Bovine Tuberculosis in Man and Beast

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Case Study

• 52 year old male
• Mexican national, arrived in the US January 2015
• Symptoms:
  • Patient began feeling sick approximately 2 months after arriving into the US.
  • Night sweats, cough, and fever
Case Study

• Chest X-ray performed on 4/9/15 showed focal density and left upper lobe cavitation.
• No history of TB or contact with TB according to patient.
• What do you suspect?
Case Study

- 4/9/15: WSLH receives two sputum specimens from the patient.
- 4/10/15: Both specimens are highly AFB-smear positive.
- 4/10/15: TB/MAC PCR is performed.
  - Rapid PCR test to detect *M. tuberculosis* complex and *M. avium* complex directly from patient specimens.
  - This fee-exempt diagnostic PCR testing is performed automatically for all new smear positive patients, same day in most cases.
Case Study

• 4/10/15: TB PCR is positive
• 4/11/15: Patient remains in respiratory isolation and is started on the standard 4-drug TB regimen: isoniazid, rifampin, ethambutol, pyrazinamide (PZA)
• What are the additional concerns?
Case Study

• **Additional Concerns:**
  • Because the patient is highly smear positive, he is considered to have highly infectious tuberculosis.
  • Local public health department will perform a contact investigation to look for active or latent TB in family members and other close contacts.
  • The patient worked at a dairy farm (since arrival from Mexico), performing nighttime feedings of the animals.
Case Study

- Due to risk factors Isolate sent to CDC for genotyping to species level.

- Identified as species M. bovis 8 days after culture confirmation of M. tuberculosis complex.
Identification of *M. bovis*

- Members of the MTBC (*M. tuberculosis*, *M. bovis*, *M. bovis* BCG, *M. caprae*, *M. microti*) are related by a >99.9% DNA homology. They are not differentiated by WSLH routine testing.

- *M. bovis* cannot be distinguished from MTBC by MALDI-TOF, 16S DNA sequencing, HPLC, or colony morphology.
  - *M. bovis* may grow more slowly than *M. tuberculosis*.

- Mono-resistance to PZA is a clue that isolate may be species *M. bovis*.
  - Patient’s drug susceptibility pattern shows resistance to PZA
Identification of *M. bovis*

- Specialized molecular testing needed
  - CDC
  - Michigan Community Health Department Laboratory
  - USDA
- Spacer oligonucleotide typing (Spoligotyping): detects variability in the direct repeat (DR) region in members of the *M. tuberculosis* complex.
- Multiplex real-time PCR assay detects the presence or absence of regions of difference (RD) between genomes of members of *M. tuberculosis* complex.
M. bovis in humans

- Can cause active human TB and/or Latent TB just like M. tuberculosis.
- Accounts for roughly 2% of all human TB cases in the US. As high as 10% in some countries.
  - Mexico = 7.6%
- Routine pasteurization effectively controls zoonotic transmission as direct animal to human is believed to be rare.
- Can cause cutaneous infection via direct contact of infectious fluid to open wound (butcher shop).
- Treated with normal TB meds. Inherently resistant to pyrazinamide. (Therapy lengthened to 9 months)
M. bovis in humans

• Risk factors for *M. bovis infection* include: Hispanic origin, consumption of unpasteurized dairy, and close animal contact.
  • Patient states that he does not recall consuming unpasteurized dairy products.

• Important to differentiate between *M. bovis* vs. *M. tuberculosis*:
  • Patient therapy
  • Transmission to dairy herd
Bovine Tuberculosis

- *M. bovis* is more transmissible to cattle than *M. tuberculosis* and can be transmitted from human to cow.
- Disease analogous to human TB.
  - Commonly involves lungs
  - Slow disease progression and difficult diagnosis
  - Spread between cattle and other mammals via airborne particulates
Bovine Tuberculosis in Cattle

• Can result in severe economic loss due to livestock disease/death and resulting trade restriction.
  – If cows are found to be positive entire herds can be quarantined and product movement can be blocked.
  – Herd may need to be depopulated as the only method that insures disease elimination.

