Gingival manifestations of tuberculosis in pediatric patients: series of 4 cases

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Objective. The aim of the study was to evaluate the gingival manifestations of tuberculosis (TB) in the oral cavity in pediatric patients.

Study Design. Four pediatric patients were enrolled in the study. Clinical symptoms, auxiliary examinations, treatments, and outcomes were recorded and analyzed. Four pediatric patients who presented with atypical gingival lesions were thoroughly examined for local and systemic signs and symptoms, and a detailed history was obtained. All relevant investigations led to a definitive diagnosis of oral tuberculous lesions. On the basis of the final diagnosis, antitubercular therapy (ATT) was started for all the pediatric patients, and outcomes were measured.

Results. All 4 patients responded very well to the treatment, with complete resolution of the lesions within 6 months after the initiation of ATT.

Conclusions. Health care professionals should rule out TB as one of the differential diagnoses in pediatric patients with atypical gingival lesions. ATT is strongly recommended for the treatment of oral TB to achieve good clinical outcomes. Rapid molecular tests based on nucleic amplification should be utilized for the diagnosis of TB in children and also for extrapulmonary TB because they are much faster and reliable compared with conventional methods. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128:508−514)

Tuberculosis (TB) has existed for millennia and still remains a global health problem. It is one of the most common chronic granulomatous infectious diseases and a major cause of death in developing countries. According to the World Health Organization report in 2017, it is the 9th leading cause of death worldwide and has been ranked even above HIV/AIDS as the leading cause of death in the past 5 years. India is one of the 14 countries on the list of high-burden countries for TB, TB/HIV, and multidrug-resistant TB. Globally, in 2016, there was an estimated 10.4 million cases of TB, and countries with the highest rates of TB incidence, in descending order, were India, Indonesia, China, the Philippines, and Pakistan, together accounting for 56% of the global incidence rate. India accounts for highest burden of TB, with an estimated incidence of approximately 2.79 million affected individuals and 0.4 million TB-related deaths reported in 2016.[1]

Susceptibility to TB in developing countries results from multiple variables, including poverty, economic recession, malnutrition, and multidrug resistance. Early detection and prompt treatment are crucial for the management of this highly infectious and communicable disease.[2] Oral manifestations of TB are uncommon; they are observed in 0.5% to 5% of the patients suffering from this disease.[3-5] Oral TB may be either primary or secondary.

In the primary form, the oral cavity is the initial site of infection as a result of direct inoculation of bacteria, whereas secondary orofacial TB arises subsequent to the spread of tuberculous infection from another site through the lymphatic and hematogenous routes. The secondary form is more commonly seen than the primary one.[5]

Oral TB is a frequent cause of missed or complicated diagnosis in general medical settings. The proper evaluation of various oral presentations of tuberculous infection, even in the absence of systemic signs and symptoms of pulmonary TB, can aid in the diagnosis of TB. Oral medicine specialists are at the frontline of the battle against TB and can make an important contribution to the control of this epidemic infection.[6] The present case series describes 4 pediatric cases of oral TB with gingival manifestations.

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CASE 1

A 13-year-old female presented with painless swelling of the gingiva in the upper left region, along with mobility of teeth and swelling of 2 months' duration on the left side of the neck. The patient also gave a history of self-exfoliation of the upper left maxillary first premolar 1 month ago, after which the swelling increased in size. There was no history of fever, weight loss, weakness, or loss of appetite. Medical and family histories were noncontributory.

Extraoral examination revealed left submandibular lymph node enlargement, approximately 3 × 3 cm in size, which was tender, mobile, and firm in consistency. There was no gross extraoral swelling, but on palpation, tenderness of the left maxillary region was observed. On intraoral examination, a multilobular, erythematous gingival enlargement was seen buccally to the depth of vestibule from the upper left canine to the second molar anteroposteriorly, extending palatally but not crossing the midline (Figure 1A). On palpation, the swelling was found to be nontender and firm in consistency. All teeth in the segment were grade 1 mobile. Another soft, nontender, smooth swelling was present in the upper labial vestibule in relation to the central incisors (Figure 1B). There was no active discharge of pus or blood.

