Disclosures

- No relevant financial relationships
- No off-label/investigative use of commercial product/device
Learning Objectives

Explain the diagnosis of MDR/XDR TB including the interpretation of rapid molecular tests for drug resistance and drug susceptibility test results to ensure a timely, accurate diagnosis.

Identify solutions to programmatic problems related to treatment of MDR/XDR TB including special issues that may occur in low incidence states and other special situations.
Patient History

- 25 y/o Somali male
- Moved to the United States in 1996
- 2007
  - Diagnosed as LTBI, completed one month of INH in Massachusetts
- 2008 through 2014
  - Patient was a University Student in Kenya and Somalia
- February 2014
  - Diagnosed by a Somali physician with active pulmonary TB
  - Started on a single tablet, once daily 3-drug coformulation treatment (presumed to be ‘Rifater’ = INH/RIF/PZA)
Polling Question

Appropriate Treatment regimen?
- Yes
- No
- Don’t know
July 2014

- Concerned his treatment was not working. Decided to move back home and live with his family in North Dakota. Stopped taking medication.
- Flew from Somalia to the United States with layovers in Addis Ababa, Dulles and O’Hare.
- Wore a mask on the plane.
- Arrived in North Dakota.
One day after arrival
Sought medical care at Local Public Health Unit

Testing Done
CXR revealed extensive upper lung infiltrates present
Sputum specimens collected
AFB smears
- August 2, 2014: 1+
- August 3, 2014: 1+
- August 4, 2014: Few

Home isolation
Living with mother and 3 siblings
Polling Question

Is home isolation appropriate for this patient?
- Yes
- No
- Don’t know
Patient History

August 2014

- Has consultation with new infectious disease physician.
  - Physician has concerns of drug resistance due to incomplete prior LTBI treatment and incomplete treatment of active TB disease.
  - Patient denies SOB, night sweats, fever or weight loss – has an infrequent cough
  - HIV negative
  - INH/RIF/PZA/EMB prescribed with B6 therapy
  - Physician wonders if the state can provide Moxifloxacin if needed.
### Patient History
- **Mid-August**: Positive for MTB complex
- **A few days later**: MDDR results received

### Laboratory Results

<table>
<thead>
<tr>
<th>Locus (region) examined*</th>
<th>Result</th>
<th>Interpretation (based on in-house evaluation of 550 clinical isolates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rpoB (RRDR)</td>
<td>Mutation: TCG&gt;T TG; Ser531Leu</td>
<td>Rifampin resistant. (100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are RMP-R.)</td>
</tr>
<tr>
<td>inhA (promoter)</td>
<td>No mutation</td>
<td>Isoniazid resistant. (100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are INH-R.)</td>
</tr>
<tr>
<td>katG (ser315 codon)</td>
<td>Mutation: AGC&gt;ACC; Ser315Thr</td>
<td></td>
</tr>
</tbody>
</table>
Patient History

- Consult with Mayo Physicians
  - Dr. Michael Corbett (Sanford) consulted with Dr. John Wilson (Mayo)
- July 2014 CXR
- Hospitalized after MDDR results received
Patient History

- August 2014
  - CT completed with signs of dense consolidation with some volume loss in the RUL with multiple cavitations.
Patient History

August 2014

- Results for MDDR received
- Treatment regimen changed
- Patient started on:
  - Amikacin IV
  - Moxifloxacin
  - Linezolid
  - Cycloserine & Vit. B6
  - Ethionamide
  - Pyrazinamide included, pending phenotypic susceptibility results
### Phenotypic Susceptibility Testing

**Phenotypic Susceptibility Testing performed at National Jewish**

- Cycloserine, Clofazimine and Linezolid - Susceptible

**RESULTS:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percent Resistance</th>
<th>Interpretation</th>
<th>Percent Resistance</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid 0.2 ug/ml</td>
<td>100</td>
<td>R</td>
<td>Kanamycin 5.0 ug/ml</td>
<td>0</td>
</tr>
<tr>
<td>Isoniazid 1.0 ug/ml</td>
<td>100</td>
<td>R</td>
<td>Ethionamide 10.0 ug/ml</td>
<td>0</td>
</tr>
<tr>
<td>Isoniazid 5.0 ug/ml</td>
<td>50</td>
<td>R</td>
<td>Capreomycin 10.0 ug/ml</td>
<td>0</td>
</tr>
<tr>
<td>Rifampin 1.0 ug/ml</td>
<td>100</td>
<td>R</td>
<td>PAS 2.0 ug/ml</td>
<td>0</td>
</tr>
<tr>
<td>Ethambutol 5.0 ug/ml</td>
<td>0</td>
<td>S</td>
<td>Ofloxacin 2.0 ug/ml</td>
<td>0</td>
</tr>
<tr>
<td>Streptomycin 2.0 ug/ml</td>
<td>100</td>
<td>R</td>
<td>Amikacin 4.0 ug/ml</td>
<td>0</td>
</tr>
<tr>
<td>Streptomycin 10.0 ug/ml</td>
<td>100</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin 2.0 ug/ml</td>
<td>see comments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin 2.0 ug/ml</td>
<td>0</td>
<td>S</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Susceptibility Testing Method: MGIT 960**

**Pyrazinamide 100 ug/ml**

- Resistant

**Comments:**

- Molecular Detection of Drug Resistance (MDDR) report was issued 6/25/2014.

