Primary Tuberculosis: An Unusual Finding in the Oral Cavity

Renu Tanwar[1], Asha R Iyengar[2], KS Nagesh[3], Parul Jhamb[4]

[1] 1MDS. Senior Lecturer, Department of Oral Medicine and Radiology. [2]MDS. Professor.† [3]MDS. Head of Department and Principal.† [4]MDS. Senior Lecturer, Department of Oral Pathology.**
** SGT Dental College, Budhera, Gurgaon, Haryana, India.*
† Department of Oral Medicine and Radiology, DAPMRV Dental College, Bangalore, India.

Abstract
The unusual involvement of the oral cavity in tuberculosis and the non-specific nature of its presentations mean that diagnosis of tuberculosis is often delayed and is an unexpected finding. The aim of this paper is to present a case of primary tuberculosis and discuss the implications of the manifestations and diagnosis of oral tuberculosis. This paper presents an unusual case of a painless, papillary, erythematous lesion in the anterior region of a maxillary edentulous ridge. When the patient concerned was first seen by the author, the lesion had been present for six months. There was cervical lymphadenopathy and it was diagnosed initially as a malignant lesion. Eventually, after biopsy and ultrasound examination, the diagnosis of primary oral tuberculosis was reached. The patient was managed solely by anti-tubercular drug therapy.

Key Words: Primary Tuberculosis, Langhans Cell, Giant Cells, Granulomatous Lesion, Oral Tuberculosis

Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis.* It is transmitted primarily through the respiratory tract. Tuberculosis is a global health problem, with eight million people newly infected annually and three million people dying from diseases related to complications arising from the disease. Its incidence in underdeveloped countries is increasing, and this is thought to be because of associated poor hygiene conditions [1,2].

Tuberculosis mainly affects the pulmonary system but it can also involve extra-pulmonary sites, including the head and neck region. A review of the English-language literature suggests that oral tuberculosis generally has been regarded as a rare entity (affecting approximately 0.05% to 5.00% of patients with the disease). Thus, the disease rarely features in the differential diagnoses of head and neck lesions [3-7].

A case report of a tuberculosis lesion in the oral cavity is presented here, with an unusual clinical presentation of a painless erythematous growth in the anterior region of a maxillary edentulous ridge that caused the patient to seek professional care and led to diagnosis of oral tuberculosis. In contrast to the published reports of oral tuberculosis, in which it presented as oral ulceration or was located in the vestibular area near the corner of the mouth or lower lip [5,8], this lesion was present in the maxillary buccal vestibule and did not involve the alveolar bone.

Case Report

A 49-year-old Indian female patient of lower socioeconomic status reported with a complaint of an ill-fitting upper denture as a result of a growth, which had been present for six months. The patient also complained of multiple pea-shaped swellings in her neck, which had been present for nine months. A through medical history did not reveal any evidence of weight loss, chills, night sweats, or cough. On extra-oral examination, multiple upper cervical lymph node enlargements were observed with maximum of 2 cm in size and palpation revealed matted, non-tender and non-fixed lymph nodes of the submandibular and anterior cervical chain on both sides (*Figure 1*). An intra-oral examination revealed a solitary, erythematous, ill-defined papillary growth that was granular in appearance, with

Corresponding author: Dr Renu Tanwar, WZ572B/1, Naraina Vihar, New Delhi-110028, India; e-mail: renuomdr@gmail.com or drashaiyengar@yahoo.co.in

dimensions of 1 cm x 3 cm. It was located in the maxillary facial vestibule and extended along the edentulous ridge from 14 to 24. It obliterated the vestibule and did not involve the maxillary ridge superio-inferiorly (*Figure 2a* and *b*). The surface of the growth was shiny; no bleeding, ulceration, or pus drainage were observed. It was not tender and was soft in consistency when palpated.