Laboratory investigations revealed increased erythrocyte sedimentation rate (ESR; 38 mm/hr). A dose of 5 tuberculin units (0.1 mL) of purified protein derivative (PPD; RT23) was injected intradermally by using a 26-gauge needle, and values were read 48 hours later. A positive reaction measuring 15 × 11 mm was noted. Posteroanterior chest radiography revealed no abnormal findings. Computed tomography showed a moth-eaten appearance and involvement of the upper left maxilla. Fine-needle aspiration cytology from the left submandibular lymph node showed abundant granulomas, consisting of epithelioid cells, macrophages, and lymphocytes (Figure 1C). Focal areas of central necrosis were observed in some granulomas. Acid-fast positive bacilli (AFB) in clusters were noted, suggesting tuberculous lymphadenitis (Figure 1D). In view of these findings, a working diagnosis of primary tuberculous osteomyelitis was made. Subsequently, antitubercular therapy (ATT) was administered according to the Directly Observed Treatment, Short Course guidelines, with phase I (intensive phase) regimen, which included isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months. This was followed by phase II (continuation phase), which included isoniazid, rifampicin, and ethambutol for 4 months. Follow-up after 6 months showed complete resolution of the oral lesion and the left submandibular swelling (Figures 1E and 1F).

CASE 2

A 13-year-old female reported with painless swelling of the gingiva around her lower anterior teeth. The swelling had been present for 6 months, but there was no history of fever, weight loss, weakness, or loss of appetite. Family history revealed her elder sister being treated for gastrointestinal TB with an ATT regimen for the past 9 months.

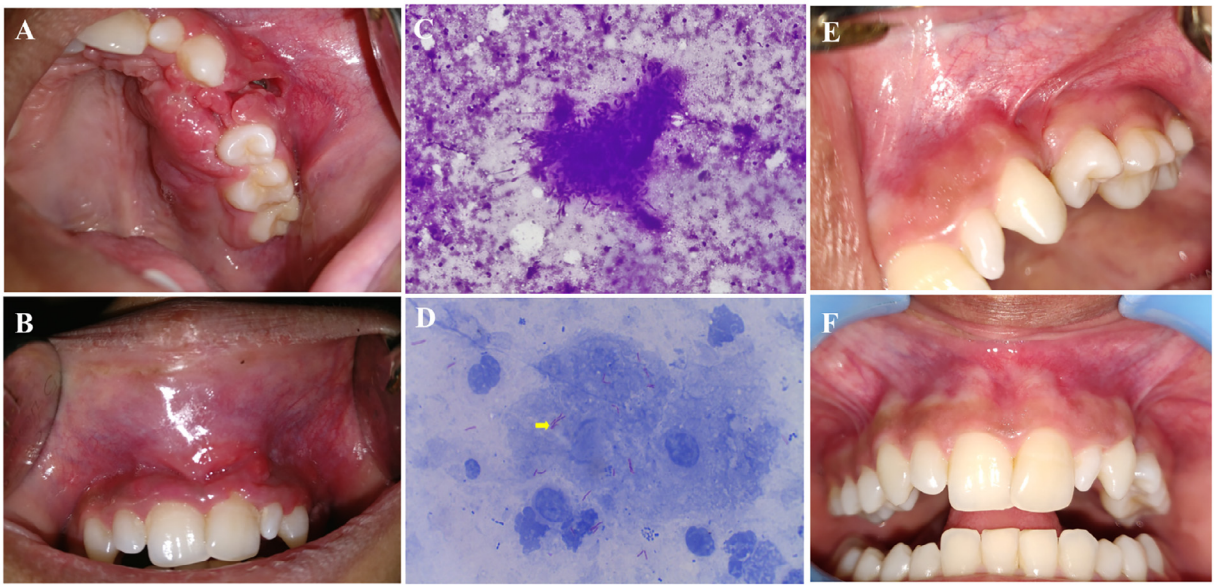

Fig. 1. **A, B,** Pretreatment intraoral photographs showing granulomatous gingival enlargement in left maxillary region and swelling in maxillary labial vestibule. **C,** Giemsa-stained microphotograph (× 40) showing epithelioid cell granuloma in a background of caseous necrosis. **D,** Ziehl-Neelson–stained microphotograph (× 100) showing acid-fast tuberculin bacilli *(yellow arrow)*. **E, F,** Post-treatment intraoral photographs showing complete resolution of lesion.

