Pathology Section

ORIGINAL ARTICLE

A Disguised **Tuberculosis** of the **Oral Buccal Mucosa**

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ABSTRACT

Tuberculosis (TB) is a major cause of ill health and death worldwide. It is a chronic granulomatous disease that can affect any part of the body, including the oral cavity. Oral lesions of TB, though they are uncommon, are seen in both the primary and secondary stages of the disease. The authors present here, a case of TB of the buccal mucosa, manifesting as a non healing, non painful ulcer. The diagnosis was confirmed, based on the histopathology, sputum examination and immunological investigation. The patient underwent anti-tuberculosis therapy and her oral and systemic conditions improved rapidly. Although the oral manifestations of TB are rare, the clinicians should include TB in the differential diagnosis of various types of oral ulcers. An early diagnosis with prompt treatment can prevent complications and potential contaminations.

Key Words: Oral, Buccal mucosa, Tuberculosis

INTRODUCTION

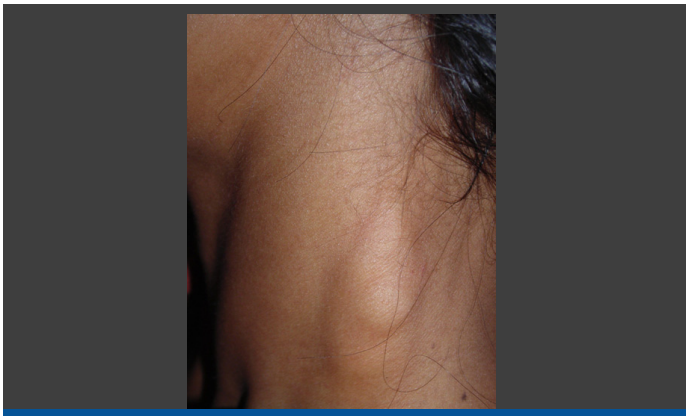
Tuberculosis (TB) is a communicable chronic granulomatous disease which is caused by Mycobacterium tuberculosis [1]. Tuberculosis is a global health problem with 8 million people being infected annually and 3 million people dying from diseases which are related to TB complications [2]. India alone accounts for nearly one fifth of the global burden of tuberculosis [3]. The incidence of TB in the underdeveloped countries is increasing, and this is thought to be because of associated poor hygienic conditions and a greater prevalence of acquired immunodeficiency syndrome (AIDS) [4], [5]. TB is usually acquired by mycobacterium tuberculosis and less frequently by the ingestion of unpasteurized cow's milk that is infected by Mycobacterium bovis or by other atypical Mycobacteria [6].

Depending on the organ system which is involved, tuberculosis is classified clinically as pulmonary and extra-pulmonary. Pulmonary tuberculosis remains the most common form of the disease. Extrapulmonary involvement in tuberculosis is uncommon, accounting for approximately 10% to 15% of all the TB cases [7]. TB mainly affects the lungs but it also affects the intestines, meninges, bones, joints, lymph glands, skin and other tissues of the body [8]. Oral tuberculous lesions are infrequent and it is estimated that only 0.05-5% of the total tuberculosis cases may present with oral manifestations [9]. The aim of this article is to report a case of primary tuberculosis and to emphasize the importance of early diagnosis with various diagnostic tests, so as to lessen the risk of exposure by contact with an infected patient.

CASE REPORT

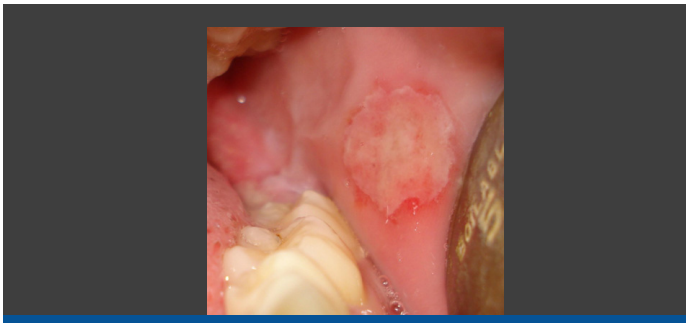
A 35 year old female was referred to the oral and maxillofacial pathology department with the chief complaint of painless, non healing oral ulcers on the left buccal mucosa of five months duration, which had increased in size. Her detailed medical history revealed that she had experienced regular weight loss (around 3 kg) over the past three to four months. She also complained of cough and a feeling of malaise during the past 15 to 20 days. However, her family history was not contributory and she was not on any kind of systemic medication.

