

Primary Tuberculous Osteomyelitis of Jaw-A Case Report of 7 Year Old Child

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ABSTRACT: Tuberculosis is a chronic granulomatous disease caused by bacilli *Mycobacterium tuberculosis*. TB is life-threatening disease in developing countries like India. Worldwide TB is the 13th leading cause of death and the second leading infectious killer after covid-19. In 2022, an estimated of 10 million people fell ill with Tuberculous (TB) worldwide. In 2020, 30 high TB burden countries accounted for 86% of new TB cases. Eight countries account for two-thirds of the total, with India leading the count, followed by China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh and South Africa. Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. Only about one in three people with drug-resistant TB accessed treatment in 2020. Globally TB incidence is falling at about 2% per year and between 2015 and 2020 the cumulative reduction was 11%. This was over halfway to the end TB Strategy milestone of 20% reduction between 2015 and 2020. Oral TB is a rare phenomenon with an incidence of 1.4% and is seen in 5% of total TB cases. About less than 2% of oral TB present as osteomyelitis of mandible. Subclinical TB is a disease that occurs due to viable *M. tuberculosis* bacteria that do not cause clinical TB-related symptoms but causes other abnormalities that can be detected using existing radiologic or microbiologic assays and hence the diagnosis of extrapulmonary TB remains demanding, World TB day is on March 24 to honor Dr. Robert Koch discovery of *M. tuberculosis*. This case report explains the most common yet rare clinical presentation of Tuberculosis.

Keywords: Primary Tuberculosis, Juvenile Tuberculosis, Osteolytic lesion of mandible, Tuberculous Osteomyelitis, Extra Pulmonary Tuberculosis.

INTRODUCTION

Tuberculosis is a systemic disease caused by *Mycobacterium tuberculosis*. It affects the pulmonary (primary TB), extrapulmonary (secondary) sites. Oral Tuberculous lesion is usually secondary to pulmonary involvement (Neville *et al.*, 2016). Oral TB is a rare lesion for the following reasons, the presence of intact stratified squamous epithelium restricts the penetration of *Tubercle bacilli* into the connective tissue, the rinsing action of saliva, antimicrobial factors, enzymes in saliva along with alteration in the local pH causing the unfavourable environment for bacterial colonization (Gupta *et al.*, 2015). However, certain systemic factors that favour chances of oral infection in TB include 1. Lowered host resistance, 2. Increased virulence of the organism, 3. Local trauma and pre-existing conditions such as leukoplakia, periapical granuloma, cysts, abscesses, periodontitis, extracted tooth sockets and jaw fractures (Neville *et al.*, 2015).

PATIENT INFORMATION

A 7-year-old girl reported to the department of oral medicine and radiology with the chief complaint of swelling in her left side of the face for the past one month. The swelling was sudden in onset and insidious in growth started as a small swelling and gradually increased in size to reach the present state. Patient's mother also gave history of visiting a local dentist for the same complaint, for which he prescribed antibiotics and analgesics and suggested removal of decayed tooth for which she was negligent, after a while when the swelling increased in size and when it started to associate with discharge of pus through the skin of the face, the mother visited the dentist, extraction was performed, yet the swelling did not regress hence the patient was brought to our department.

On extra oral examination a diffuse swelling of approximately 3×4 cm in size was noted in left side of the face extending anteroposteriorly from para

