Mayo Clinic Center for Tuberculosis

Tuberculosis in North Dakota - TB Case Studies

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TB Case Manager Training Course - August 4-5, 2016
Disclosures

- No relevant financial relationships
- No off-label investigational uses
Objectives

• Review epidemiology of TB cases in North Dakota
• Identify public health challenges and opportunities in a low incidence state
• Discuss the importance of performing a good contact investigation
Case Study #1

Contact Investigation
Patient History

- 30-40 y/o, foreign born
- Student at a ND college
- Third ER visit in 2 weeks
  - Severe headache
    - Rapid HIV positive
    - Abnormal CXR
- Transported by ambulance to Medical Center
Hospital Admission

• Positive for Cryptococcus
• CD4 109 count
• CD4 8%
• HIV RNA VL 307,000
• Bronchoscopy performed
  • AFB smear – 1+
  • Nucleic Acid Amplification Test – Positive
  • Culture – Positive for Mycobacteria tuberculosis
Contact Investigation

- 53 college students/faculty identified
  - QFT – 24 tested (no foreign-born)
    - Positive – 10
    - Indeterminate – 1
    - Negative - 13
  - TST – 12 Students
    - Positive – 0
    - Negative - 12
Case Study #2

TB and One Health
Patient History

• 20-30 y/o
• Farm/Ranch Worker
• Work VISA (Mexico)
• Presents to local clinic
  • Cold/flu Symptoms
  • Elevated glucose
• Referred to infectious disease physician
Patient History

- Diabetes mellitus
- Cough x 1 month
- Fever
- Weight loss
Testing

- QFT – positive
- CXR and CT – infiltrates with cavitation
- 1+ AFB smear
- Nucleic Acid Amplification Test – Positive
- Self-Isolate
Nucleic Acid Amplification Test (NAAT)

• Positive
  • *Mycobacterium tuberculosis*
  • *Mycobacterium bovis*
  • *Mycobacterium Bacillus Calmette-Buerin*
  • *Mycobacterium africanum*
  • *Mycobacterium canetti*
  • *Mycobacterium microti*

• Negative
  • *Mycobacterium avium complex*
  • *Mycobacterium fortuitum*
  • *Mycobacterium gordonae*
Treatment started

- Isoniazid – 300 mg
- Rifampin – 600 mg
- Ethambutol – 1200 mg
- Pyrazinamide – 1500 mg
- B6 – 50 mg

- DOT – nearest TB Nurse more than 30 miles
  - Contract with local clinic to provide mediation
Patient Interview

- Patient Interview
  - Farm hand acted as interpreter
  - Worked with close contact to cattle for 5 years
  - Each year travels back to Mexico for 2 months
  - Shares a mobile home with 3 other workers
  - Milks 150 cows twice a day
- Signed release to share information with employer and North Dakota Department of Agriculture
Contact Investigation

- Tested 13 named contacts - July
  - 11 QFT, 2 positive
  - 2 TST, no reactors

- Tested 11 negative contacts – October
  - No conversions
Late 2013

- *Mycobacterium bovis* identified
  - Pyrazinamide resistant
  - Isoniazid resistant
- Changed treatment regimen
  - Rifampin – 600 mg
  - Ethambutol – 1200 mg
  - Moxifloxicin – 400 mg
  - B6 – 50 mg
- Treatment to extend until Fall 2014
Cure TB – San Diego County

- Medications provided to patient

- Letter written from health department

States Sending/Receiving TB Referrals
2010 – 2013

- 78% (39/50) states in US and 97% (31/32) states in Mexico sent or received a CureTB referral
- In 2012, services were expanded to Central America.
- Services have also been provided for Canada, Ecuador and Peru.

Legend
- Referral Source
- Referral Destination
National Veterinary Services Laboratories

SNP Table detailing the SNP differences between the most closely related isolates. An in-depth analysis of the 3 ND isolates show no evidence that 14 SNPs that are divergent (in positions 1264009 through 517735) exist in any of the isolates at low levels as a mixed population, consequently direction of transmission cannot be resolved by these data,
SNP Table detailing the SNP differences between the most closely related isolates. An in depth analysis of the 3 ND isolates show no evidence the 14 SNPs that are divergent (in positions 1264009 through 517735) exist in any of the isolates at low levels as a mixed population, consequently direction of transmission cannot be resolved by these data.
Case Study #3

