

## Oral ulcer: an uncommon site in primary tuberculosis

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### ABSTRACT

Tuberculosis is a chronic infectious disease and a major cause of morbidity and mortality worldwide. It can affect any part of the body, including the oral cavity. Oral lesions of tuberculosis, though uncommon, have been observed in both primary and secondary stages of the disease. This article presents a case of primary tuberculosis manifested as a non-healing, tender ulcer on the lingual mucosa of the edentulous right mandibular arch molar zone, an uncommon site. The diagnosis was confirmed after histopathology examination, polymerase chain reaction and purified protein derivative tests and chest radiograph. A recommended treatment plan of six months with four anti-tuberculous antibiotics was commenced. Clinically, the oral ulcer disappeared three months after the commencement of treatment. The resurgence of tuberculosis should compel clinicians to include the disease in the differential diagnosis of various types of non-healing oral ulcers.

**Keywords:** Mandibular lingual mucosa, oral ulcer, primary tuberculosis.

**Abbreviations and acronyms:** PCR = polymerase chain reaction; PPD = purified protein derivative; TB = tuberculosis.

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### INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis*.<sup>1–7</sup> About one-third of the world's population is affected, with eight million people infected annually and three million dying per year from tuberculosis complications.<sup>1,2,7–10</sup>

The disease declined sharply in the early 1980s but resurged due to a combination of factors such as the HIV epidemic, increased immigration from countries with endemic tuberculosis, transmission of tuberculosis in crowded or unsanitary environments, and a decline in health care infrastructure.<sup>1,6,10–13</sup>

Tuberculosis is usually caused by *Mycobacterium tuberculosis*, by direct person-to-person spread through airborne droplets and, less frequently, by ingestion of unpasteurized cow milk infected by *Mycobacterium bovis* or by other atypical *Mycobacteria*.<sup>1,2,9,10,12–14</sup>

Depending on the infected site, tuberculosis is classified clinically as pulmonary and extrapulmonary. Pulmonary tuberculosis remains the most common form of the disease but other sites may be involved, including the lymphatic, skeletal and central nervous systems, the skin, kidneys, pharynx and gastrointestinal tract.<sup>1–3,6,8,10,14</sup> Extrapulmonary involvement in tuberculosis is uncommon, accounting for approximately 10% to 15% of all infected people.<sup>2,5</sup> The global

prevalence of human TB due to *Mycobacterium bovis* has been estimated at 3.1% of all human TB cases.<sup>14</sup>

Oral tuberculosis lesions are uncommon. They are found in 0.05% to 5.00% of tuberculosis cases.<sup>6,7,9,12</sup> Most cases appear as a chronic painless ulcer.<sup>1,4,15</sup> Primary oral tuberculosis without pulmonary involvement is extremely rare since most oral lesions represent a secondary infection from initial pulmonary lesions.<sup>1,4,5,11,14–16</sup>

Primary oral tuberculosis is more common in younger patients.<sup>6,8,17</sup> When present, it usually involves the gingiva,<sup>5</sup> mucobuccal fold and areas of inflammation adjacent to teeth or in extraction sites, with enlarged palpable cervical lymph nodes.<sup>1,7,13,15</sup> However, secondary oral tuberculosis is mostly present on the tongue, lips, buccal mucosa and rarely on the palate, gingival mucosa<sup>7,8,10,13,15,16</sup> and lingual frenum.<sup>5</sup>

The aim of this article was to report a case of non-healing tender ulcer of primary tuberculosis, localized on the lingual aspect of an edentulous right mandibular arch molar zone and to emphasize the importance of early diagnosis and management.

### CASE REPORT

A 65-year-old male was referred to the Oral Pathology and Oral Diagnosis Department at the Lebanese University School of Dentistry with a chief complaint

of tender, non-healing oral ulcer on the lingual aspect of the edentulous right molar mucosa of the mandible which over three months had increased in size from 1 cm to 3 cm. The ulcer was treated with miconazole (Daktarin® Oral Gel, Janssen Cilag Ltd). Topical mouthwashes of an undisclosed brand were also used for three weeks prior to referral but with no positive outcome. During this period, the patient was asked not to wear his partial removable prosthesis.