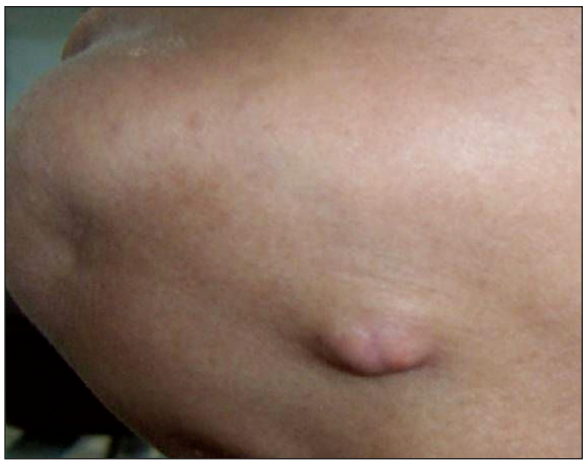

Figure 1. *Cervical lymphadenitis.*

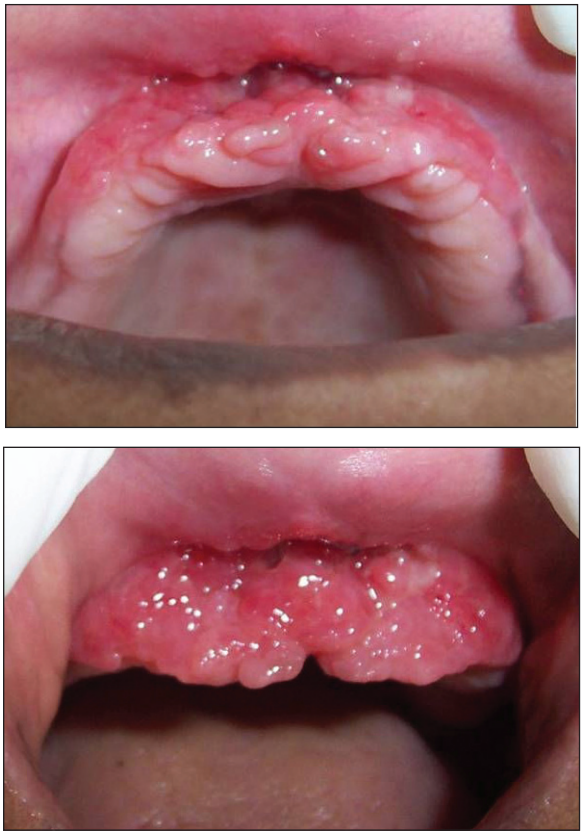

Figure 2 a, b. *Erythemous growth in maxillary facial vestibule.*

The patient gave a past dental history of extraction of upper front teeth one year previously. She had not taken any medication for the lesion. Her family history was non-relevant. Routine haematological and biochemical investigations and a chest radiograph were undertaken on the day that the patient reported to the department; they did not reveal any abnormality. No radiographic evidence of involvement of underlying bone was seen on an occlusal radiograph. Ultrasound examination of the enlarged lymph nodes was performed three days after the first visit of the patient. It revealed hyperechoic, matted lymph nodes, suggestive of tuberculosis (*Figure 3*).