Drug Resistance
Patient History

- 20-30 y/o foreign born male
- Moved to the United States in late 1990s
- 2007
  - Diagnosed as LTBI, completed one month of INH in another state
- 2008 through 2014
  - Returned to his home country and attended university
- Early 2014
  - Diagnosed by with active pulmonary TB in foreign country
  - Started on a single tablet, once daily 3-drug coformulation treatment (presumed to be ‘Rifater’ = INH/RIF/PZA)
Patient History

- Summer 2014
  - Concerned his treatment was not working and decided to move back in with his family, stopped taking medication.
  - Flew from to the United States with layovers in 3 different airports
  - Wore a mask on the plane but not in the terminals
  - Arrived in North Dakota
Patient History

- Sought medical care at Local Public Health Unit
- CXR revealed extensive upper lung infiltrates present
- Sputum specimens collected
- AFB smears
  - Day 1: 1+
  - Day 2: 1+
  - Day 3: Few
- Home isolation
  - Living with mother and 3 siblings
Consult with Infectious Disease Physician

• Summer 2014
  • 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
Laboratory Results

- Positive for MTB complex
- MDDR results received

<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;TTG; 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
- Pre-Treatment CXR

Patient was hospitalized
Patient History

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

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

**Susceptibility Testing Method:** Direct agar proportion, TH10 medium; Susceptibility is defined as ≤ 1% resistance compared to colonies that develop on drug-free media.

### 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>Cliprofloxacin 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 8/25/2014.
- These conventional agar proportion results agree with the MDDR results.
- **EXCEPTION:** Based on the SdrS31Lee 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.

- 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
- Weekly calls
- Resource

TB Nurse Case Manager

State TB Controller

Mayo Physician

Patient’s Physician
Follow up CT Chest – 8 Months Later

- Significant radiologic improvement
- Microbiologic culture conversion
- Clinically improved (significant)

Therefore, no surgery planned
Case Management

• Insurance
  • Pt had no health insurance
• Medicaid Expansion in ND
  • Coverage obtained
  • NDDOH covers co-pay and co-insurance costs
  • Prescription medications have a $3.00 co-pay.
TB Nurse 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 another state
  - Uncle – works in the oil fields
  - 10 children

- Division of Global Migration and Quarantine – 33 contacts

- Home Country – 7 contacts
Barring any setbacks -
Will complete treatment in 2016
Case Study #4

Travel History
Patient History

- Male, US born
- Lived in a TB high incidence country for 1 year, 10 years ago
- QFT – negative
- HIV - Negative
- Poorly controlled diabetic
  - Diagnosed in 2000
- Difficulty swallowing
- Smoker

- Weight loss
  - 15 pounds in last couple of weeks
- Shortness of Breath
- Night Sweats
- CXR with left apical and right midlung infiltrates
- CT Large cavitation in LUL, cavitary infiltrate in RUL
- AFB smear 4+
- Bronch Culture positive for *Mycobacterium tuberculosis*
Additional Testing

• MDDR – no mutations
• Phenotypic susceptibility – Pan Sensitive
• Genotype – PCR00385
Contact Investigation

• 18 identified
  • 13 screened – TST
    • 10 adults – all negative
    • 3 children
      • 1 negative
      • 1 positive, placed on treatment with INH
      • 1 placed on window prophylaxis
    • 5 not tested
  • Conflicting information
Hospitalized

• Electrolytes – below normal values
• Total Protein and Albumin – below normal values
• Glucose – above normal value
Hospital Admission – Week 2

- Failure to thrive
- Refuses food
- Depression
- Developing Skin breakdown
- 17 pound weight loss since admission
- Consider feeding tube
- Not ambulating in room

- Hepatic function tests are worsening
  - Bilirubin 6.0 (0.7-4.7)
  - ALT 169 (20-142)
  - AST 192 (31-97)
  - Alk Phos 359 (126-225)

- Consider changing treatment regimen
  - Aminoglycoside
  - Quinolone
  - Ethambutol
  - Reintroduce Rifampin and Isoniazid
Less than 2 months after TB diagnosis

The patient passed away.
Tuberculosis in North Dakota: TB Case Studies

1. *Mycobacterium bovis* is typically resistant to:
   - a) Isoniazid
   - b) Rifampin
   - c) Ethambutol
   - d) Pyrazinamide

2. Multidrug-resistant TB (MDR TB) is caused by an organism that is resistant to at least:
   - a) Isoniazid and Ethambutol
   - b) Isoniazid and Rifampin
   - c) Isoniazid and Pyrazinamide

3. People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active tuberculosis.
   - a) True
   - b) False
Tuberculosis in North Dakota
TB Case Studies