The patient's medical history included a diagnosis of type II diabetes in April 2010. The patient was on a low carbohydrate diet and took no medication. He was a non-smoker with no family history of infectious diseases.

Upon extraoral examination, a single enlarged submandibular lymph node on the right side was detected. It was firm, tender and fixed to deeper anatomical layers (Fig. 1).

Intraorally, there was an ulcer on the lingual aspect of the edentulous right mandibular second molar mucosa of an irregular oval shape and measuring about 1.5 × 3.0 cm. The ulcer had a well-defined and slightly elevated border that altered to ill-defined on the lower perimeter. It was covered by an inhomogeneous grey yellowish layer with a granular aspect surrounded by an erythematous halo (Fig. 2). The base and borders of the ulcer were indurated on digital palpation.

A peripheral giant cell granuloma on the alveolar crest ridge, corresponding to the first left molar, was diagnosed following a biopsy.

An orthopantomogram revealed a multitude of ill-shaped radiopacities forming a circular configuration of 1 cm diameter and superimposed with the right angle of the mandible (Fig. 3). On the left side, a few millimetres higher, there were fewer radiopacities.

Based upon both clinical and radiographic examinations, a differential diagnosis included possible



Fig. 1 Extraoral photograph of enlarged right submandibular lymph node.



Fig. 2 Intraoral photograph of an ulcer, via mirror view, with well-defined erythematous margins and covered by a yellow necrotic layer.

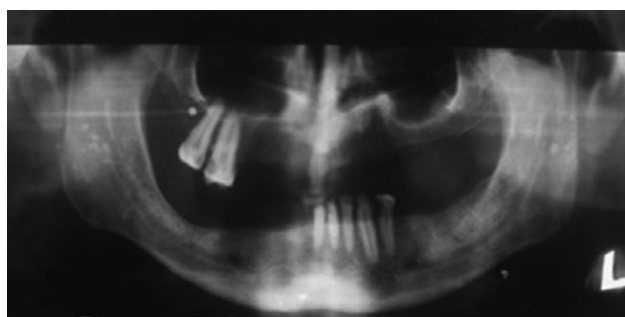


Fig. 3 Orthopantomogram of an inhomogeneous radiopaque lesion.

squamous cell carcinoma, lymphoma, giant aphthous ulcer, traumatic ulcer, infections (bacterial, fungal or viral) and drug reaction.<sup>4,11</sup> As there was no history of trauma and the ulcer was chronic, tender and non-recurrent, the possibility of traumatic or aphthous ulcer was ruled out. The patient was not on any medication and therefore the possibility of ulcer due to drug reaction was also ruled out.

A biopsy of the ulcer under local analgesia (mepivacaine with epinephrine 1/50 000) was performed. Histopathological examination showed a regular stratified squamous surface epithelium focally ulcerated. The connective tissue exhibited granulomatous inflammation containing epithelioid and multinuclear giant cells. Some of these granulomas showed a central acidophilic, granular and acellular necrosis with a leucocytic infiltrate.

This raised the possibility of granulomatous lesion, including tuberculosis or sarcoidosis. A real-time polymerase chain reaction (PCR) for DNA detection of Mycobacterium complex tuberculosis and non-tuberculosis mycobacteria was performed on paraffin embedded tissue and proved to be positive for Mycobacterium complex.

The patient was then referred to a pneumologist for further care. A chest radiograph did not reveal any characteristic tuberculous features and a purified protein derivative (PPD) test was positive with a

diameter of 15 mm. Complete blood count (CBC) was within normal limits except for a raised white cell count ( $12.5 \times 10^9$ ). The erythrocyte sedimentation rate (ESR Westergren) showed high values (60 mm in the first hour). Hepatitis C and HIV tests were negative. All the above findings were consistent with those of primary extrapulmonary tuberculosis.

The physician initiated a WHO recommended anti-tuberculous therapy ('Directly observed treatment, short course') with rifampicin (600 mg), isoniazid (300 mg), ethambutol (800 mg) and pyrazinamide (1200 mg) daily for six months. A clinically healed mucosa was obvious three months after treatment initiation (Fig. 4). At 30-months follow-up the oral ulcer had not recurred.

