XDR Case Study

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Disclosure

• Relevant Financial Relationships
  • None

• Off-Label Investigational Uses
  • Meropenem
  • Amoxicillin-clavulanate
  • Linezolid
  • Bedaquiline
Learning Objectives

• Define extensively drug resistant tuberculosis (XDR TB)

• Apply transfer of knowledge of XDR TB to a clinical case
Definitions

• Multidrug-Resistant TB (MDR TB) – resistant to at least isoniazid and rifampin

• Extensively Drug-resistant TB (XDR TB) – resistant to isoniazid, rifampin plus any fluoroquinolone and at least one of three second-line injectable drugs (i.e., amikacin, kanamycin, capreomycin)
Initial Contact

• Early September 2015
• XDR TB case currently at NIH (has been there since June 2015) but family now in Indiana
• Family has been moving around the mid-west since April 2015
• Plan is for case to join family in Indiana once stable and released from NIH
• Need physician able to care for family and case
• Need plans for care, public health issues and financial issues
September 2015 – February 2016

- Multiple telephone conference calls
- Contract with ISDH and Witham for MD services, labs, EKGs, etc.
- Contract with Local Health Department for DOT services, transportation, etc.
- Changing drug regimens
- Waiting for release of patient from NIH
XDR TB Case

- Female born in India 10/18/89
- First diagnosed with TB 2006 with fevers, productive cough, weight loss, and sputum positive for AFB
- Was told she had pulmonary TB without extra-pulmonary involvement
- Treated for 18 months in India with multidrug regimen (unknown drugs)
- Poor compliance secondary to side effects – nausea, vomiting, gas
XDR TB Case

• When completed initial therapy, symptoms returned and she was retreated for another 15-18 months in India (unknown regimen)

• Eventually traveled to Australia in 2013 and underwent medical evaluation

• Treated with either roxithromycin or doxycycline

• Did well and gained weight

• Returned to India when her visa expired

• Symptoms returned
XDR TB Case

- Re-diagnosed with TB in December 2014
- She was given the option of surgery, which she declined
- Treated with antibiotics (unknown) but also told that there was not much more the doctors in India could do for her
- Traveled with family to U.S. in April of 2015 to visit extended family in Illinois.
- Admitted to Sherman Hospital in the Chicago area on 5/21/15
XDR TB Case

• Admitted to NIH 6/5/15

• 25 yo female c/o cough and SOB. Denied fever or chills or recent wt. loss

• PE: BP 119/66, HR 121, T 35.2C, RA O2 95%, wt. 33kg
  • Gen – cachectic
  • Lungs – diminished BS on R with rales and wheezes throughout
  • Heart – distant heart sounds, tachycardia
  • GI – soft, NT, ND
XDR TB Case

• Labs:
  • Chemistries – glucose 85, sodium 139, potassium 4.1, BUN 8, creatinine 0.58, AST 23, ALT 21, Bili 0.6, albumin 3.5, CRP 3.2
  • CBC – Hgb 11.3, Hct 35%, WBC 12.27, polys 59%, lymphs 27%, monos 8%, eos 3.7%

• Imaging: CT scan done in IL “Large cystic masses bilaterally. Right apex cyst 5.2 x 5.4 cm. Left lower lobe cyst measuring 8.9 x 6.7 cm. Small amount of fluid in cysts. Bronchiectasis and non-calcified lung nodules in right lung”
XDR TB Case – 6/5/15
XDR TB Case – 6/11/15
XDR TB Case – 6/11/15
XDR TB Case

• Cultures *Mycobacterium tuberculosis*
  • July 21, 2008
    • Susceptible to: kanamycin, ofloxacin, PAS, cycloserine, clarithromycin, levofloxacin
    • Resistant to: ethionamide, prothionamide
XDR TB Case

• Cultures *Mycobacterium tuberculosis*
  • January 23, 2014
    • Susceptible to: clarithromycin, linezolid, azithromycin, kanamycin, amikacin, ciprofloxacin, roxithromycin
    • Resistant to: cycloserine, ethambutol, ethionamide, PAS, rifabutin, streptomycin, isoniazid, rifampicin, pyrazinamide, prothionamide, doxycycline
XDR TB Case

- Cultures *Mycobacterium tuberculosis*
  - June 5, 2015
    - Susceptible to: linezolid, bedaquiline, clofazamine
    - Resistant to: isoniazid, rifampin, ofloxacin, aminoglycosides
  - Subsequent cultures
    - Positive until September 7, 2015
    - First negative culture was September 14, 2015 and has been negative since
XDR TB Case

• Treatment
  • Bedaquiline: 6/12/15 – 4/27/16, 6/22/16 – 9/19/17
  • Clofazamine: 6/16/15 – 7/10/15, 7/16/15 – 5/27/16, 6/29/16 – 9/19/17
  • Meropenem and amoxicillin-clavulanate: 6/15/15 – 5/27/16, 6/7/16 – 6/14/16
  • Ethambutol: 6/22/15 – 6/29/15
XDR TB Case