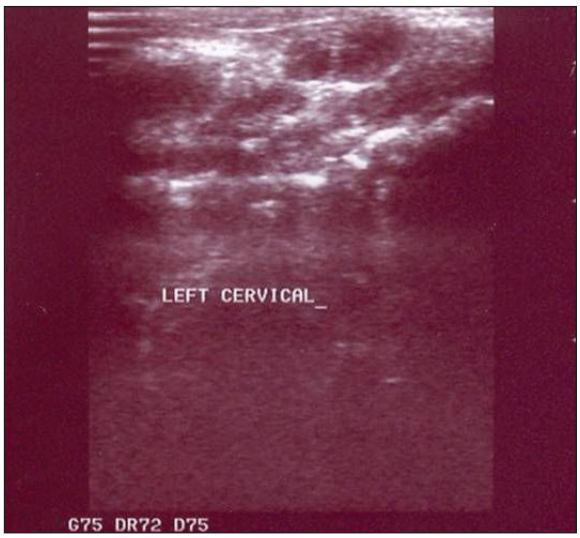

Figure 3. *Ultrasound picture of left cervical lymph nodes.*

Three weeks after the first visit, serological tests were performed for syphilis and human immunodeficiency virus (HIV), together with a sputum examination, including Zielh–Neelsen staining. They gave negative results. Biopsy of the intra-oral lesion was then undertaken. The subsequent histopathological examination showed stratified squamous epithelium and connective tissue, revealing crushing artifacts, with the presence of multiple necrotising epithelioid cell tuberculous granuloma and Langhans type of giant cell *(Figure 4).* Acid-fast bacteria (AFB) staining was also found to be negative in the biopsy specimen.

The patient was referred to Department of General Medicine at the General Hospital in Bangalore and a multidrug anti-tubercular regimen was started. This anti-tubercular therapeutic regimen was administered for six months and follow-up showed complete resolution of the oral lesion with no recurrence after two years, suggesting a successful outcome.

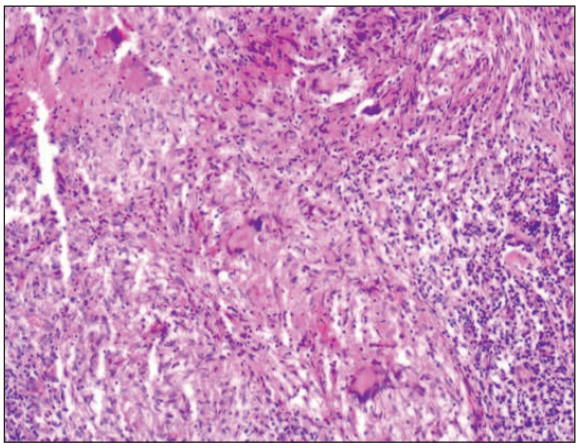

Figure 4. *Langhans giant cell containing nuclei arranged in a horseshoe-shaped pattern at cell periphery.*

The anti-tuberculous regimen for the patient was as follows. In the initial phase, the following drugs were given for two months: ethambutol hydrochloride (E): 500 mg, twice daily; isoniazid (INH): 150 mg, twice daily; pyrazinamide (Z): 750 mg, twice daily; rifampicin (RIF): 300 mg, twice daily. The initial phase was followed by continuation phase which during which the following drugs were given for a further four months: INH: 150 mg, twice daily; RIF: 300 mg, twice daily.

During follow-up, the size of enlarged lymph nodes reduced from 2 cm to 1 cm after the first three months of treatment and were of normal size after one year. The size of intra-oral lesion reduced and then completely healed. Six months after the completion of anti-tuberculous therapy, the patient was referred to Department of Prosthodontics for the construction of a new denture. No recurrence of the lesion was observed in the follow-up period of two years after completion of drug regimen (*Figure 5*).

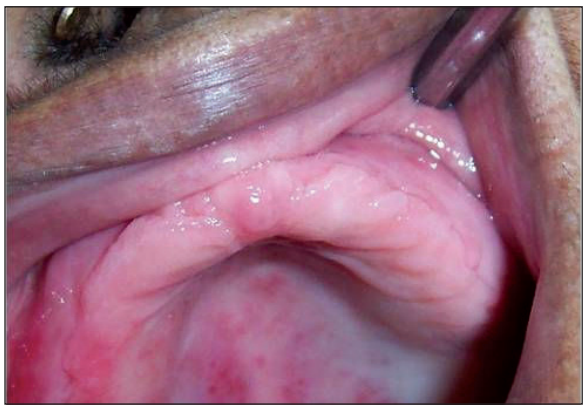

Figure 5. *Resolved oral mucosal lesion after anti-tubercular therapy.*

The patient gave written consent for her photographs and those of the lesion and its histopathological images to be used in this case report.