Extraoral examination showed bilateral submandibular lymph nodes being palpable, nontender, subcentimetric in size, mobile, and firm in consistency. Intraoral examination revealed hyperemic enlargement of the labial gingiva, lingual gingiva, and alveolar mucosa, in relation to the lower incisors and canines. Ulceration of the labial and lingual gingiva was also seen extending from the mandibular left to right canines (Figures 2A and 2B). The mandibular central incisors were grade 1 mobile, with severe amounts of deposits and calculus. Intraoral periapical radiography revealed interdental horizontal bone loss in relation to the central incisors (Figure 2D).

Laboratory investigations showed increased ESR (25 mm/hr). A dose of 5 tuberculin units (0.1 mL) of PPD RT23 was injected intradermally by using a 26-gauge needle, and values were read 48 hours later. A positive reaction measuring 22 × 20 mm was noted. Chest radiography showed bilateral, discrete, infiltrative lesions in the lungs, with prominent bronchovascular markings. Incisional biopsy was carried out in the gingiva around the mandibular central incisors, and analysis of the specimen revealed numerous ill-defined granulomatous aggregates in an inflammatory background. The granulomas showed Langhans and foreign-type giant cells (Figure 2C); AFB staining showed negative results. The cartridge-based nucleic acid amplification test (CB-NAAT) was positive for *Mycobacterium tuberculosis*. On the basis of this result, a confirmed diagnosis of secondary tuberculous gingival enlargement was made, and the patient was treated with ATT. ATT was initiated with phase I (intensive phase) regimen, which included isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months. This was followed by phase II (continuation phase), which included isoniazid, rifampicin, and ethambutol for 4 months. Following therapeutic regimen for 3 months, accompanied by scaling and root planing of mandibular teeth, there was remarkable resolution of the gingival lesions. Follow-up after 6 months showed complete resolution of the oral lesion (Figures 2E and 2F).

CASE 3

An 8-year-old female was referred with a chief complaint of nonhealing ulcer of 6 months' duration in the upper front gingival region . A diagnosis of drug-induced gingival enlargement was made because the patient had been taking phenytoin for epilepsy and she had undergone gingivectomy 4 months ago at the referring institution. Family history revealed that the patient's father had been treated for pulmonary TB 1 year ago.

On extraoral examination, the right submandibular lymph node was palpable, subcentrimetric in size, mobile, and tender. Intraoral examination revealed an erythematous lesion with a granular surface and sloughing in a few areas on the attached gingiva of the maxillary incisors, as well as multiple small sinuses and ulcerations with active pus discharge and bleeding on palpation (Figure 3A).

Laboratory investigations showed elevated ESR (25 mm/hr), A standard dose of 5 tuberculin units (0.1 mL) of PPD RT23 was injected intradermally by using a 26-gauge needle, and values were read 48 hours later. A positive

