Case Presentation Using Genotyping to Confirm a Suspected Case of Tuberculosis Cross Contamination

Case History:

Patient A was a 45-year old US-born white female with a six month history of illness characterized by a twenty pound weight loss, dry cough, shortness of breath (SOB), and chest pain. She was seen by a physician on December 12, 2003 to evaluate a spontaneous pneumothorax and rule out lung cancer. A Computed Tomography (CT) of her chest revealed large bilateral cavitary lesions. She underwent a bronchoscopy exam on December 19, 2003. An acid-fast bacillus (AFB) smear-positive specimen was obtained using bronchial-alveolar lavage (BAL). The sputum was culture-positive for *Mycobacterium tuberculosis*, and on February 20, 2004 *Mycobacterium tuberculosis* was isolated from her BAL and sputum. The isolated organism was pansensitive. She was started on isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) at the time of her TB diagnosis and received nine months of treatment due to her large cavitary lesions and advanced TB disease.

Patient B was a 56-year old US-born male. In July 2001 he was diagnosed with lung cancer and an upper and middle lobectomy was performed. On December 12, 2003 he underwent a bronchoscopy to evaluate new symptoms of SOB and new bilateral pulmonary infiltrates (on chest radiograph). A BAL obtained was AFB smear negative.

On January 7, 2004 a preliminary report from the hospital indicated that *Mycobacterium tuberculosis* complex had been isolated from the BAL specimen for Patient B. The State Lab confirmed pansensitive *Mycobacterium tuberculosis* on January 27, 2004. Patient B underwent treatment with INH, RIF, PZA, and EMB starting January 9, 2004 and continued though completion on July 2, 2004. This was a single-positive-specimen (SPS); no other sputum specimens were ever collected from Patient B.

The genotypes for Patient A and Patient B became available several months later and were reviewed by the State TB Control Program. These two patients had a unique genotype. No other matches were found in the state or neighboring states. Both their spacer oligonucleotide type (spoligotype) and Mycobacterial Interspersed Repetitive Unit (MIRU) matched; however they lived in different parts of the state and had no known epidemiological links. Further review indicated that both patients were diagnosed in the same hospital at the same time. Due to the unique matching genotype, no known social link, Patient B’s SPS, and their link to the same hospital, an investigation into possible cross contamination was launched.

The hospital was notified when the possible cross contamination was determined by the State TB Control Program. On August 18, 2004 state program staff visited the hospital to investigate. They met with the following staff: the Infection Control Nurse, the Microbiology Lab Director, the Director of Respiratory Therapy (Bronchoscopy Laboratory), and the Director of Employee Health. The hospital staff was receptive and cooperative with the investigation, and had conducted their own internal review of procedures prior to the State TB program staff’s visit.

The investigation revealed that the same bronchoscope was used on both patients. A third patient underwent bronchoscopy with this scope on December 26, 2003, but all TB smears and cultures collected on this patient were negative. Due to a change in vendors at the end of the year, this scope had not been used again.

Patient A was considered the “hot” patient; bronchoscopy was performed on December 19th (Friday). Due to the patient’s critical condition the physician requested that specimens be processed as soon as possible. The specimens were processed on December 20th (Saturday) and were not batched with other specimens. Patient B was the next patient to undergo a bronchoscopy exam on December 22nd (Monday) and that specimen was processed the same day. The state reference lab also received specimens from the two patients on different days and only for culture identification after specimen growth. Laboratory cross contamination was therefore considered unlikely as the specimens were not processed in any lab at the same time. Continued on Page 6
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The hospital conducted a review of its bronchoscopy laboratory procedures; there was no new staff in the Bronchoscopy Laboratory. Procedures called for single-patient use of a lidocaine spray and nozzle when anesthetizing the patient’s airway. All accessory instruments used during procedures were also single-patient use. Bronchoscopes were all cleaned by hand prior to disinfection and scopes were disinfected with Cidex (with appropriate soak times and solutions).

Those involved with the investigation believed that bronchoscope contamination was the likely source of Patient B’s positive tuberculosis culture; however since the scope in question had long since been discarded there was no conclusive evidence. Lab contamination was improbable since specimens were processed two days apart in the hospital and arrived at the state reference lab after isolate growth. The hospital took these concerns seriously and used this issue to develop a quality improvement process aimed at assuring that cross-contamination is minimized during bronchoscope processing, handling, and cleaning/disinfection. They were open to suggestions by the State TB Control Program staff to decrease this risk in the future. Both Patient A and Patient B completed anti-tuberculosis treatment.

Key Concepts:

Universal genotyping allows programs to identify links between TB patients that would otherwise be unrecognized. Key to this investigation was access to genotyping results of both specimens and recognition by the State TB Control Program of the significance of a single positive specimen that matched a highly infectious TB patient. All TB Control Programs should have procedures in place to readily detect genotyping matches and SPSs, and launch timely investigations of possible cross-contaminations (CDC 2004). It should be noted that this investigation was not completed until eight months after the contamination due to delays in laboratory procedures at the time and lack of an automated surveillance system. The national web-based program, TB GIMS, will substantially improve a TB Program’s ability to recognize possible cross contamination cases faster and intervene earlier.

An estimated 0.1 – 3% of active TB diagnoses are based on false positive specimens or cross contamination of specimens. False-positive TB diagnoses result in needless treatment for the patient, delays in an accurate diagnosis, and misrepresentation of the actual incidence of TB. (Djelouadji, Z., et al 2009) In this instance, bronchoscope contamination resulted in the likely nosocomial infection with M. tuberculosis for Patient B.

Cross contamination of specimens via contaminated bronchoscopes are less frequent than laboratory cross contamination, but certainly possible. Several examples have been published in the literature. Any possibility of bronchoscope contamination should result in a thorough review of infection control procedures (Djelouadji, Z., et al 2009; Shoch, O. D. et al 2003; and Larson, J. L. et al 2003) as happened in this event.

TB GIMS will enhance the utility of genotyping data for state TB programs. In addition to gaining ability to identify cross contamination events, genotyping can (CDC 2004):

- Establish criteria for outbreak-related case definitions
- Identify additional persons involved in a TB outbreak
- Distinguish recent infection (with development of disease) from activation of an old infection
- Determine completeness of contact investigation
- Uncover interjurisdictional and atypical transmissions of tuberculosis

For questions please contact the Heartland National TB Center or email tbgims@cdc.gov.

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