symphysis region to the angle of mandible (Fig. 1 and 2), superoinferiorly from the zygomatic inferior border of mandible extending into the submandibular region. The skin appears erythematous with evidence of pus discharge. Left submandibular lymph nodes were palpable, firm, tender, mobile and skin over node was pinchable. On intra oral examination, a swelling was noted in relation to 34,35 region with obliteration of buccal sulcus in relation to 34, 35 region and raised floor of the mouth with surface ulceration on linguogingival aspect of 36 (Fig.3). There was also presence of bone exposure on the buccogingival aspect of 36, no evidence of any discharge intraorally. Hard tissue examination revealed evidence of eruption of 34,35, root stump in relation to 84,54,64. Based on the age of the patient, history of presenting illness, past dental history, extra oral and intra oral examination a provisional diagnosis of Garre's osteomyelitis was given. Following the provisional diagnosis, an IOPA (Fig. 4) and Occlusal (Fig.5), OPG (Fig. 6) were taken which revealed ill-defined radiolucency extending from 73 (distal aspect) to 36 (distal aspect), buccal cortical plate expansion with periosteal reaction (presenting as a thin radiopaque line parallel to the buccal cortex). Owing to the wide extension of lesion in the radiograph, the history was revisited during which patient's mother confounded that all the presentation had been there for about 3 months. CBCT was taken considering the involvement of bone lesion, cortical expansion and periosteal reaction.



Fig. 1 and 2. A diffuse swelling of approximately 3*4 cm in size was noted in left side of the face.



Fig. 3. 34, 35 region and raised floor of the mouth with surface ulceration.

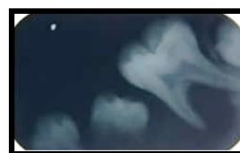


Fig. 4



Fig. 5.

Fig. 4 and 5. Occlusal radiograph revealed bi-cortical expansion.



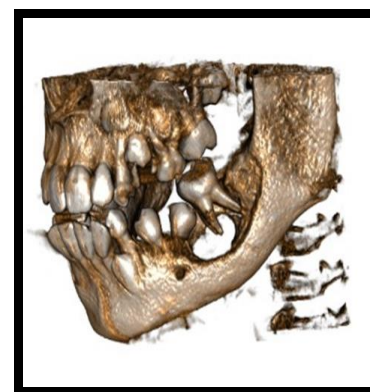
Fig. 6. OPG revealed Diffuse radiolucency from the distal of 73 with intense radiolucency surrounding the mesial root of 75.



(A)



(B)



(C)

Fig. 7A. shows axial section of mandible at the level of middle third of the tooth revealed an Osteolytic lesion extending from the erupting 35, extending anteroposteriorly from distal aspect of 73 to distal root of 36, superoinferiorly from alveolar mucosa to 0.5cm above the inferior border of mandible with effacement of buccal cortical plate with periosteal reaction and widening of inferior alveolar nerve. Fig. 7B shows sagittal section of left mandible showing osteolysis with root resorption of 36. Fig. 7C shows 3D reconstruction of mandible.

The following are the radiographic differential diagnosis that were suggested. Considering the age, duration of the swelling, extent of the lesion, radiographic presentation Ewings Sarcoma, Central

Hemangioma, Osteosarcoma, Eosinophilic Granuloma and Lymphoma of mandible were ruled out through USG, FNAC and incisional biopsy. Complete blood investigation revealed neutrophilia.

Further probing into the history as sarcoma was included, the patient mother reluctantly expressed that the presenting complaints was there for more than a year thereby we further narrowed the differentials into eosinophilic granuloma and also included Tuberculous osteomyelitis in the differential diagnosis taking into account the duration of history, clinical/ radiographic presentation, history of tuberculosis in the family.



Fig. 8. Mantoux test was positive with 15 mm.

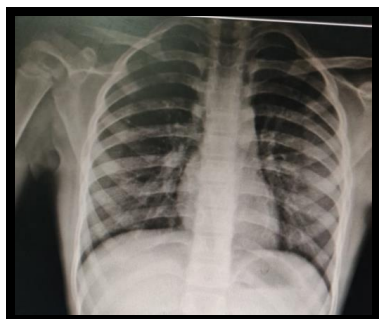


Fig. 9. Chest Xray appears to be normal.