Discussion

Tuberculous involvement of the oral cavity is extremely rare, with incidence ranging from 0.05%-5.00% [4,9]. Tuberculous lymphadenitis constitutes a component of head and neck disease in up to 90% of patients and presents as single or multiple enlarged lymph nodes that may be firm, fluctuant, or matted with fistula formation [5,9-11].

The World Health Organization (WHO) estimates approximately 20 million active cases of tuberculosis, 80% of which occur in the developing countries. The regions with the highest incidence of tuberculosis are the Indian subcontinent, South-East Asia, and Africa. The epidemiology of tuberculosis differs considerably with ethnicity. Age has also been implicated as an important risk factor, as well as differing ethnic and socio-economic grouping [12]. Poorer populations are twice as likely to have tuberculosis and three times less likely to access care for this disease [13].

Oral tuberculosis most commonly results from contact of the oral tissues with infected sputum or haematogenous dissemination in an older individual with pulmonary disease. In contrast, cases of primary infection arising through direct mucosal invasion by mycobacteria are uncommon and typically are seen in young patients, who often present with cervical lymphadenopathy with or without cutaneous sinus formation [6]. An intact and healthy oral mucosa seems to provide a sufficient barrier to mycobacteria, with saliva also helping to control the organisms [8].

The sites demonstrating the most frequent involvement with primary tuberculosis are the gingivae, vestibular mucosa, and extraction sockets. Mucosal lacerations and dental extractions have been implicated as predisposing an individual to the development of oral tuberculosis [7].

Traditionally, the diagnosis of tuberculosis has been made on the basis of clinical and radiographic findings. The diagnosis of orofacial tuberculosis can be quite challenging, mainly because of a lack of definite signs and symptoms. According to Pandit *et al.* (1995), when considering the overall prevalence of tuberculosis in the Indian population, the presence of epithelioid cell granuloma is indicative of the disease unless proven otherwise, which is similar to our findings. It is also reported that the

percentage of cases showing AFB positivity declines when more epithelioid cell granulomas are observed [14].

Dimitrakopoulos *et al.* (1991) reported two cases of primary tuberculosis of the oral cavity where smears and culture for AFB, from the oral lesion and the sputum, were negative [15]. They confirmed the diagnosis solely on the basis of history and histopathologic examination, which only revealed giant cells and epithelioid cells. In their manuscript, they have quoted various reasons cited by different authors for the difficulty in microbiologic detection of the tubercle bacilli. This may be due to (a) high immunity of the patient resulting in destruction of the bacilli, (b) their enclosure by local tissue reaction and the very small numbers of tubercle bacilli in oral lesions, which is why direct examination of scrapings stained with the Ziehl–Neelsen stain are usually negative, and (c) previous long-term treatment with antibiotics [11,15].

In our patient, the histopathology revealed the presence of an epithelioid cell granuloma, which is very typical of tuberculosis. It was noted that the patient was responding to treatment. Also in the present case, the patient was managed solely with anti-tubercular chemotherapy.

Oral cavity tuberculosis is difficult to differentiate from other conditions on the basis of clinical signs and symptoms alone. When evaluating such cases, clinicians should consider both infectious processes, such as primary syphilis and deep fungal diseases, and non-infectious processes such as chronic traumatic ulcer and squamous cell carcinoma. If there is no systemic involvement, an excisional biopsy is indicated to establish a definitive diagnosis [6,16].

Multinucleated giant cells of Langhans type are frequently seen in various granulomatous lesions such as bacterial, fungal and autoimmune diseases, including tuberculosis, leprosy, syphilis, sarcoidosis, Crohn's disease, eosinophilic granuloma, cheilitis granulomatosis and certain fungal diseases [17].

In case of any discordance in histopathologic diagnosis, a Ziehl–Neelsen stain, a complete medical and dental history, a clinical correlation and an immune-based assay can be used to rule out other lesions with Langhans type of giant cells. For example, unlike tuberculosis, sarcoidosis lacks caseous necrosis and acid-fast organisms.

