region) | No mutation | Cannot rule out PZA resistance. (86% of PZA-R isolates in our in-house evaluation of 550 clinical isolates have a mutation at this locus.) |
| gyrA (QRDR) | No mutation | Cannot rule out fluoroquinolone resistance. (80% of FQ-R isolates in our in-house evaluation of 550 clinical isolates have a mutation at this locus.) |
| rs (1400 region) | No mutation | Cannot rule out resistance to injectable drugs (kanamycin, capreomycin, amikacin). (In our in-house evaluation of 550 clinical isolates: <ul style="list-style-type: none"> • 91% of AMK-R isolates have a mutation in the rs locus; • 87% of KAN-R isolates have a mutation in either the rs locus or the eis locus; • 55% of CAP-R isolates have a mutation in either the rs locus or the tlyA locus.) |
| eis (promoter) | No mutation | |
| tlyA (entire ORF) | No mutation | |


Diagnostic Testing

| Specimen Collection Date | Specimen Type | Results |
|--------------------------|-------------------|---|
| 7/7 | Lymph node biopsy | <ul style="list-style-type: none">• 9/6 (61 days) CDC MDDR results, multiple mutations<ul style="list-style-type: none">• Confirms INH resistant result• No pncA mutation: discordant PZA result• 9/16 (71 days): WSLH final results, INH and PZA resistant• 10/19: genotype results: not consistent with M. bovis• 11/16 (132 days): culture based DST confirms PZA resistance• PZA MGIT Growth Units = 261/400 and 228/400 |

Ongoing challenges:

- Appropriate treatment
- Minimizing drug side effects; current weight loss
- Liberian contact
- Immigration status
- Employment and healthcare benefits



An aerial photograph of Madison and Dane County, Wisconsin, overlaid with a yellow boundary line. The map features various colored overlays: green for forested areas, blue for water bodies, and red and purple for specific land use or geological features. The text "Questions? Thank you!" is centered in white.

Questions? Thank you!