Saturday Night Fever

Shaka Brown
Capital Congress
Sick sucks.

September 5, 2013
160lbs?! Wtf! Can I put a burger on an IV drip?
August to October 2013

Symptoms:
• Severe fatigue
• Night sweats
• Low grade fever
• Weight loss – 50 lbs in 3 months
• I’ll be fine
• And then…
October 8, 2013
Visit to the doctor

- Visited primary care physician (PCP)
- Diagnosed with epididymitis – treated with ciprofloxacin
- Other testing performed, all negative - including HIV testing
- Mild improvement but still had severe fatigue and weakness
- Returned to PCP who provided a letter and instructions to visit the Emergency Department (ED)
Shaka Zulu – October 31, 2012
THE DIAGNOSIS
Hospital course
Hospital Course

Admission notes

- Presented to the ED on 11/14/2013: fever, shortness of breath with dry cough, 50 lb. weight loss over 3 months, and testicular infection with ongoing edema
- MEDICATIONS: none
- ALLERGIES: none
- PMH (Past Medical History): negative
- PSH (Past Surgical History): negative
- SOCIAL HISTORY: AA male born in US. Travel to more than 37 countries as international dancer. Alcohol socially. Denies tobacco. Denies illicit drug use.
TB Anywhere...
TB Anywhere...

- Lungs
- Kidneys
- Muscle Tissue
- Bone Marrow
- Eyes
- Prostate
- Testes
- Ear
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- Psoas
- ...
Laboratory Testing

- Given CT appearance, sputum was obtained on 11/17
- RESULTS: AFB Smear (+), TB PCR (+)
- REFERRAL: Specimen was sent to the Florida State Public Health Laboratory where molecular MDR screen testing (by Hain MTBDRplus assay) showed no katG or inhA mutations but was rpoB indeterminate
- REFERRAL: Specimen was sent to CDC MDDR Program which identified a rpoB mutation interpreted as “low level but probably clinically relevant rifampin resistant”
## Results for Molecular Detection of Drug Resistance (Sanger Sequencing, complete panel); Conventional Drug Susceptibility Test in progress.

<table>
<thead>
<tr>
<th>Locus (region) examined*</th>
<th>Result</th>
<th>Interpretation (based on in-house evaluation of 500 clinical isolates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>j (rrDRR)</td>
<td>Mutation: CAD=AAC His52His</td>
<td>Low-level but probably clinically relevant rifampin resistance has been linked to the NAS3/RR gene mutation detected in the spoligotypes; isolates with this mutation may test as susceptible by conventional techniques.</td>
</tr>
<tr>
<td>ethB (MET400/Gly405)</td>
<td>No mutation</td>
<td>Cannot rule out ETH resistance. (98% of ETH-R isolates in our in-house evaluation of 500 clinical isolates have a mutation at one or both of these loci.)</td>
</tr>
<tr>
<td>iap (promoter, coding region)</td>
<td>Unable to interpret data. No result</td>
<td>Cannot rule out PZA resistance. (98% of PZA-R isolates in our in-house evaluation of 500 clinical isolates have a mutation at this locus.)</td>
</tr>
<tr>
<td>gyrA (GRDR)</td>
<td>No mutation</td>
<td>Cannot rule out fluoroquinolone resistance. (86% of FQR isolates in our in-house evaluation of 500 clinical isolates have a mutation at this locus.)</td>
</tr>
<tr>
<td>ms (1400 region)</td>
<td>No mutation</td>
<td>Cannot rule out resistance to injectable drugs (kanamycin, capreomycin, amikacin). (In our in-house evaluation of 500 clinical isolates: 91% of AMK-R isolates have a mutation in the ms locus; 87% of KAN-R isolates have a mutation in either the ms locus or the rhl locus; 55% of CAP-R isolates have a mutation in either the ms locus or the tlyA locus.)</td>
</tr>
<tr>
<td>rrs (promoter)</td>
<td>No mutation</td>
<td></td>
</tr>
<tr>
<td>tlyA (entire ORF)</td>
<td>Unable to interpret data. No result</td>
<td></td>
</tr>
</tbody>
</table>

* The term 'locus' refers to a specific genetic location on a chromosome where a gene or set of genes is located. The term 'result' refers to the outcome of a genetic test, whether it indicates the presence or absence of a mutation. The 'interpretation' column provides a clinical context for the genetic result, indicating the potential implications for drug resistance.
Hospital Course continued

- Placed on TB medication
- On 11/19/13 fell in hospital room and hit head on a trash can
- 11/20/13
Brain MRI – 11/24/13
Is this TB as well? Just treat as TB or perform a biopsy to make sure there is no other disease process?