• Close contact within Dairy operations make exposure and transmission greater concerns, think TB in prisons.
Bovine Tuberculosis in Cattle

• Careful eradication programs have rendered most developed nations ‘nearly’ m. bovis free.
  – In 1917 US established the Cooperative State-Federal Bovine Tuberculosis Eradication Program.
  – Restricted movement, ante mortem testing (CFT), quarantine measures, herd culling, and post-mortem meat inspection.

• There remain areas in the world where bovine TB is poorly controlled.

• Wildlife maintenance hosts such as white-tailed deer (US) and badgers (UK) make complete eradication difficult.

- 1994- Endemic M. bovis found circulating in White-tail deer reservoir host.
- 1998- Three herds of cows infected
- 2002- Human cases diagnosed and linked to cattle outbreak.
- If an Bovine tuberculosis outbreak is detected in a state it cannot regain its status as Accredited-Free(AF) until two years after the last affected herd is depopulated or released from quarantine.
California outbreak (2007-2009)

- In 2007-2009 an outbreak occurred which spanned multiple dairy herds across California.
- Five herds were investigated and quarantined, two of the herds were confirmed to be directly infected by cattle sales between operations.
- CFT screening was performed on over 400,000 cows and over 10,000 registered positive reactions. At a cost of almost $2 Billion.
- Human employees spreading disease to cattle is a suspected source of infection in one of the herds, though not confirmed.
Bovine Tuberculosis Testing in California

Caudal Fold Tuberculin Test

Positive Responder

Reactor
Quarantine Herd
Appraise and remove animal from herd AND
Whole herd retest a minimum of 60 days after removal of reactor.

Suspect
Quarantine Suspect
1. Producer decides to repeat test in 60 days OR
2. Send directly to slaughter for enhanced inspection

Comparative Cervical Test AND/OR Gamma Interferon Blood Test

Necropsy

Diagnosed with BOVINE TB
Histopathology compatible
PCR positive for M. TB complex and/or
Culture positive M. bovis
Herd Quarantined and classified Affected.

Reactor Negative
No evidence of bovine TB
Additional herd testing required

Suspect Negative
No evidence of bovine TB
(No further action)

Approved Herd Plan
Herd remains under quarantine. Test and removal of reactor animals. Herd plan for a minimum of 4 years

Complete Herd Depopulation
Herd appraisal and producer compensation

Whole Herd Test
1 year after repopulation

Null
Wisconsin Dairy Industry

• Wisconsin is home to over 10,000 dairy farms (most in the US) and 1.27 million cows.

• The dairy industry contributes $43.4 billion to the WI economy, or $82,500 per minute.

• 99% of Wisconsin dairy farms are family owned.
Patient Follow-up

- Herd will be screened using the caudal fold tuberculin (CFT) test
  - A small amount of purified protein derivative (PPD) is injected into the fold of skin at the base of the tail
- 31 cattle at patient's workplace we screened.
- 5/21/15: one dairy cow tested positive and was killed to prevent further transmission.
Patient Follow-up

- Patient treatment included INH, rifampin and ethambutol
  - PZA discontinued due to inherent resistance of *M. bovis*
  - Treatment lengthened from 6 months to 9 months
- The patient’s last culture positive specimen was collected on June 17\(^{th}\) (2 months after diagnosis)
- However, smears remain intermittently positive as of August 19\(^{th}\).
Conclusions

• It is important to quickly diagnose tuberculosis and differentiate *M. bovis* in workers associated with the dairy industry

• *M. bovis* can be transmitted from humans to cattle and poses a threat to dairy herds in the US

• Wisconsin has programs in place for
  • rapid diagnostic testing in humans (WSLH),
  • rapid identification of *M. bovis* (USDA)
  • rapid testing of cattle
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Questions?
References

• U.S. Department of Agriculture Bovine Tuberculosis fact sheet

• CDC M. bovis fact sheet

• The Center for Food Safety and Public Health M. bovis fact sheet
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