

Usage of Molecular Pathology in a Rare Oral Tuberculosis Diagnosis

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To the Editor: A patient presented with oral mucosa, ulcerated pain, and limitation of mouth opening from January 2016. Local doctors diagnosed him with oral ulcer and prescribed courses of related medicine which did not relieve symptoms. Frozen section of oral mucosa (March 31, 2016) showed granulomatous reaction [Figure 1]. He was referred to our hospital.

Physical examination showed malnutrition, chronic sick look, ulcerated oral mucosa, and purulent secretion. Erythrocyte sedimentation rate was 34 mm/h. Tuberculosis (TB) antibody was positive. Lymphocyte count was as follows: Th cell 23.5% (normal range: 27–51%) and B-cell 2.6% (normal range: 5–18%). Interferon- γ release assays: A155 B191. Then, molecular pathology of oral mucosa was tested and it showed *Mycobacterium tuberculosis* (MTB) DNA positive. Oral TB was diagnosed.

A comprehensive diagnosis was not finished yet. Oral mucosa may be infected when sputum passed mouth. Hence, the primary lesion may be in lung. After diagnosing oral TB, chest computed tomography and sputum test were performed, which showed high-dense nodes and fibers and MTB *rpoB* positive. Lung TB was diagnosed then.

Furthermore, MTB in saliva could be swallowed into digestive tract, so gastrointestinal TB may be secondary to oral TB. Gastroscopy and feces were tested and the results showed negative. Apart from anti-TB medicine, oral hygiene care was provided. After 1.5 months, oral lesion disappeared, sputum turned negative, and digestive tract continued to be normal.

Only approximately 0.05–5.00% of the total TB cases manifest orally.^[1] Pathological lesions are commonly found on tongue, followed by labial mucosa, hard palate, gingiva, and buccal mucosa. Ulcers are the most common manifestations.^[2] In primary oral TB, mouth can be the initial site of infection. Secondary oral TB arises from another site and may be inoculated with sputum. Oral mucous membrane presents natural resistance to *Mycobacterium* invasion, which attributes to cleansing action of saliva, salivary enzymes, tissue antibodies, oral saprophytes, and thickness of protective epithelial covering. A breach in these defense mechanisms by abrasions, poor oral hygiene, extraction socket, periodontal

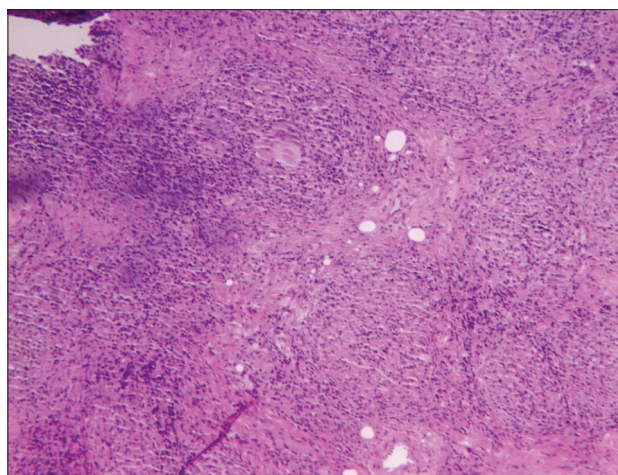


Figure 1: Frozen section of oral mucosa (March 31, 2016) showing granulomatous reaction (HE, original magnification $\times 50$).

disease, pulpal exposure, or overhanging restoration may lead to oral TB.

Oral TB is nonspecific in its presentation and often overlooked, which leads to therapy delaying. Similar oral features can occur in numerous other settings including infection by fungi and unusual bacteria, traumatic aphthous or herpetic ulcers, neoplastic processes such as Hodgkin's disease, Kaposi sarcoma, and squamous cell carcinoma.^[3] Although presumptive diagnosis of TB can be based on histopathological examination and bacilli stains, mycobacteria can be demonstrated only in 27–60% of cases.^[4] Microbe culture shows good results, but may last for 4–6 weeks.

As genetic technique develops, molecular biology technique is used in pathology diagnosis. Molecular pathology is a new method

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combining pathology and molecular biology methods. After extracting DNA from tissue, pathogenic target genes are amplified using polymerase chain reaction to detect pathogen. *IS6110* gene fragment has been found in MTB and *Mycobacterium bovis* but not in other mycobacteria, so it is used as a specific target gene for identifying MTB. Moreover, *IS6110* is multiple copies, which can enhance sensitivity. It shows that using *IS6110* as a target gene in molecular pathology technique to diagnose TB patients has higher positive rate (51.5%), when compared with acid fast stain (31%) and auramine O fluorescent dyes (40.5%) with $P < 0.05$, and could distinguish non-TB *Mycobacterium* from MTB.^[5] In China, molecular biology technique confines to sputum samples, and traditionally, pathology diagnosis confines to histomorphology and pathogen investigation, both of which may have low sensitivity and specificity.^[4] Molecular pathology may be a better choice, especially for rare disease diagnosis, where diagnosis often depends on pathology.

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Conflicts of interest

There are no conflicts of interest.

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