Intraoral biopsy was performed. Specimen was subjected to immunohistochemistry to rule out the radiological differential diagnosis with specific tumor markers (CD99, CD45, CD65, CD20, CD3, S100, CD1A). All were negative and reported as granulomatous lesion gene Xpert was found to be positive. Considering the family history, clinical presentation, radiological investigations, histopathological investigations the final diagnosis of Tuberculous Osteomyelitis of mandible was proposed. Under pulmonology opinion and care, antitubercular drugs which includes isoniazid 50 mg, rifampicin 75mg, ethambutol 400 mg, were prescribed. Patient is still under follow up. At the 3rd month post treatment patient showed reduction in the size of swelling and erupting 34, 35 (Fig. 10 and 11). At 6th month follow up OPG revealed reduction in the radiolucency at the site of lesion suggesting new bone formation (Fig. 12). Review after 12 months CBCT was taken. Axial section and sagittal section at the level of middle third of the tooth showed intact lingual cortical plate with new bone formation and eruption of 34, 35 (Fig. 13 A and 13 B).

POST TREATMENT



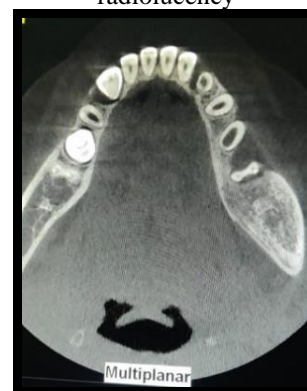
Fig. 10. Reduction in size of swelling.



Fig. 11. Erupting 34, 35.



Fig. 12. OPG revealed decrease in size of the radiolucency



(A)



(B)

Fig. 13.A and B. CBCT revealed showed intact lingual cortical plate with new bone formation and eruption of 34, 35.

DISCUSSION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis*. The rate of infection based on race, geographical environment differs. Based on that the rate of infection in Hispanics, blacks, and Asians was respectively 7.6%, 8.4%, and 21.2% higher than in whites respectively. Immigration of people from developing countries resulted in transmission of endemic infectious diseases. Despite the dramatic improvement in the public health measures to control this infectious disease there is no significant decline in the incidence of it. Most infections are the result of direct person-to-person spread through airborne droplets from a patient with active disease (WHO 2004). Subclinical TB comprises a large fraction of prevalent disease at the population level, has meaningful infectious potential, follows a heterogeneous clinical trajectory, and is difficult to diagnose using passive systems Kendall *et al.* (2021).

The primary site of infection is lungs and they are caused by air borne droplets transmission from the infected individual. The infection must be distinguished from the active disease, about 5% of the infection progress into active disease. Current estimates suggest that about one-third of the world population has latent TB (WHO, 2004). In about 95% of cases, after about 3 weeks of uninhibited growth, the immune system suppresses bacillary replication, usually before symptoms or signs develop (Grover and Takkar 2008). The smallest particles (1-5 μm) enters the lung and are engulfed by macrophages. In response to antigen presentation CD4, T lymphocytes produce an array of cytokines including interferon resulting in formation of granulomas which displace central caseous necrosis. The formation of granuloma leads to the appearance of primary lesion Ghon's Focus. If bacilli spreads through lymph/blood it forms the secondary foci in other organs such as TB-Lymph Adenitis/Scrofula, TB-Osteomyelitis, involving spine called Potts disease, liver, kidney, nails called Lupus Vulgaris (WHO, 2004).

Multiple foci of infection that are disseminated through vascular supply appearing as millet seeds in radiographic examination termed as *Miliary Tuberculosis*. The term consumption is used when the disease is progressive and wasting syndrome is noted. Oro facial presentation of tuberculosis disease involves swelling, pain, loosening of teeth, displacement of tooth bud, ulcer, involvement in salivary gland, TMJ. Occurrence of TB in the oral cavity is less than 2% in which occurrence in the mandibular jaw is the rarest form, here we discussed one such rarest form of TB.

In our case, the patient never had any other routine symptoms of TB that could lead to differential diagnosis of Tuberculous osteomyelitis. On repeated revisit to the history along with multi-investigatory procedure lead to the diagnosis of TB osteomyelitis but there was lot of pressure and anxiety for the parents until diagnosed. The diagnosis was given following the histopathological examination ruling off other differential diagnosis already discussed.

