Evaluating the Sensitivity of MTBC Detection in Extrapulmonary Specimens by Real-time PCR During an Outbreak of Spinal Tuberculosis

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Objective

In June 2021, the CDC reported a multistate cluster of tuberculosis associated with patients who had recently undergone spinal surgery. All surgeries were associated with a single lot of bone repair product. The product was later found to be contaminated with viable MTBC.[1]

Healthcare facilities in Indiana received 45 units of FiberCel bone graft product, which was implanted into 33 patients, primarily for spinal fusion repair surgeries. Because many of the patients presented with surgical site infections, testing of extrapulmonary specimens was critical for patient treatment and TB prevention efforts.

Study Design

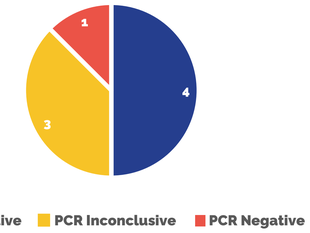
All specimens were first digested and decontaminated using standard methods (as applicable for the specimen type) and then extracted for PCR using a heat inactivation step, lysis buffer and the Roche MagNA Pure™ Compact instrument. PCR analysis was performed using a lab-developed, real-time PCR assay on the Applied Biosystems QuantStudio™ Dx Real-Time PCR instrument. Cultures were inoculated for each specimen using MGIT broth and LJ-Gruft slants. PCR results were compared to culture results to assess sensitivity. Inconclusive PCR results (CT value >37) were counted as positive results for the purpose of calculating the culture correlation rate since inconclusive results typically correlate to positive cultures of MTBC per our laboratory data (Table 1).

Table 1: Overall Test Results

Patient	Specimen	Specimen Type	AFB Smear Result	TB PCR Result	Culture Result
Patient A	A-1	Wound	Acid Fast Bacteria not found	Inconclusive	Mycobacterium tuberculosis complex
Patient A	A-2	Anterior Cervical Spine	Acid Fast Bacteria Found 1-10 per field	Inconclusive	Mycobacterium tuberculosis complex
Patient A	A-3	Anterior Cervical Spine	Acid Fast Bacteria Found <1/field (very few)	Negative	Mycobacterium tuberculosis complex
Patient B	B-1	ACDF Surgical Wound	Acid Fast Bacteria Found <1/field (very few)	Positive	Mycobacterium tuberculosis complex
Patient B	B-2	ACDF Surgical Wound	Acid Fast Bacteria Found 1-10 per field	Positive	Mycobacterium tuberculosis complex
Patient C	C-1	Cervical Wound	Acid Fast Bacteria Found <1/field (very few)	Inconclusive	Mycobacterium tuberculosis complex
Patient D	D-1	Deep Cervical Fascia	Acid Fast Bacteria Found <1 per field	Positive	Mycobacterium tuberculosis complex
Patient E	E-1	Deep Neck Cervical	Acid Fast Bacteria Found >10 per field	Positive	Mycobacterium tuberculosis complex
Patient F	F-1	Lumbar Abscess	Acid Fast Bacteria not found	Negative	No Mycobacteria isolated
Patient G	G-1	Lumbar Fluid	Acid Fast Bacteria not found	Negative	No Mycobacteria isolated

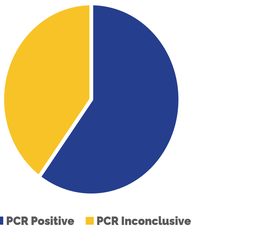
Results

Figure 1
Culture Positive Specimens

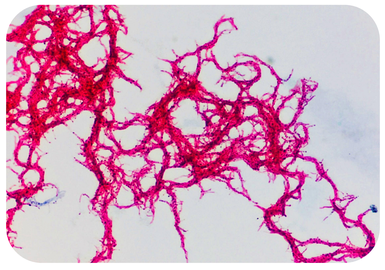


In June and July 2021, ten extrapulmonary specimens from seven patients were received and tested at IDOH Laboratory. Of these, eight specimens from five patients were found to be culture positive for MTBC (Figure 1). Specimens consisted of cervical spinal tissue and wounds, with the majority being smear positive (counts ranging from <1/field to >10/field). MTBC DNA was detected in at least one specimen from each of the five culture positive patients. The PCR-to-culture correlation rate per patient was calculated at 100% (Figure 2).

Figure 2
PCR Results for Culture Positive Patients



MTBC culture in MGIT™ broth.



Conclusion

In this limited data set, real-time PCR was found to be highly sensitive in the detection of MTBC in extrapulmonary specimen types. PCR positive results correlated 100% with positive culture results for each patient. This data demonstrates that real-time PCR is an effective means of determining the presence of MTBC in extrapulmonary specimens.

Many TB laboratories are unable to perform NAA testing on extrapulmonary specimens due to limitations in validation data. Without NAAT results, confirmation and diagnosis of TB infection must usually be delayed until culture results are available. This delay can have an adverse impact on TB control efforts because extrapulmonary TB infections often make up a significant proportion of overall cases. Implementing NAA testing of extrapulmonary specimens has the potential to significantly increase the sensitivity and speed of a TB diagnosis.

[1] https://www.cdc.gov/hai/outbreaks/TB-bone-allograft.html