

# Primary Tuberculous Gingival Enlargement: A Rare Entity

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## ABSTRACT

With the advent of effective drug therapy, tuberculous lesions of the oral cavity have become so rare that they are frequently forgotten. Primary gingival tuberculosis is extremely rare and usually manifests as ulcer. We report the first case of primary tuberculosis manifesting as gingival enlargement, which was the only presenting sign of tuberculosis. Diagnosis was based on histopathology (hematoxylin and eosin staining), complete blood count, polymerase chain reaction assay and immunologic investigation with the detection of antibodies against *Mycobacterium tuberculosis*. The possibility of gingival enlargement due to drugs, leukemia, fungus and sarcoidosis was ruled out. Antituberculous therapy over 6 months was followed by surgical excision of the residual enlargement under local anesthesia. After 1-year follow-up there was no recurrence of the disease. This case emphasizes the need for dentists to include tuberculosis in the differential diagnosis of gingival enlargement so that they may play a role in its early detection.

**MeSH Key Words:** diagnosis, differential; tuberculosis, oral/diagnosis; tuberculosis, oral/drug therapy

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Tuberculosis is a chronic granulomatous infectious disease caused by *Mycobacterium tuberculosis*; it can affect any part of the body including the oral cavity. Extrapulmonary tuberculosis is rare, occurring in 10% to 15% of all cases.<sup>1</sup> Since the introduction of effective drug therapy, tuberculous lesions of the oral cavity have become so rare that this manifestation of the disease is often forgotten.<sup>2,3</sup> Oral tuberculosis can be primary or secondary. Primary oral tuberculous lesions are extremely rare and generally occur in young adults with associated caseation of the dependent lymph nodes; the lesion itself remains painless in most cases.<sup>4,5</sup> In contrast, secondary oral tuberculosis is seen in about

0.05% to 1.5% of cases and usually in older adults.<sup>6,7</sup> In oral tuberculosis, the most commonly affected site is the tongue; other sites include the lip, cheek, soft palate, uvula, gingiva and alveolar mucosa.<sup>8</sup> The lesions are seen as superficial ulcers,<sup>9,10</sup> patches,<sup>3</sup> indurated soft tissue lesions<sup>11</sup> or even lesions within the jaw in the form of tuberculous osteomyelitis.<sup>12</sup>

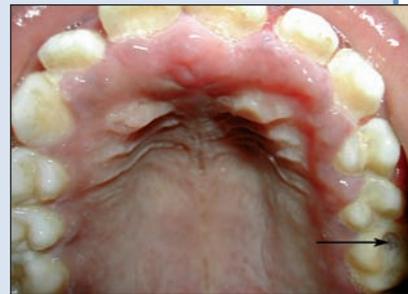
There have been no published reports of primary tuberculosis of the oral cavity manifesting as gingival enlargement. We report the first case of primary tuberculous gingival enlargement as an early presenting sign of tuberculosis, with no regional lymph node involvement and no evidence of systemic tuberculosis.



**Figure 1:** Diffuse enlargement of both arches and lobulated appearance of mandibular gingiva.



**Figure 2:** Diffuse enlargement of gingiva extending up to the second molar.



**Figure 3:** Gingival enlargement associated with carious maxillary left first molar.

### Case Report

A 10-year-old girl reported to the department of periodontics, Government Dental College and Hospital, Bangalore, with progressive, nonpainful swelling of the gingiva on the left side and the front of both arches of 6 months duration.

The patient had a history of rising temperature in the evening and weakness over the last 3 months. She had experienced loss of appetite over the last 4 months and a weight loss of about 4.5 kg during the last 8 months.

Her medical history revealed no systemic problems, no cough with expectoration, no history of dental trauma or any surgery in the affected area. The patient had not been treated for this condition. One of her nieces had been treated for tuberculosis 9 months previously.

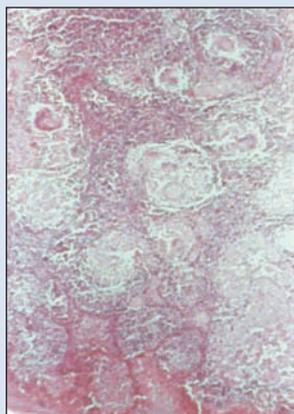
Extraoral examination revealed no significant cervical lymphadenopathy. Intraoral examination showed diffuse enlargement of upper and lower gingiva on the labiobuccal, palatal and lingual sides extending up to the second molar (Figs. 1 and 2). Surprisingly, the gingiva on the right side was not affected. On palpation, the swelling was slightly tender and firm. The rest of the oral cavity was normal; oral hygiene was fair, except for a deep caries in the upper left first molar (Fig. 3).