- These conventional agar proportion results agree with the MDDR results.

- **EXCEPTION:** Based on the Ser531Leu mutation detected in rpoB in the MDDR analysis, this isolate is probably resistant to rifabutin. This conflicts with the result obtained by agar proportion testing (rifabutin-S).

- **EXCEPTION:** embB — Asp354Ala mutation; AP DST — EMB-S. 12% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are EMB-S by agar proportion testing.

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**Patient History**

- Phenotypic Susceptibility Testing performed at National Jewish
- Cycloserine, Clofazimine and Linezolid - Susceptible
Case Management

Planning Meeting with LPHU

- Medical Officer, Director of Nursing, TB Nursing Staff, Emergency Preparedness Response Staff
  - Housing
  - DOT
  - Food
  - Transportation
  - Insurance
  - Contact Investigation Progress
Case Management

- Mayo Nurse Consultant, Shea Rabley
  - Weekly calls
  - Resource
Case Management

Housing
- Worked with Emergency Preparedness Response coordinator
- No hotels/motels with appropriate ventilation available
- Shortage of housing available for rent
- Explored options in other cities
- 12 month lease required by all rental companies
  - Lease signed October 1st
- Furnished with Thrift Store items, donated items and a few items purchased by EPR
- Phone, Computer with internet access, Cable
Case Management

DOT

- Patient discharged from hospital mid-October 2014
- 7-day a week initially
- Self-administered Amikacin IV (observed by PHN)
- vDOT performed for evening dose
- DOT administered at clinic on days of drug levels
- December 2014
  - 3 consecutive negative cultures obtained early December 2014
  - 5-day a week DOT
Polling Question

Is vDOT appropriate for this patient?

- Yes
- No
- Don’t know
Case Management

DOT

- Side effects and adverse reactions to 2\textsuperscript{nd} line medications noticed by nurse
- Nurse noted increased irritability, anxiety and depression
  - End of October 2014
  - d/c Cycloserine (Oct. drug level 23; not elevated)
- OPAS Paser Granules started
No longer infectious

3 negative AFB smears end of October
• 10 weeks

With MDR, require 3 negative culture results
• Early December culture negative
January 2015
- d/c Amikacin due to tinnitus in right ear
- Ethambutol added
  (discordant MDDR, phenotypic DST results)

→ Moxi/LZD/ETH/PAS/EMB with (B6, Synthroid)
Polling Question

What is the best strategy for managing side effects during treatment for MDR TB?

- Stop offending agent immediately
- Change to a different medication class immediately
- Try to ameliorate side effects to maximize efficacy of most effective medications as there are few medications for the treatment of MDR TB.
Case Management

Food

- Dietician made list of suggested foods to purchase
- Each week groceries ordered and delivered
- Occasional fast food lunch
Transportation

- Ready Wheels, non-emergency transportation service – part of ambulance service
- Drivers notified to wear N-95 masks
- $50.00 round-trip
- No bus line available
- Local physician raised questions for surgery consideration
  - Denver, 850 miles
  - Rochester, 320 miles
Follow up CT Chest February 2015

- Significant radiologic improvement (Aug ‘14 – Feb ‘15)
- Microbiologic culture conversion
- Clinically improved (significant)

Therefore, no surgery planned
Case Management

Insurance
- No health insurance
- Medicaid Expansion in ND
- December 2014
  - Coverage obtained
  - NDDOH covers co-pay and co-insurance costs
- Prescription medications have a $3.00 co-pay.
Case Management

- Lack of Social Worker
- TB Case Nurse Manager played a dual role
  - Arrange transportation
  - Food
  - Appointments
  - Coordination with other agencies
  - Worked with ER and EMS to develop a plan if transport needed
  - Work with the family
Contact Investigation

14 Contacts
- Mother and Aunt
- Father in Massachusetts
- Uncle – works in the oil fields
- 10 children

Division of Global Migration and Quarantine – 33 contacts

Somalia – 7 contacts
Contact Investigation

Unable to use INH or RIF

Treat LTBI contacts with Moxifloxacin
Challenges

Move home with mother and siblings
- vDOT, no internet
- Concerns for medication storage
Success Story

- Started treatment regimen
  August 2014

- Completed treatment
  August 2016

- 106 weeks
Thank You!