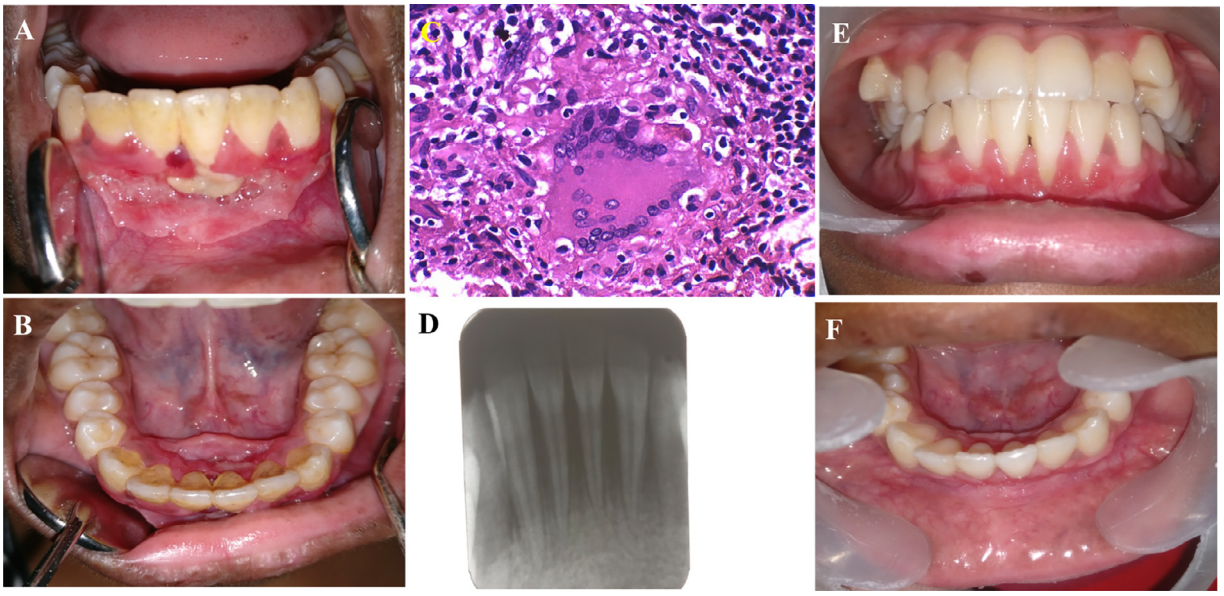

Fig. 2. **A, B,** Pretreatment intraoral photographs showing hyperemic enlargement of mandibular labial and lingual gingiva with ulceration. **C,** Hematoxylin and eosin (H&E)−stained photomicrograph (× 40) showing numerous ill-defined granulomatous aggregates in an inflammatory background. **D,** Intraoral periapical radiograph showing interdental horizontal bone loss in relation to central incisors. **E, F,** Post-treatment intraoral photographs showing complete resolution of lesion.

