

TB or not TB, that is the question

2018 WMLH State Conference
Oct 10, 2018

PATIENT #1

History

- No known prior TB history.
- Foreign born, came to the US when a teenager.
- 4 week hx of cough, sputum, fevers, intermittent night sweats, and weight loss.
- Had not been on meds prior to this illness. No prior weight loss.

1/2/18 Physician outside hospital network

- RADIOLOGY FINDINGS:
 - PA and lateral views of the chest obtained on 01/02/2018 are reviewed without available comparison.
 - There is fairly extensive coarse reticular and patchy infiltrate within the right upper lobe as well as milder patchy and reticular infiltrate within the left upper lobe and right middle lobe. A small right basilar pleural effusion is present. No evidence of pneumothorax. Heart size is within normal limits.
- IMPRESSION:
 - Bilateral lung infiltrates noted, most prominent within the right upper lobe compatible with pneumonia.
- Since out of network do not know if labs were ordered

1/5/18 Clinic within hospital network

- Another chest x-ray was performed and reviewed.
 - Secondary to the area of involvement in the appearance and did question the patient if he had any exposure to her risk for tuberculosis which he denied. He states he's not any travel out of the country over the past 6 months.
 - Radiology had concerns about pneumonia and possible tuberculosis pattern on the chest x-ray. Recommendations were for pulmonary consult ASAP.

- Patient had a sputum culture ordered, patient declined lab work at that time.
 - Patient wanted to collect at home and submit to lab in morning
- Patient advised to avoid any respiratory interaction secondary to the concern about spreading infection
- Patient referred to pulmonologist

1/6/18

- Seen at clinic within hospital network to submit specimen:
 - Routine Sputum culture ordered at sent to other hospital lab in network to work up for suspected pneumonia
 - Reported out “Moderate Normal Flora”

Pulmonology:

- 1/8/18 Scheduled appointment with Pulmonologist – did not show up
- Patient seen by Pulmonologist 1/9/18:
 - Noticed that C AFB not ordered or sent to main micro lab in hospital network
 - Called to have sputum sent to main micro lab and have C AFB performed

1/10/18 – Micro Lab

- Sputum from 1/6/18 processed for C AFB
 - Patient had Many AFB seen on Auramine O stain
 - Cepheid MTB/RIF performed
 - MTB: Detected
 - RIF: Not Detected
- Local Health Department was notified
 - Orders for patient to be put on TB medications on 1/11/18

Lab information

- 1/10/18:
 - Smear and MTB/RIF positive
- 1/15/18:
 - VersaTrek Myco positive with Roping AFB and Bacteria
 - Subculture: BAP, 7H11, LJ
 - Reprocessed VersaTrek 1/16/18

- 2/12/18:
 - Smear of reprocessed VersaTrek Bottle
 - AFB seen
 - Subculture of VersaTrek
- 2/19/18:
 - *M. avium* growing
 - See MTB slight growth, unable to separate out from *M. avium* colonies
 - State was able to isolate out MTB from primary specimen we had sent them to perform susceptibility testing

PATIENT #2

History

- 80 Y female with left sided moderately differentiated squamous cell lung cancer (not on chemo, s/p recent radiation therapy)
- Hypothyroidism
- Osteoporosis,
- Coronary Artery Disease and Peripheral Artery Disease
- Right hip tendonitis

ED Visit 12/30/17

- Patient presents to ED after falling out of bed.
 - Patient does not recall falling and son states she has fallen 4 times in last 2 weeks
 - Patient has pain in right hip
- Patient says has had cough for last 2 years as well as increased SOB
 - Patient received Oxygen in ED and said felt an improvement
 - CXR ordered

ED Visit

- New bilateral lung opacities with a superimposed infectious/inflammatory process suspected bilaterally were seen on chest x-ray.
- Patient admitted to inpatient floor for suspected pneumonia
 - Respiratory Virus NAAT: Negative
 - Blood culture: Negative
 - *Legionella* and *S. pneumoniae* urine antigens: Negative

