

TB diagnosis: Are we culturing enough biopsies?

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, and there are between 200 and 250 new cases diagnosed in BC yearly. Approximately 21% of TB cases in BC are extrapulmonary, with lymphadenitis being a common extrapulmonary site. TB can be suspected based on clinical, microbiological, and histopathological findings. Risk factors include prior TB infection, TB exposure, or residence in or travel to a TB-endemic area.¹ Microbiological confirmation of TB can be by culture of *M. tuberculosis* or molecular detection of *M. tuberculosis* DNA in patient samples.¹ Histopathological findings associated with TB are necrotizing granulomata and positive AFB stain, although non-necrotizing granulomata can also be found.²

Every year there are multiple requests at the Mycobacteriology Laboratory of the BC Centre for Disease Control Public Health Laboratory (BCCDC PHL) to attempt molecular-based diagnosis of TB on formalin-fixed paraffin-embedded (FFPE) tissue samples that were sent for histopathological examination without concurrent tissue culture, and were later suspected of TB based on histopathology. However, this diagnostic route compromises patient care since molecular testing is less sensitive than culture for *M. tuberculosis*, does not confirm organism viability, and limits options for drug susceptibility testing.¹ To estimate how frequently TB diagnosis may be missed, we reviewed lung and

thoracic lymph node biopsy handling practices (635 patients) and associated laboratory and clinical findings and engagement in TB care of those suspected or diagnosed with TB based on biopsy findings (23 patients) in two BC hospitals for 2018. The same review was conducted on all patients whose FFPE samples were sent to the Mycobacteriology Laboratory at the BCCDC PHL for TB molecular testing (48 patients) in 2018.

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We found that 4% to 14% of lung and thoracic lymph node biopsies were sent for mycobacterial culture, in addition to histopathological evaluation. Patients with tissue culture and histopathology were significantly more likely than those with histopathology only to be diagnosed with TB and undergo assessment and treatment by provincial TB services, based on biopsy results. High clinical suspicion for TB prior to biopsy in patients whose biopsies were sent for mycobacterial culture likely drove these differences. Less than 1% of lung biopsy patients were referred to TB services for assessment based on histopathological findings only (presence of granulomata in tissue), resulting in diagnosis and treatment of three additional patients. Out of 48 patients tested by molecular testing for TB at BCCDC PHL in 2018, 44 patients were assessed by the TB services, six were diagnosed with TB based on molecular testing of FFPE samples, with three of those being on peripheral lymph node biopsies. An additional five patients were treated for TB in the absence of microbiological diagnosis, based on clinical and histopathological suspicion alone.

Our review demonstrates that a small portion of TB patients in BC received a sub-optimal diagnostic workup due to lack of tissue culture. To further reduce this number,

physicians ordering biopsies should consider TB in the differential and evaluate each patient for TB risk factors prebiopsy (especially in cases of peripheral lymphadenitis), and ensure cultures are performed for biopsies of patients with clinical suspicion of TB. ■

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This article is the opinion of the BC Centre for Disease Control and has not been peer reviewed by the BCMJ Editorial Board.