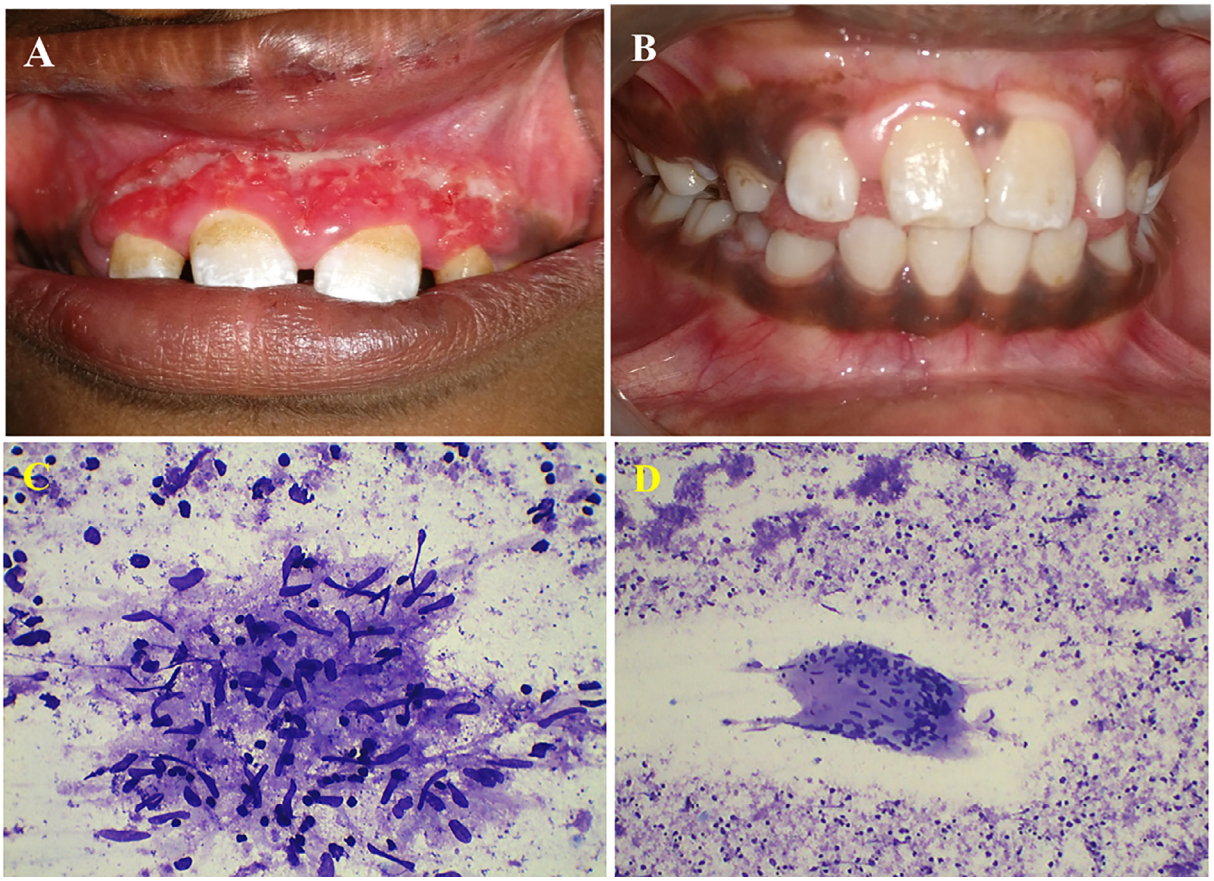

Fig. 3. **A,** Pretreatment intraoral photographs showing ulcerative lesion with pus discharge in maxillary labial gingiva and vestibular region. **B,** Post-treatment intraoral photographs showing complete resolution of lesion. **C, D,** Giemsa-stained photomicrograph showing granuloma with elongated epithelioid cells along with few aggregates of lymphocytes (**C,** × 40; **D,** × 10).

reaction measuring 35 × 28 mm was noted. Posteroanterior chest radiography revealed clear bilateral lung fields. A cytological smear was obtained from the lesions, which were suspected to be granulomatous lesions or epithelial dysplasia (Figures 3C and 3D).

CB-NAAT was performed and yielded a positive result for *M. tuberculosis*. On the basis of this finding, a confirmed diagnosis of primary TB of the gingiva was made, and the patient was administered ATT. ATT was initiated with phase I (intensive phase) regimen, which included isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months. This was followed by phase II (continuation phase), which included isoniazid, rifampicin, and ethambutol for 4 months. Complete resolution of the lesion was seen within 6 months after initiation of ATT (Figure 3B).

CASE 4

A 10-year-old female presented with gingival swelling of 2 years' duration. Initially, there was generalized gingival bleeding on slight provocation, which was insidious in onset. This was followed by enlargement of the gingiva around the mandibular and maxillary teeth. History revealed no fever, cough, weakness, and/or loss of appetite, but there was some loss of weight. There was a positive family history for TB, with the patient's grandfather having been treated for pulmonary TB.

Extraoral examination revealed bilateral submandibular lymphadenopathy. Intraoral examination showed generalized gingival enlargement of the marginal and interdental gingiva around the buccal surface of the mandibular and maxillary teeth and of the palatal gingiva around the maxillary teeth extending up to cervical one-third of the tooth surface (Figures 4A and 4B). The gingival surface was smooth, lobulated, deep red in color, firm, and slightly tender.

Laboratory investigations revealed an increased ESR (30 mm/hr). A dose of 5 tuberculin units (0.1 mL) of PPD RT23 was injected intradermally by using a 26-gauge needle, and values were read 48 hours later. A positive reaction measuring 12 × 16 mm was noted. Chest and panoramic radiography revealed no significant findings.

Fine-needle aspiration cytology from the submandibular lymph node revealed granulomas in a reactive background, but AFB staining result was negative and