On extra oral examination, a single cervical lymph node of the left side was found, which was palpable and enlarged; however, there was no sign of tenderness or fixation to the surrounding tissues [Table/Fig 1]. Intra orally, there was an ulcer on the left buccal mucosa, measuring about 1.5 x 1.5 cm in dimension, with a shallow ulcerated base and well defined margins.



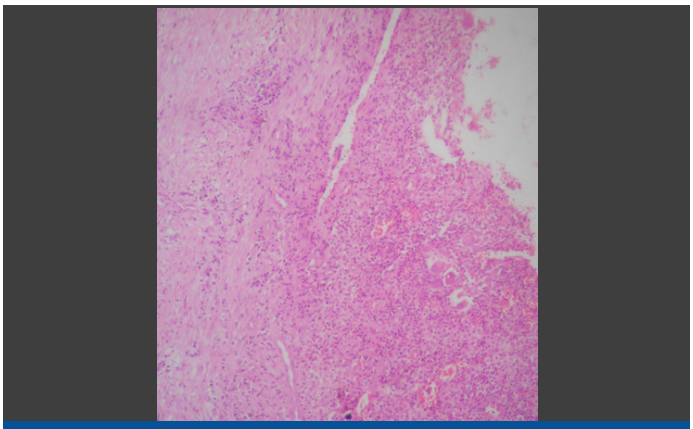
[Table/Fig 1]: Extraoral photograph shows enlarged cervical lymph node

The ulcer was covered by a yellow pseudomembrane and was surrounded by an erythematous halo [Table/Fig 2]. There was no other abnormality elsewhere in the oral cavity. Based upon the clinical examination, a differential diagnosis which included aphthous ulcer, traumatic ulcer, infections (bacterial, fungal and viral), drug reaction and malignancy, including primary squamous cell carcinoma and lymphoma was made. Since there was no history of any kind of trauma and the ulcers were chronic, painless and non recurrent, the possibility of traumatic and aphthous ulcers was ruled out. Moreover, the patient was not on any systemic medication, thus ruling out the possibility of ulcers due to drug reaction.

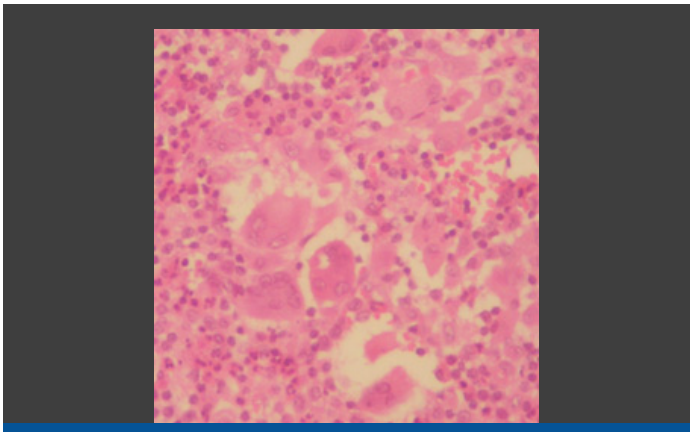


[Table/Fig 2]: Intra orally photograph shows an ulcer with well defined margins on the left buccal mucosa covered by a yellow pseudomembrane

[Table/Fig 3]

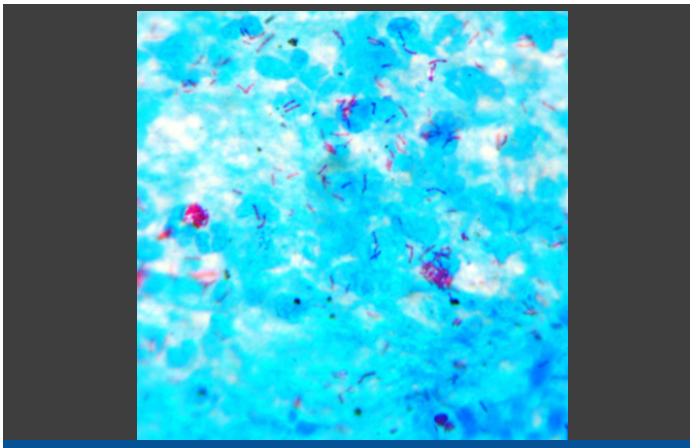


[Table/Fig 3 (a)]: Histopathological slide shows granulomatous inflammation with Langhan's giant cells and focal caseous necrosis (hematoxylin and eosin stain)



[Table/Fig 3 (b)]: Langhan's cells containing nuclei arranged in a horse-shoe shaped pattern at cell periphery