Inpatient stay

- Patient transferred to the MICU 1/4/18 due to worsening of symptoms
 - Bronchoscopy performed 1/5/18
 - While on the floor she continued to require O2 10-15l but she remained stable with no other respiratory complaints
- Stable for transfer back to inpatient floor on 1/7/2018
- Patient discharged 1/13/18 to rehab facility
 - Patient was told to follow up with a pulmonologist

Lab Results 1/5/18 BAL

- Culture respiratory/SA-MRSA NAAT:
 - Culture: 50K CFU/ML *C. albicans*, <10K CFU/ML MOF
 - SA-MRSA NAAT: Negative for both
- Fungal culture:
 - 4+ *C. albicans*, 4+ *C. glabrata*
- Pneumocystis DFA: Negative
- Respiratory virus NAAT & Atypical Pneumonia NAAT: Negative
- AFB Culture.....

AFB Culture

- 1/6/18: No AFB Seen on concentrated smear
- Liquid media:
 - Went positive 1/16/18: Bacteria and yeast seen
 - VersaTrek bottle reprocessed 1/16/18
 - Reprocessed bottle:
 - Went positive 1/23/18: NOS, performed Blind sub and put back in instrument
 - 1/30/18 “dry” colonies seen on blind sub, Kinyoun Positive
 - MALDI TOF: *M. tuberculosis*

MTB isolate

- Notified Pulmonology department 1/30/18
 - Patient had missed appointment with them
 - Called rehab facility to make sure patient was put in isolation, reduced prednisone, and referred patient for ID consult
- Facility ordered Quantiferon test:
 - Test came back negative

MTB isolate

- After reporting tech was suspicious since 2nd MTB patient within <1 month
 - On average see 2 – 4 new **pulmonary** MTB cases yearly
 - 2nd in first month of the year
- Tech did some investigating and saw patient 1 and patient 2 had liquid media reprocessed on the same day

Investigation

- Medical Director called on 1/30/18 regarding possible cross contamination
- 1/31/18 WSLH TB Lab contacted to help with investigation of possible cross contamination
 - Both patient samples sent to WSLH for TB Genotyping 2/1/18

WSLH Response

- Made sure that isolates sent for TB Genotyping were processed right away
- 2/8/18 preliminary results received from WSLH
 - Patient #2 isolate had similar banding pattern from Patient #1
 - Results suggestive of laboratory contamination
- 2/15/18 confirmation with 2nd method that isolate from Patient #1 was same as Patient #2

ID consult

- Patient did not show for appointment 2/5/18
- ID were previously notified by Medical Director regarding possible laboratory cross contamination event.
 - ID decided to wait on Genotyping results before treating patient
- 2/8/18 ID informed of laboratory contamination event

ID Consult notes from 2/8/18

- Called to inform patient that the test on the BAL showing possible MTb was a laboratory contamination event. There is no evidence she has tuberculosis.
- Left message on voice mail and gave call back numbers for the ID clinic in case she wants to discuss further.

What is TB Genotyping?

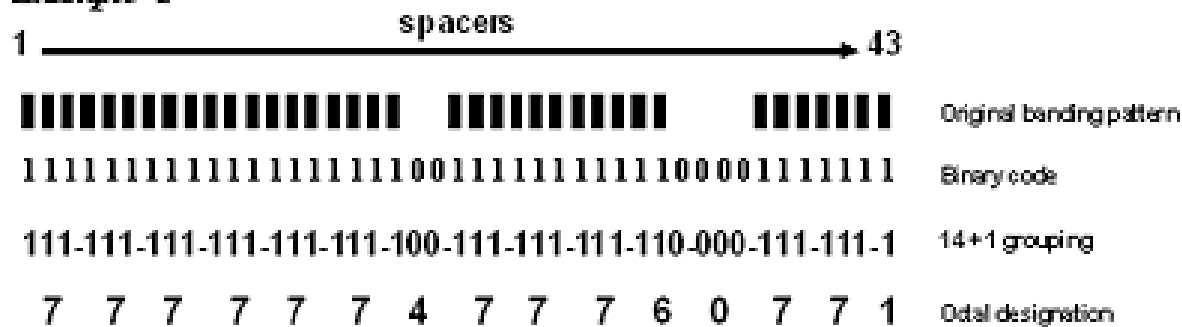
- 2 – 3 Methods involved:
 - Spoligotyping (spacer oligo typing)
 - Variable number of tandem repeat (VNTR) - Mycobacterial interspersed repetitive unit (MIRU) analysis
 - IS6110-based restriction fragment length polymorphism (RFLP) analysis