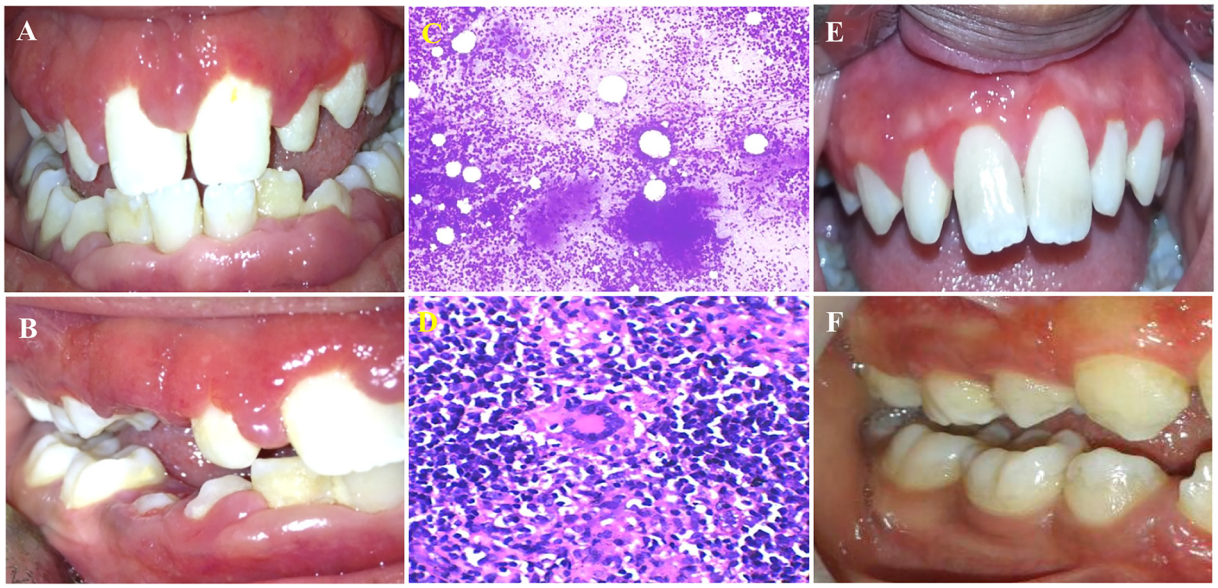

Fig. 4. **A, B,** Pretreatment intraoral photographs showing generalized gingival enlargement. **C,** Hematoxylin and eosin (H&E)−stained photomicrograph (× 10) showing abundant granulomas. **D,** Photomicrograph (× 40) showing Langhans giant cell in the center with epithelioid macrophages and lymphocytes. **E, F,** Post-treatment intraoral photographs showing complete resolution of lesion.

was suggestive of granulomatous lymphadenitis. Incisional biopsy of the mandibular anterior buccal gingiva was performed. Histopathologic examination revealed noncaseating granulomas with Langhans-type giant cells, plasma cells, lymphocytes, and epithelioid cells, suggestive of a granulomatous lesion, and AFB staining showed negative results (Figures 4C and 4D). Polymerase chain reaction was carried out to identify specific sequences of *M. tuberculosis*, and positive results confirmed the presence of *M. tuberculosis*. A final diagnosis of primary tuberculous gingival enlargement was made, and ATT was initiated with isoniazid, rifampicin, and pyrazinamide for 2 months, followed by isoniazid and rifampicin for the following 7 months. After completion of the 9-month regimen, and after waiting for another 2 months, gingivoplasty was performed to shape and contour the residual gingival enlargement. On subsequent follow-ups, remarkable healing was evident (Figure 4E and 4F).

DISCUSSION

TB is a chronic granulomatous infectious disease caused by *M. tuberculosis* and remains a major cause of morbidity and mortality in developing countries, especially in the Indian subcontinent. Although TB affects the lungs in the majority of cases, it can also affect other parts of the body, including the oral cavity.[7]

Oral manifestation of TB is a rare occurrence, reported in approximately 0.5% to 5% of all cases of TB. The primary form is rare and more commonly found in children and adolescents. It commonly involves the gingiva and is associated with regional lymphadenopathy. In contrast, the secondary form is more common in middle-aged and older patients.[8-10] Any site of the oral cavity and associated structures, such as the tongue (more common in the secondary form), palate, lips, oral mucosa, jaws, sinuses, and temporomandibular joint, can be involved.[11] The intact squamous epithelium of the oral cavity resists direct penetration by *M. tuberculosis*, and this explains the rarity of oral lesions in TB. This resistance may also be attributed to the thickness of the oral epithelium, the cleansing action of saliva, local pH, and antibodies in saliva.[12,13] In primary oral TB, the mode of entry of the organism may be through a break in the mucous membrane caused by mechanical insult or tears resulting from trauma, chronic irritation, and inflammation. Pre-existing periodontal disease may favor the localization of *M. tuberculosis*. Close contact with infected family members could also explain the primary infection seen in the 3 cases of the present series, where a positive family history was present. In secondary oral involvement, the bacilli can travel from the lungs via the lymphatic or hematogenous route.[5,14]

In countries with a high prevalence of TB (e.g., India), it is important to be aware of the different manifestations of oral TB. Its nonspecific presentation may pose difficulties in its early diagnosis and can result in further spread of the infection. Oral tuberculous lesions can present as ulcers, tuberculous fissures, papillomas, tuberculomas, and cold abscesses. Oral TB can involve different sites of the orofacial region, including the mandible, maxilla, lymph nodes, salivary glands, gingiva, and tongue (Table I). The nonspecific presentation of oral TB makes differential diagnosis difficult because it

Table I. Summary of clinical and follow-up details of all cases of oral tuberculosis in this case series