If syphilis is suspected histopathologically, vascular changes such as proliferative endarteritis and a proliferation of endothelial cells resulting in constriction of the vascular lumen are seen. Warthin–Starry stain can be used to identify the causative organism.

Leprosy lesions are associated with the involvement of superficial nerves leading to anaesthesia and paraesthesia, which may cause unrealised trauma leading to ulcers and secondary infection [17,18].

Cheilitis granulomatosis involves only lips, most often the lower lip, but skin and mucous membrane remain intact. Histopathologically, sarcoid-like non-caseating granulomas are present.

Crohn's disease manifests itself as granulomatous nodules and ulcers in the oral cavity along with associated gastrointestinal symptoms. Histopathology reveals the presence of non-caseating epitheloid granulomas with Langhans giant cells. Schaumann and asteroid bodies may also be present [17,18].

Fungal lesions such as histoplasmosis, blastomyosis and coccidiomycosis should also be considered during diagnosis of an oral tuberculosis lesion. Microscopically, organisms can be identified with stains such as haematoxylin and eosin (H&E), para-aminosalicylic acid (PAS), or methenamine silver. Sporangia may be found free within necrotic tissue or within the epitheloid cells and giant cells of the granuloma. Fungal cultures can be an aid in identification of specific fungal species [17,18].

The same basic principles for the treatment of pulmonary tuberculosis apply to extra-pulmonary tuberculosis. For tuberculosis at any site, a course of treatment of from six to nine months with regimens that include INH and RIF is recommended; the single exception is meningitis, for which 9 to 12 months of treatment is recommended [9,16,19,20].

In the present case, the patient reported with a painless erythematous lesion in the maxillary facial vestibule. This is an unusual presentation for oral tuberculosis because most cases reported in literature are related to painful ulceration, with the most commonly involved sites being either tongue or gingivae. As the patient gave a history of traumatic extraction in relation to maxillary anterior teeth, inflamed and irritated mucosa could have favoured localisation of the organisms leading to development of this lesion. The diagnosis of primary oral tuberculosis in our patient was made by biopsy because the clinical features of the oral lesions were non-specific and chest radiographs and sputum

examination, including Zielh–Neelsen staining, were negative for pulmonary involvement. Histopathology of the lesion demonstrated multinucleated giant cells, especially Langhans giant cells and histiocytes. Ultrasound investigation of cervical lymph nodes demonstrated the size of the enlarged lymph nodes and the presence of central hypodensity. An anti-tubercular therapeutic regimen was administered for six months and follow-up showed complete resolution of oral lesion with no recurrence after two years, suggesting a successful outcome.

Conclusion

Tuberculosis remains a devastating disease throughout the world. Efforts to eradicate it have been thwarted by poverty, lack of healthcare access, drug resistance, immuno-suppressed populations (e.g., HIV-infected persons), and global migration. As presented in this paper, in cases of inflammatory or malignant lesions of the oral cavity, oral tuberculosis should be considered within a diferential diagnosis and incisional biopsy should be performed. In order to differentiate between the possibilities of primary versus secondary tuberculosis of the oral cavity, a radiograph of the chest should be taken. In cases of primary or secondary oral tuberculosis, early detection, diagnosis, and treatment are of the utmost importance. Effective management requires prompt recognition using a combination of clinical, radiographic, microbiological, and histopathologic signs and the initiation of appropriate multidrug therapy. In addition to effective treatment of patients with active tuberculosis, public health management strategies include contact investigation and testing of persons who came into close contact with patients with active tuberculosis before initiation of therapy and reduction of the population-based burden of tuberculosis through timely treatment and follow-up.

Acknowledgement

The authors thank the staff of the Department of Oral Pathology, DAPMRV Dental College, Bangalore for assistance in the histopathologic examination of the lesion.