An incisional biopsy of the ulcer was performed under local anaesthesia. Histopathological examination of the excised specimen showed an ulcerated, stratified, squamous surface epithelium in association with the fibro vascular connective tissue. The connective tissue exhibited a granulomatous inflammation containing epitheloid cells, Langhan's giant cells and a lymphocytic infiltrate with areas of caseous necrosis [Table/Fig 3]. This raised the possibility of a granulomatous infection, including tuberculous, sarcoidosis or fungal infections. Subsequent stains for fungi (PAS and Grocott Silver) and bacteria (Gram stain) were negative. However, several acid-fast bacilli were identified by doing a Ziehl-Neelsen's stain, in the sputum. [Table/Fig 4]



[Table/Fig 4]: Several acid-fast bacilli in the sputum (Ziehl-Neelsen stain)

The blood tests were within normal limits, except for a raised white cell count (11.1x 10^9) and a raised erythrocyte sedimentation rate (95 mm/hour). The hepatitis C virus test and theVDRL (Veneral Disease Research Laboratory) and HIV tests were negative. An ELISA (Enzyme-Linked Immunosorbent Assay) test confirmed the presence of antibodies against mycobacterium tuberculosis. However, the chest X ray did not reveal any characteristic finding. These features were consistent with those of a tuberculous granulomatous lesion.

Based on all the above observations, the patient was referred to a physician who initiated a WHO recommended category 1 anti-tubercular therapy DOTS (Directly Observed Treatment, Short Course) with rifampicin (450 mg), isoniazid (600 mg), ethambutol (1200 mg) and pyrazinamide (1500 mg) for two months, with three times doses per week, followed with a continuation phase with isoniazid (300 mg) and thioacetazone (150 mg) for six months. The patient reported to our department after 6 months with a relatively normal buccal mucosa.

DISCUSSION

Tuberculosis is a major cause of ill health and death worldwide. The risk of infection however, is much greater among people in the lower socioeconomic groups [9]. Every year, approximately 2.2 million individuals develop tuberculosis in India, of which around 0.87 million are infectious cases and it is estimated that annually there are around 330,000 deaths due to TB [3]. TB has become the most common opportunistic infection in areas where the HIV infection is prevalent [4].

Tuberculosis of the oral cavity is an uncommon occurrence, may be because of an intact squamous epithelium of the oral mucosa which makes penetration difficult for the tuberculosis bacilli and provides protection against the infection [10]. Although the mechanism of primary inoculation has not been definitely established as yet, it appears that the organisms are most likely to be carried in the sputum and that they enter the mucosal tissue through a small tear in the oral mucosa as a result of chronic irritation or inflammation, which may favour the localization of the organisms [6]. The local predisposing factors include poor hygiene, local trauma, dental extraction, leukoplakia, jaw fracture, cyst and abscess [11]. In the present case, the bacteria might have spread through local trauma or poor oral hygiene.

Primary oral TB lesions are extremely rare and are usually seen in children but they may also be seen in adults. They typically involve the gingiva and are associated with regional lymphadenopathy. The secondary TB lesions are more frequent and involve the tongue, followed by the palate, lip, the buccal mucosa, the gingiva and the frenula [9],[12],[13]. The oral manifestations of TB are seen as superficial ulcers, patches, indurated soft tissue lesions or even as lesions within the jaw, that may be in the form of TB osteomyelitis [7], [14]. The chronic ulcerative form is the most common among these oral lesions [1].

This case is unusual in the sense that a painless ulcer on the buccal mucosa lead to the diagnosis of tuberculosis. The primary lesions of TB manifest in the oral cavity as non healing chronic ulcers. Clinicians should be aware when diagnosing such lesions with a non healing tendency; tuberculosis should be considered in the differential diagnosis. It is vital for the clinicians to conduct a complete physical examination, including the signs and symptoms of pulmonary TB, with various diagnostic tests, as listed in [Table/Fig 5] and by performing a biopsy. A histopathological study is needed to exclude carcinomatous changes and to confirm the diagnosis of TB. In the present case, the most likely differential diagnosis included a primary squamous cell carcinoma, traumatic ulcer, syphilitic ulcer and lymphoma, but the presence of a granulomatous inflammation with Langhan's giant cells and focal caseous necrosis in the histological specimen was typical of TB. Other orofacial granulomatous conditions such as sarcoidosis, syphilis, deep mycotic infection, cat-scratch disease, foreign-body reactions and Wegener's granulomatosis also give a similar granulomatous reaction. We confirmed the diagnosis of TB by doing a sputum examination (smear microscopy), immunological tests (ELISA) and by histopathological

examination.