Spoligotyping

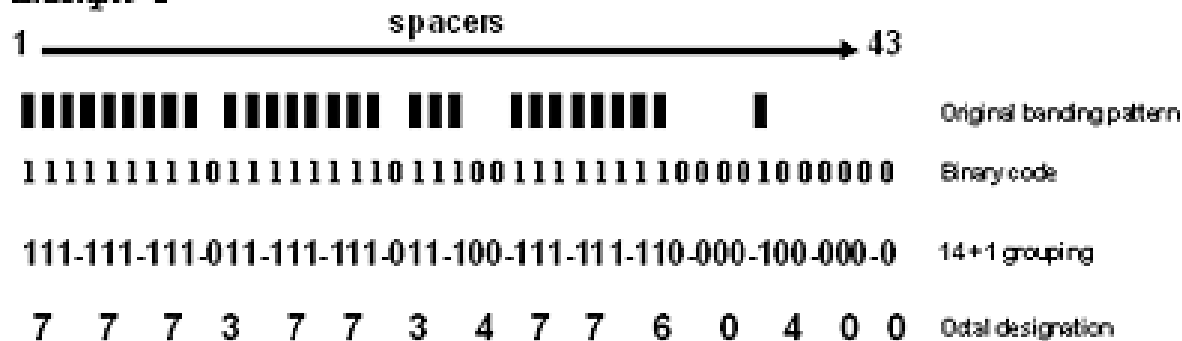
- PCR amplification of a highly polymorphic direct repeat locus in the *M. tuberculosis* genome
- Performed on a membrane and looks at banding pattern
 - Looks for the absence (no band) or presence (dark band) of certain unique spacer sequences in this region
 - Breaks down banding pattern into a digital code
 - 43 regions looked at and broken down into a binary code
 - 1 for band, 0 for absence of band
 - Binary code of 43 regions broken down into a “14 + 1” code
 - Binary code put in groups of 3, with 1 band extra
 - 14 + 1 code broken down into octal designation that is compared to other isolates
 - 4+2+1 equation (000 = 0; 001 = 1; 010 = 2; 011 = 3; 100 = 4; 101 = 5; 110 = 6; 111 = 7)

Spoligotyping example

Example 1



Example 2



VNTR - MIRU

- VNTR Typing:
 - Based on analysis of DNA segments containing “tandem repeated” sequences
 - The number of copies of the repeated sequence varies among strains
- MIRU:
 - Class of tandem repeated sequences
 - Looks for the number of repeated sequences at 24 specific loci
 - Reported as a two 12 digit code