## DISCUSSION

Tuberculosis is a major cause of morbidity and mortality worldwide. The risk of infection is much greater among people in lower socio-economic groups,<sup>2,5,11</sup> rural dwellers or people with occupational exposure.<sup>14</sup> The primary form of TB is most often localized to the lungs.<sup>8,10</sup> This was the first case of primary oral TB observed since 1994 at the Department of Oral Pathology and Diagnosis, School of Dentistry, Lebanese University, Beirut, Lebanon.

Primary oral TB lesions are extremely rare and usually observed in children<sup>17</sup> but may also be seen in adults.<sup>2</sup> They typically involve the gingiva,<sup>5</sup> mucobuccal fold and areas of inflammation adjacent to teeth or in extraction sites.<sup>1,2,6</sup> They are usually associated with enlarged regional lymph nodes.<sup>1,2</sup> In the present case, the patient was a 65-year-old male diagnosed with type II diabetes in 2010. Extraoral examination revealed a single enlarged submandibular lymph node.

Primary oral tuberculosis is an uncommon occurrence, probably because the intact squamous epithelium of the oral mucosa acts as a mechanical and biological barrier. It provides protection against infection from tuberculosis bacilli;<sup>5,7,14</sup> the inhibitory effect of saliva is also considered to be an additional reason of the relative resistance against tuberculous

bacilli.<sup>5,7,8</sup> Although the mechanism of primary inoculation has not yet been well established, it appears that tuberculosis bacilli are most likely carried in sputum or unpasteurized milk and enter the mucosal tissue through a small tear in the oral mucosa.<sup>5,14</sup> Local predisposing factors include poor dental hygiene, periodontitis, leukoplakia, traumatic ulcers, recent opened dental extraction sites and jaw fracture.<sup>1,2,8</sup> In the present case, the most likely mode of primary inoculation was through a traumatic ulcer due to an ill-fitting removable prosthesis and contaminated milk.

This case is unusual in that a non-healing tender ulcer on the lingual mucosa aspect of the edentulous right mandibular molar led to the diagnosis of primary extrapulmonary tuberculosis. In the literature, the presence of primary oral tuberculosis lesion in this region is rarely described.<sup>6</sup> Differential diagnosis of this non-healing chronic ulcer initially included a squamous cell carcinoma, which is more frequent in this region. Mahajan and co-workers<sup>6</sup> reported a non-healing ulcer on the retromolar trigone as an uncommon site for secondary tuberculosis associated with HIV.

It is vital for dentists to perform a biopsy and conduct a complete physical examination including signs and symptoms of pulmonary TB. Histopathological study is needed to exclude carcinomatous changes and confirm definite diagnosis of TB.<sup>2,6</sup> In the present case, aphthous ulcer, traumatic ulcer, infections (bacterial, fungal and viral) and drug reaction were ruled out due to the absence of non-recurrent ulcer, traumatic history and systemic medication.

In our case, histopathology revealed a granulomatous lesion. This raised the possibility of orofacial granulomatous conditions such as tuberculosis, sarcoidosis, tertiary syphilis, deep mycoses and foreign body reaction. The definitive diagnosis of tuberculosis was confirmed by a PPD and PCR tests.

## CONCLUSIONS

Primary and secondary tuberculosis of the oral cavity is relatively rare and has largely become a forgotten diagnosis in oral lesions. Dental practitioners need to be aware that TB may occur in the oral cavity. Tuberculosis should be considered in the differential diagnosis of any suspicious, indurated non-healing ulcer of the oral cavity, especially when treating patients from a lower socio-economic background.<sup>5,14</sup> In addition, efforts should be made to control oral TB by early detection and referral of the patient to a specialized physician for proper diagnosis and management.<sup>5</sup> An early diagnosis with prompt treatment will usually result in complete cure.<sup>8</sup> Appropriate and effective infection control programmes in dental practice should be maintained.



Fig. 4 Intraoral view six months after treatment.

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