• Side effects with medications
  • Ethambutol – mild transaminitis
  • Linezolid – peripheral neuropathy
  • Meropenem/Amoxicillin-clavulanate – Fanconi syndrome (proteinuria/glycosuria/hypophosphatemia)
  • Clofazamine – mild transaminitis but resolved at lower dose
XDR TB Case

• Other medical conditions/complications
  • Fatigue/Gas/Abd discomfort
  • Dyspnea on exertion – PFTs reveal restrictive lung disease
  • Pneumonia – Acinetobacter pitti and Enterobacter cloacae
  • Sinus tachycardia with mild prolonged QTc
  • Iron deficiency anemia
  • Failure to thrive – admission weight 33 kg, discharge weight 46.9 kg
  • Hearing loss – bilateral moderately high frequency
XDR TB Case

• Taken off respiratory isolation 11/18/15
• Pt released from NIH 7/5/16
• Since release has been back to NIH every 2-3 months
• Has been seen by local MD every 1-2 months
• Initially had weekly labs and monthly EKGs.
• Had daily DOT by local health department in person or via skype
XDR TB Case – 9/12/16
XDR TB Case – 9/12/16
XDR TB Case

• Taken off clofazamine and bedaquiline at September 2017 NIH visit
• To be followed for another 1-2 years
• Will be seen again at NIH in 6 months
• To have monthly AFB smears and cultures
• Routine labs per local MD
XDR TB Case

- Current problems
  - Dyspnea on exertion
  - Cough
  - Failure to thrive
  - Fatigue
  - Gas/abdominal discomfort
XDR TB Case

• Current medications:
  • Albuterol Nebs
  • Azithromycin (for pulmonary inflammation)
  • Cetirizine
  • Fexofenadine
  • Fluticasone/Salmeterol
  • Ipratropium Nebs
  • Montelukast
  • MVI
Contacts – Parents and Siblings

- Father – DOB 2/22/69
  - Initial skin test 6/15 – 0 mm
  - Second skin test 7/15 – 9 mm
  - IGRA 9/15 – positive
  - CXRs – all negative
  - Treated with 12 weeks rifapentine/INH DOPT
  - Followed clinically for 24 months with every 3 month visits and every 6 months CXR
  - Final visit and CXR 9/17
Contacts – Parents and Siblings

• Mother – DOB 9/22/70
  • Initial skin test 6/15 – 0 mm
  • Second skin test 7/15 – 8 mm
  • IGRA 9/15 – positive
  • CXRs – all negative
  • Treated with 12 weeks rifapentine/INH DOPT
  • Followed clinically for 24 months with every 3 month visits and every 6 months CXR
  • Final visit and CXR 9/17
Contacts – Parents and Siblings

- Sister - DOB 5/26/92
  - IGRA 6/15 – positive
  - IGRA 9/15 – positive
  - CXRs – all negative
  - Treated with 12 weeks rifapentine/INH DOPT
  - Followed clinically for 24 months with every 3 month visits and every 6 months CXR
  - Final visit and CXR 9/17
Contacts – Parents and Siblings

- Brother - DOB 3/31/99
  - Initial skin test 6/15 – 24 mm
  - IGRA 6/15 – positive
  - IGRA 9/15 – positive
  - CXRs – all negative
  - Treated with 12 weeks rifapentine/INH DOPT
  - Followed clinically for 24 months with every 3 month visits and every 6 months CXR
  - Final visit and CXR 9/17
Contacts – Cousins

• Second cousin, his wife and 2 children were host family in Indiana

• Wife and children never had contact with XDR case. They all had negative IGRAs and normal CXR. They were not treated.

• Cousin had positive IGRA and normal CXR. His last contact with XDR case was in 2009 just before he immigrated to the U.S. We opted to treat him with moxifloxacin for 12 months as the index case was still susceptible to moxifloxacin at the time of the last exposure. CXR remained negative and he has done well.
Questions

• Extensively Drug-resistant TB means the *Mycobacterium tuberculosis* organism is resistant to which of the following?
  - A. Isoniazid and Rifampin
  - B. Isoniazid, Rifampin and Ciprofloxacin
  - C. Isoniazid, Rifampin, Ciprofloxacin and Cycloserine
  - D. Isoniazid, Rifampin, any fluoroquinolone, and at least 1 of 3 second-line injectable drug
Questions

• In general, how long after sputum conversion to negative does one with XDR TB need to be treated?
  • A. one year
  • B. two years
  • C five years
  • D. ten years
Questions

• In general, how long does one need to follow contacts of XDR TB cases?
  • A. one year
  • B. two years
  • C. five years
  • D. ten years
XDR TB Case

Discussion & Questions

Thank You