Contributions of each author

- AA commissioned work, gave advice and checked drafts.
- BB gave advice and checked drafts.
- RT, ARI and KSN all wrote sections of the manuscript.
- RT accessed and prepared the figures.
- PJ provided the histopathologic diagnosis of the specimens.

Statement of conflict of interest

As far as the authors are aware, there is no conflict of interests.

References

1. Phelan JA, Jimenez V, Tompkins DC. Tuberculosis. *Dental Clinics of North America*. 1996; **40**: 327-341.

2. Yepes JF, Sullivan J, Pinto A. Tuberculosis: medical management update. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 2004; **98**: 267-273.

3. Ito FA, de Andrade CR, Vargas PA, Jorge J, Lopes MA. Primary tuberculosis of the oral cavity. *Oral Diseases.* 2005; **11**: 50-53.

4. Mignogna MD, Muzio LL, Favia G, Ruoppo E, Sammartino G, Zarrelli C, *et al*. Oral tuberculosis: a clinical evaluation of 42 cases. *Oral Diseases.* 2000; **6**: 25-30.

5. Al-Serhani AM. Mycobacterial infection of the head and neck: presentation and diagnosis. *Laryngoscope.* 2001; **111**: 2012-2016.

6. Eng HL, Lu SY, Yang CH, Chen WJ. Oral tuberculosis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endododontics.* 1996; **81**: 415-420.

7. Wang WC, Chen YK, Lin LM. Tuberculosis of head and neck: A review of 20 cases. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endododontics.* 2009; **107**: 381-386

8. Piasecka-Zeyland E, Zeyland J. On inhibitory e?ect on human saliva on growth of tubercle bacilli. *Tuberculosis.* 1937; **29**: 24-25

9. Popowich L, Heydt S. Tuberculous cervical lymphadenitis. *Journal of Oral Maxillofacial Surgery.* 1982; **40**: 522-524.

10. Mohapatra PR, Janmeja AK. Tuberculous lymphadenitis. *Journal of the Association of Physicians of India.* 2009; **57**: 585-590.

11. Iqbal M, Subhan A, Aslam A. Frequency of tuberculosis in cervical lymphadenopathy. *Journal of Surgery Pakistan (International)*. 2010; **15**: 107-109.

12. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. *Journal of the American Medical Association.* 1999; **282**: 677-686.

13. World Health Organization (WHO). *Regional Consultation on Social Determinants of Health. A Report.* New Delhi: WHO Regional Office for South-East Asia; 2005.

14. Pandit AA, Khilani PH, Prayag AS. Tuberculous lymphadenitis, extended cytomorphological features. *Diagnostic Cytopathology*. 1995; **12**: 23-27.

15. Dimitrakopoulos I, Zouloumis L, Lazaridis N, Karakasis D, Trigonidis G, Sichletidis L. Primary tuberculosis of the oral cavity. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endododontics.* 1991; **72**: 712-715.

16. Respiratory and ear, nose and throat diseases. In: Scully C, Cawson RA. *Medical Problems in Dentistry.* 5th ed. Chennai, India: Reed Elsevier India; 2005. p. 342-344.

17. Samar G, Jafari Sh, Moazamie N. Tuberculosis of the cervical lymph nodes: a clinical, pathological and bacteriological study. *Acta Medica Iranica* 1998; **36**: 138-140.

18. Marx RE. Stern D. *Oral and Maxillofacial Pathology. A Rationale for Diagnosis and Treatment.* Hanover Park, IL: Quintessence; 2003. p. 39-52, 90-106.

19. Peralta FG. [Tuberculosis infections of the head and neck]. *Acta Otorrinolaringológica Española.* 2009; **60**: 59-66. [Article in Spanish]

20. von Arx DP, Husain A. Oral tuberculosis. *British Dental Journal*. 2001; **190**; 420-422.

21. Sia G, Wieland L. Current concepts in the management of tuberculosis. *Mayo Clinic Proceedings*. 2011; **86**: 348-361.