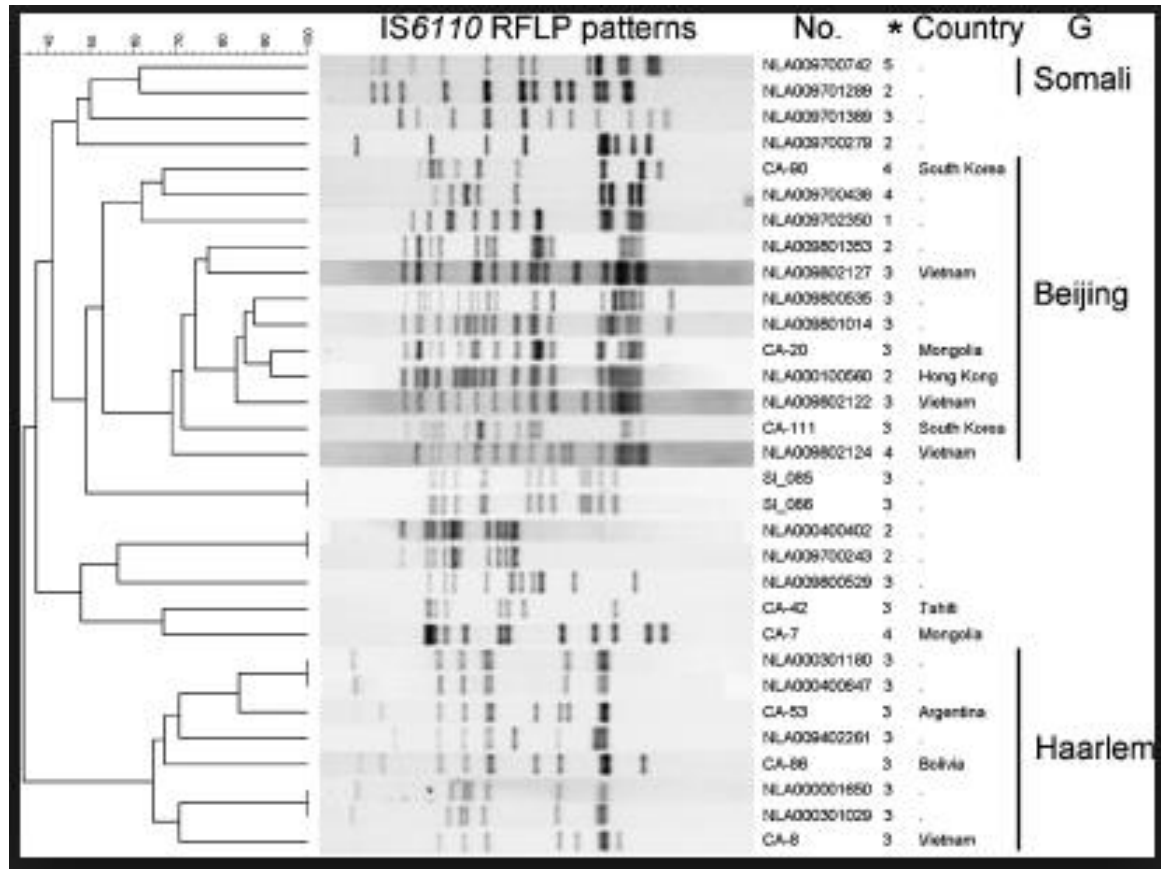
VNTR – MIRU Example

Example 1												
MIRU locus name	02	04	10	16	20	23	24	26	27	31	39	40
No. of repeats	2	3	2	2	3	4	2	5	3	3	2	2
MIRU designation	232234253322											

RFLP

- Detects variations in a specific section of the *M. tuberculosis* genome
 - Insertion element *IS6110*
- Method:
 - DNA is purified from *M. tuberculosis*
 - A restriction enzyme is added that cuts the DNA into hundreds of different fragments as specific sequences
 - Fragments separated by size on agarose gel and transferred to a membrane
 - Probe is used to detect fragments containing *IS6110*
 - Each copy of *IS6110* produces one band

RFLP Example



TB Genotyping – Why Use It

- Discover unsuspected transmission relationships between TB patients
- Establish criteria for outbreak-related case definition
 - Identify additional persons involved in outbreak
 - Determine completeness of contact investigations
- Detect laboratory cross-contamination event
- Distinguish between reactivation vs new infection

Laboratory Cross-Contamination

- CDC:
 - 2% of all *M. tuberculosis* cultures represent false-positive results due to laboratory cross-contamination
- When to suspect false-positive result:
 - Single confirmed culture
 - Clinical presentation is inconsistent with lab result
 - No clinical improvement despite adequate TB therapy

Common Causes of Cross-Contamination

- Use of common flask for reagents
- Aerosol creation or spills during processing
 - Contamination of equipment or supplies (pipettes, syringe, loops) inside BSC
 - Contamination of centrifuge carriers
- Processing of large batches
 - Breakdown in SOP practices
 - Lack of spacing with specimen tubes in processing racks
- Failure of BSC
- Mislabeled
 - Wrong persons culture inoculated

Lessons Learned

- Investigating potential reasons for event
 - Mislabeled vs Cross Contamination
 - Technologist was training
- Importance of Critical Thinking
 - Awareness of MTB prevalence
- Importance of notification of possible event
- Importance of utilizing partners like WSLH

Questions?