The initial clinical examination showed inflammatory gingival enlargement. The differential diagnosis included enlargement due to drugs (e.g., phenytoin, nifedipine, cyclosporine, etc.), infection (bacterial, fungal and viral) and hematologic malignancy, such as leukemia. The possibility of drug-induced enlargement was ruled out based on the medical history. Results of a complete blood count were within normal limits except for a marginal rise in leukocyte count ( $13 \times 10^9/L$ ) and an elevated erythrocyte sedimentation rate (ESR) of 56 mm/h (Westergren method), which ruled out leukemia-associated enlargement and raised the possibility of one of the commoner causes of high ESR, tuberculosis.

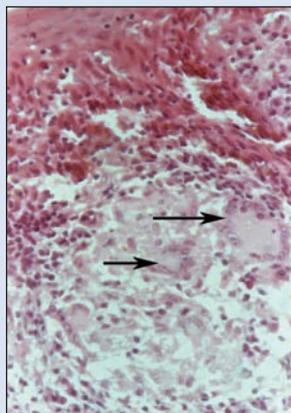
An incisional biopsy was performed on the upper labial gingiva in relation to the maxillary right central incisor. Histopathologic examination revealed clusters of epithelioid cells surrounded by a chronic inflammatory type of infiltrate. There was no evidence of caseating necrosis, but numerous Langhans-type giant cells were visible in the clusters of epithelioid cells suggestive of a “hard tubercle” (Figs. 4 and 5). To eliminate the possibility of localized granulomatous changes superimposed on an area of gingival enlargement, incisional biopsy was repeated in the remaining 3 quadrants. Histopathology showed similar granulomatous changes in all tissue specimens examined.

Microscopic examination raised the possibility of chronic granulomatous infection, including *M. tuberculosis*, fungal etiology or sarcoid granuloma. Sections stained with periodic acid-Schiff and Grocott-Gomori stains for bacteria and fungi were negative. Levels of serum calcium and angiotensin-converting enzyme were not elevated, which ruled out sarcoidosis. A tuberculin (Montoux) test was positive, suggesting tubercular infection. Chest radiography (posteroanterior view) revealed no abnormalities. Culture of sputum, obtained by forceful coughing, was negative for *M. tuberculosis*. Special staining of formalin-fixed, paraffin-embedded tissue specimens for mycobacteria, i.e., Ziehl-Neelsen and Auramine-Rhodamine stain, was negative. A fresh tissue sample from the enlarged gingiva was also cultured, but failed to show any signs of the *Mycobacterium*. An immunologic test to detect antibodies against *Mycobacterium* in the patient's serum (ELISA) was positive. In view of these findings, a working diagnosis of primary tuberculous gingival enlargement was made.

Polymerase chain reaction (PCR) assay was carried out using 6 5- $\mu$ m sections of paraffin-embedded tissue to identify specific sequences of *M. tuberculosis* complex, with adequate controls. DNA extraction and isolation were performed using standard protocols. The DNA was



**Figure 4:** Low-magnification micrograph showing numerous non-caseating granulomas.



**Figure 5:** Higher-magnification micrograph of granulomatous process with Langhan's giant cells and epithelioid cells.



**Figure 6:** Photograph showing no recurrence after 1-year follow-up.

used as an amplifying target for the sequence IS-6110, which is specific for *M. tuberculosis*. Positive PCR results confirmed the presence of *M. tuberculosis* in the tissue samples.

Thus the diagnosis of primary gingival tuberculosis was confirmed and, in consultation with a physician, anti-tubercular therapy was initiated with isoniazid (10 mg/kg body weight), rifampicin (10–20 mg/kg), pyrazinamide (20–35 mg/kg) and ethambutol (25 mg/kg) for 2 months followed by isoniazid (10 mg/kg) and rifampicin (10–20 mg/kg) for the following 4 months. During this period, the patient was instructed not to undergo any surgical procedure within the oral cavity and was warned about the chance of transmitting the disease to others via salivary contamination. Further, basic periodontal therapy, which included scaling and root planing, and oral hygiene were instituted. This resulted in significant regression of the enlarged gingivae in both arches. After completion of the 6-month regimen, gingivoplasty was performed to shape and contour the residual enlargement under universal aseptic conditions. No recurrence of the lesion occurred during 1-year follow-up (Fig. 6).