Case No.	*Sex/Age*	*Location*	*Family history*	*Blood profile*	*Mantoux test*	*Cytologic smear/ Histopathology*	*Radiographic examination*	*CB-NAAT/ PCR*	*Treatment*	*Follow-up duration (in months)*	*Clinical outcome*
1.	F/13	Maxillary gingiva and bone	Negative	Neutropenia, Raised ESR (38 mm/hr)	Positive (15 × 11 mm)	Abundant granulomas with AFB-positive bacilli	Chest radiograph - normal, CECT showed moth-eaten appearance in left maxilla region	Positive	Antitubercular therapy	24	Complete resolution
2.	F/13	Mandibular anterior gingiva	Positive—elder Sister (undergoing treatment)	Raised ESR (25 mm/hr)	Positive (22 × 20 mm)	Granulomas with Langhans and foreign body−type giant cells and negative AFB staining	IOPA radiography showed horizontal bone loss in lower central incisors Chest radiography showed bilateral discrete infiltrative lesions in lungs	Positive	Antitubercular therapy	16	Complete resolution
3.	F/8	Maxillary anterior gingiva	Positive—father (H/O pulmonary TB 1 year back)	Raised ESR (25 mm/hr)	Positive (35 × 28 mm)	Abundant granulomas with negative AFB staining	Chest radiography—normal	Positive	Antitubercular therapy	20	Complete resolution
4.	F/10	Generalized Gingiva	Positive—grandfather (H/O pulmonary TB 1 year back)	Raised ESR (30 mm/hr)	Positive (12 × 16 mm)	Abundant granulomas with negative AFB staining	Chest radiography—normal Panoramic radiography—normal	Positive	Antitubercular therapy and gingivoplasty	36	Complete resolution

AFB, acid-fast bacilli; *CB-NAAT,* cartridge-based nucleic acid amplification test; *CECT,* contrast-enhanced computed tomography; *ESR,* erythrocyte sedimentation rate; *H/O,* history of; *IOPA,* intraoral periapical; *PCR,* polymerase chain reaction; *TB,* tuberculosis.

can include such diseases as malignancies, syphilitic ulcers, traumatic or major aphthous ulcers, sarcoidosis, Wegner granulomatosis, and actinomycosis.

There is always a need for a rapid and sensitive test for early detection of *M. tuberculosis*, as culture techniques are complex and time-consuming. Also, sputum-based tests are unsuitable for detection of extrapulmonary and pediatric TB. Pediatric TB is paucibacillary in nature, and the yield of identifying TB bacilli with the use of the traditional method of sputum microscopy is very low.[14] In the present cases, *M. tuberculosis* DNA was detected with the help of CB-NAAT because it is known to be highly sensitive and specific compared with tissue culture techniques. CB-NAAT is a cartridge-based, fully automated nucleic acid amplification test for TB detection and rifampicin resistance testing, which can provide results in less than 2 hours compared with the turnaround time of 8 to 10 weeks with conventional drug-sensitivity testing. The Government of India's Revised National TB Control Programme is also currently using CB-NAAT to diagnose pulmonary TB, pediatric TB, extrapulmonary TB, rifampicin resistance, and multidrug-resistant TB in high-risk populations, such as HIV-positive individuals, as recommended by the World Health Organization in its 2013 policy recommendations.[15]

After the diagnosis of oral TB, patients should be treated with antitubercular drugs to achieve good clinical results before any surgical procedure is undertaken. In all of the cases presented here, patients were treated with ATT according to the Directly Observed Treatment Short-Course guidelines, with the phase I (intensive phase) regimen including isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months. This was followed by phase II (continuation phase), which included isoniazid, rifampicin, and ethambutol for 4 months. Although a 6-month treatment may be sufficient for many patients, each case should be assessed and extension of relevant treatment determined on an individual basis.

Tuberculous lesions in the oral cavity are a rare finding, usually indicative of underlying pulmonary TB.[16] The appropriate identification of oral TB is important not only for the patient but also for health care professionals and the community at large because the patient is a potential source of disease spread. Therefore, in all cases of oral cavity TB, even in the absence of any systemic signs and symptoms, pulmonary TB should be ruled out.

CONCLUSIONS

Tuberculous oral lesions are relatively rare and can be of primary or secondary origin. Clinicians need to be aware of this possibility and should consider TB in the differential diagnosis of gingival enlargement, persistent and atypical lesions of the oral cavity not responding to the conventional antibiotic, anti-inflammatory treatment, and mass lesions with unusual appearances. Through early detection and appropriate treatment or tuberculous oral lesions, dental clinicians can contribute to the control and spread of TB.

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