To conclude, tuberculosis of the oral cavity is relatively rare and has largely become a forgotten diagnosis of oral lesions. Dental practitioners need to be aware that TB may occur in the oral cavity and that it should be considered in the differential diagnosis of any ulcerated, indurated, non healing lesion of the oral cavity, especially in the lower socioeconomic groups. In addition, efforts should be made to control oral TB by early detection and referral of the patient to a physician for proper management. Also, appropriate and effective infection control programmes in dental surgery should be encouraged. [Table/Fig 5]

Diagnostic Tool	Method/Inference	Advantages	Limitations
1.Tuberculin skin test (TST) a) Heaf test [15] b) Mantoux test [16]	Heaf gun injects multiple samples of testing serum over the flexor surface of the forearm in a circular pattern of six. Read at 3-7 days. Graded into 4 types 5 tuberculin units injected intradermally and read 48 to 72 hours later Postive when induration 5-15mm	Easier to interpret, with less inter-observer variability Less training is required to administer and to read the test. Used for screening purpose. Helpful in diagnosis of active TB. More precise than radiographic interpretation Easy to perform.	Multi puncture method 6 pricks-6 injections Not recommended in: Infants under 12 weeks old Past Mantoux reactions ≥ 15 mm Previous TB disease
2.Radiograph [17]	Areas of calcifications, cavities or radiolucency (darkened area) are seen in chest Infiltrate or consolidation		Exposure to x-rays. It has poor sensitivity. Cannot distinguish between active TB or healed TB in case of scar formation
3.Staining a) Ziehl-Neelson (ZN) staining [18] b) Auramine fluorescence [19]	Acid-fast bacilli are seen as bright red rods against blue, green or yellow background depending upon counterstain. Visualize acid-fast bacilli as bright rods against dark background using fluorescence microscopy	Simple method Non invasive Economical Contrast bacilli can be readily seen under high dry objective. More sensitive Less tiring Quick results for large number of slides.	Mycobacteria less than 10^4 per ml gives negative result Saprophytic mycobacterium may present similar appearance. Equipment required is expensive Used as a screening tool not as a final diagnosis
4. Enzyme-linked immunosorbent assay (ELISA) [20] Interferon release assays (IGRAs) [21] a) QuantiFERON-TB Gold b) T-SPOT.TB	Detects the presence of IgG and IgM antibodies when cultured with highly purified A 60 antigen extracted from mycobacteria Amount of interferon-gamma (IFN- γ) in response to contact with the TB antigens is measured Number of peripheral blood mononuclear cells used in the assay is quantified and enumerates individual T cells producing IFN-γ after antigenic stimulation thus gives an overall measurement of the antigen load on the immune system	More sensitive than staining Simple method Faster results Results within 24 hours Does not boost responses measured by subsequent tests, which can happen with tuberculin skin tests (TST). Is not affected by prior BCG (Bacille Calmette-Guérin) vaccination. Faster (results within 24 hours) Allows physicians to treat and control the disease much better	A60 antigen is common antigen to various species of mycobacteria leprae, tuberculosis and bovine Blood samples must be processed within 12 hours after collection while WBC is still viable. More data on the effectiveness of these tests in HIV-infected patients, young children, and other vulnerable groups are needed To process within six hours of venipuncture
5.Culture [22] a) Lowenstein-Jensen Media (LJ medium) b) BACTEC	When grown on LJ medium, M. tuberculosis appears as brown granular colonies (sometimes called "buff, rough and tough"). Detects the presence of oxygen in fluorescence by scanning it after every hour. Positive sample may contain 10^5-10^6 CFU/ml.	Less expensive than BACTEC Less chances of contamination Early detection Differentiate M.Tuberculosis from other Mycobacterium species More sensitive than conventional LJ media	Takes 4-6 weeks to get visual colonies on media. Can not differentiate between M.Tuberculosis from other Mycobacterium species Expensive More medical technologist required Risk of contamination is more
6.Polymerized chain reaction (PCR) [23], [24]	Help in detection of infectious agents and the discrimination of non-pathogenic from pathogenic strains by virtue of specific genes	Very small size of DNA is amplified easily. High sensitivity of PCR permits virus detection soon after infection and even before the onset of disease.	Neither localization within tissues nor staging of Mycobacterial disease is possible.

[Table/Fig 5]: Diagnostics techniques in tuberculosis

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DECLARATION ON COMPETING INTERESTS: No competing Interests

Date of Submission: **Nov 30, 2010**
Peer Review Completion: **Jan 05, 2011**
Date of Acceptance: **Jan 10, 2011**
Date of Final Publication: **Apr 11, 2011**