## Discussion

Tuberculosis remains the leading cause of death worldwide from a single infectious organism. Approximately 32% of the world's population is infected with tuberculosis and an estimated 2 million people die annually from this treatable disease.<sup>13</sup>

In the Indian population, the average prevalence of all forms of tuberculosis has been reported to be 5.05 per 1,000, the prevalence of smear-positive cases is 2.27 per 1,000 and the average annual incidence of smear-positive cases is 84 per million.<sup>14</sup>

Although oral tuberculosis has been well documented, tuberculous lesions of the upper aerodigestive tract have become rare. As a consequence, clinicians are not sensitized to the disease as part of a differential diagnosis, and there are undoubtedly patients in whom the correct diagnosis and therapy are delayed or missed entirely.

The mechanism of primary inoculation into the oral mucous membrane is not clearly understood. One reason for the rare occurrence of tuberculosis of the gingiva may be that the intact squamous epithelium of the oral cavity resists direct penetration by bacilli.<sup>9</sup> This resistance has been attributed to the thickness of the oral epithelium, the cleansing action of saliva, local pH and antibodies in saliva.<sup>1</sup> Even if the onset of infection is by hematogenous spread, injured or inflamed tissue tends to localize bloodborne bacteria. However, the mode of entry of the organism may be through a break in the mucous membrane caused by local trauma.<sup>15</sup> Where the infection involves bone, the mode of entry is thought to be through an extraction socket. However, there is general consensus that secondary tuberculosis spreads by a hematogenous route.<sup>16</sup>

This is the first case report of gingival tuberculosis appearing as diffuse gingival enlargement instead of the usual manifestation as an ulcer<sup>17</sup> or localized granular mass.<sup>18</sup> In our case, there was no neck node involvement secondary to the primary involvement. Pre-existing tuberculous infection in the periapical tissues of the carious maxillary left first molar might have spread to the gingival tissues hematogenously or through the inflamed gingival tissues (Fig. 3).<sup>19</sup> This view corresponds to that expressed by other researchers.<sup>16</sup> Tuberculosis is likely considered only when a histologic specimen reveals a granulomatous lesion. This granulomatous lesion would then lead

to consideration of other orofacial granulomatous conditions such as sarcoid, Crohn's disease, deep mycoses, cat-scratch disease, foreign-body reactions, tertiary syphilis and Melkersson-Rosenthal syndrome.

Diagnosis of oral tuberculosis is difficult as the clinical presentation may take various forms and the typical constitutional features are absent in most cases. In our case, a positive tuberculin test indicated previous exposure to tuberculosis bacilli. An immunological test for antibodies to *M. tuberculosis* was positive. However, anti-tubercular antibodies may occur in those who have been exposed to the organism; thus, this test is not considered to confirm a diagnosis of active disease.

Histopathologic examination and identification of the bacilli using special stains lead to presumption of a diagnosis of tuberculosis. But there is a need for rapid and sensitive detection of *M. tuberculosis* in tissue specimens, as culture techniques lack sensitivity, present technical difficulties and require a wait of 4–6 weeks for results.<sup>20</sup> Moreover, for patients in whom diagnosis depends on tissue examination rather than detection of *M. tuberculosis* in body secretions, DNA amplification would be useful for detecting *M. tuberculosis* in formalin-fixed, paraffin-embedded tissue samples.<sup>21</sup> Tuberculous granuloma that are negative for *M. tuberculosis* using culture techniques or special stains may be positive for its DNA. In the case presented here, a recently introduced, sophisticated technique, PCR, was used to detect this DNA, as it is known to be highly sensitive and specific compared with tissue culture techniques.<sup>22</sup> It is known to detect DNA even when only a few genomes are present.<sup>21</sup> The working diagnosis of tuberculous gingival enlargement based on the histopathologic examination was thus confirmed by PCR.

## Conclusions

Tuberculosis infection of the gingivae is relatively rare; oral lesions would most commonly be secondary to pulmonary tuberculosis. Hence, to characterize oral lesions as primary tuberculosis, a thorough examination to rule out other primary sites should be attempted. With the recent increase in the incidence of tuberculosis, clinicians need to be aware of this possibility, consider tuberculosis in the differential diagnosis of gingival enlargement and, thus, play a role in the early detection of this disease. ♦

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