Brain CT showed:

- Multiple hypodense regions in the bilateral subcortical white matter, left basal ganglia, and left middle cerebellar peduncle
- A slight mass effect noted on the fourth ventricle with no evidence of obstruction
- A steroid was added to the treatment regimen
Hospital Course continued

- Experiencing tingling and shooting pain in feet, imbalance, and poor urine control
- Neurology consult concluded ‘severe sensory abnormalities in feet bilaterally with associated gait instability’ and performed spinal MRI
Spine MRI – 12/2/13
MRI on 12/2/13 revealed L4-5 spondylitis with paraspinal abscess with compression on S1
Three ring enhancing lesions identified within the thoracic spinal cord
• The lesions at T10 and T12 were felt to be intermedullary in nature
• Unclear whether the lesion at T5-T6 was intramedullary within the dorsal cord/or leptomeningeal in nature
# Laboratory Testing

<table>
<thead>
<tr>
<th>Drug</th>
<th>FSPHL</th>
<th>MIC</th>
<th>Suscept Cutoff</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>&lt;0.25</td>
<td>&lt;2.0</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>&lt;0.03</td>
<td>&lt;0.25</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>&lt;0.12</td>
<td>&lt;1.0</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Ethionamide</td>
<td>1.0</td>
<td>&lt;2.0</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Kanamycin</td>
<td>1.2</td>
<td>&lt;2.5</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>&lt;0.12</td>
<td>&lt;0.25</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>1.0</td>
<td>&lt;1.0</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>&lt;0.3</td>
<td>&lt;1.2</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>0.25</td>
<td>&lt;2.0</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Moxifloxain</td>
<td>0.5</td>
<td>&lt;0.12</td>
<td>No Interpret</td>
<td></td>
</tr>
<tr>
<td>PAS</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>Susceptible</td>
<td></td>
</tr>
<tr>
<td>Cycloserine</td>
<td>16</td>
<td>&lt;8.0</td>
<td>No Interpret</td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>No pncA mutation</td>
<td></td>
<td>Susceptible</td>
<td></td>
</tr>
</tbody>
</table>
Treatment for MDR-TB

• Medications determined based on diagnosis of potentially RIF resistant, disseminated TB
  1. Amikacin 1gm IV 3x weekly
  2. Rifabutin 300mg PO daily
  3. Isoniazid 300mg PO daily
  4. Cycloserine 250mg PO daily
  5. Pyridoxine 200mg PO daily
  6. Levofloxacin 750mg PO daily
  7. Ethambutol 1200mg PO daily
  8. Pyrazinamide 1500mg PO daily
Treatment – what does that look like? What is DOT?
Discharge – March 2014

• Packed a bag for one night stay in mid November 2013…
April to July 2014

• Readmitted in April with a 3-day headache and slurred speech. Brain lesion in left frontal lobe shown to have increased in size. Steroid treatment resolved symptoms (5 day hospital stay)

• Readmitted in July with continued and increased headaches, fatigue, lack of coordination and bilateral weakness. Large legion in left frontal lobe larger and now multilobulated, indicating that an abscess may be forming (16 day hospital stay)
Brain MRI – 4/24/14 and 7/7/14
Brain lesion is not getting better! Is this IRIS or drug resistant TB?

- Neurosurgery was consulted to perform a left pterional craniotomy for resection of the insular mass
- PATHOLOGY: Necrotizing granulomatous inflammation, AFB stains (-)
- TB LAB: TB PCR (-) x2, AFB smear and culture (-)
July 2014

- Steroids and more drugs added to the TB regimen: linezolid and ethionamide
  1. Isoniazid 500mg PO daily
  2. Rifabutin 300mg PO daily
  3. Levofloxacin 750mg PO daily
  4. Ethionamide 500mg PO BID
  5. Cycloserine 250mg PO daily
  6. Linezolid 300mg PO daily
  7. Pyridoxine 200mg PO daily
- Discharged on July 23
- Brain MRI repeated September 26
TB treatment is a slow process

Plan for 18-month treatment from date of last culture-positive specimen on 11/20/13

... 5/20/2015 couldn’t come fast enough

It’s like a marathon!
A Reason
May 2015

- Successfully completed 18 months of MDR-TB treatment (and a marathon)
Thank you!

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