Most of the cases of Tuberculosis of maxillofacial bones are secondary to pulmonary tuberculosis. However, in our case there is no clinical and radiographic evidence of pulmonary involvement which is similar to the case reported by Kamath *et al.* (2015) and primary orofacial TB could be due to the self-inoculation or hematogenous spread to the extraction site (Mignogna *et al.*, 2000). Detecting subclinical TB provides an opportunity to provide care early in the disease history, which should benefit individuals by preventing extensive lung damage and the risk of post-TB sequelae and benefit society by interrupting transmission (Frascella *et al.*, 2020). Extrapulmonary tuberculosis is observed more frequently in children compared with adults because the risk of lymphohematogenic spread is high, especially in young children, the sensitivity of diagnostic tests is low in pediatric patients, and tuberculosis may mimic many other disease entities. It is recommended that treatment should be initiated after the assessment of clinical and radiologic findings together when it is not possible to prove the disease through laboratory findings (Kaba *et al.*, 2019).

An extensive investigation is required to confirm the diagnosis of Tuberculosis specially when it involves extra pulmonary organs. The traditional diagnostic method involves symptom screening, the sensitivity for TB in prolonged cough more than 2 weeks has sensitivity of 24% and specificity was 96% (Fatima *et al.*, 2020). The main drawback of symptom screening is its poor sensitivity. The chest x-ray is always a part of TB diagnosis, yet the sensitivity is offset by poor specificity. Therefore, when certain chest x-ray findings can be indicative of tuberculosis, it remains insensitive and nonspecific test (Fatima *et al.*, 2020). Culturing the organism and subjecting it for the drug sensitivity is done to detect the antibiotic inhibiting the growth of the organism by 99%. The multi-drug resistance TB were detected using this method. Apart from the traditional method of investigating new diagnostics were introduced to detect the presence of TB in the affected individual. The tuberculin skin test (TST) has been used to detect latent Tuberculosis. In BCG vaccinated population, the standard recommendation by Revised National Tuberculosis Program (RNTPC) guidelines 10 mm of induration of PPD-RT 23 is considered positive (Grover and Takkar 2008). Interferon gamma release assays (IGRAs) were developed to find more specific test that would not contain antigens from Bacilli-Calmette- Guerin (BCG). IGRA have been specifically employed for diagnosing latent TB infection (Dutta and Karakousis 2014). However, they are also employed in assessing active TB. Isolated blood mononuclear cells is used to test T – SPOT. TB which has sensitivity of 83% and specificity of 61%. In another test called QuantiFERON- TB Gold In- Tube (QFT-GIT) uses the whole blood, it has sensitivity of 69% and specificity of 52% (Fatima *et al.*, 2020).

The sensitivity and specificity of Xpert study using sputum sample is 89 % and 99% respectively. Our patient was also subjected to Xpert and turned out to be positive. Other test includes PCR (Polymerase Chain

Reaction), Colorimetric redox indicator (CRI), nitrate reductase assay (NRA), microscopic observation drug susceptibility (MODS). Technologies like bacteriophage assay and Loop Isothermal Amplification (LAMP) are under the process recommendation from WHO (Fatima *et al.*, 2020). However, unfortunately the catastrophic costs faced by the families of TB patients according to the results of 23 national surveys ranged from 13% to 92%, on total of more than 20% of their income (WHO 2004). Identifying TB and planning the treatment at the earliest has been aided by the new laboratory technologies. In our patient, irrespective of various other differential diagnosis the extensive laboratory and the histopathological examination revealed the confirmatory diagnosis of TB Osteomyelitis at the earliest possible. Taking all the side effects of the drugs into account and after assessing the ophthalmology examination our patient was given ATT under DOTS (Directly Observed Treatment, Short – Course)

According to the literature the first line of drugs for Tuberculosis is Rifampin 10mg/kg/day, Pyrazinamide 25mg/kg/day, Isoniazid 5mg/kg/day and Ethambutol 15-20mg/kg/day. The second line of treatment included Kanamycin, Amikacin, Streptomycin, Levofloxacin. For multi drug resistance tuberculosis the drug of choice would be Bedaquilin, Linezolid, Delamanid, Pretomanid and for latent Tuberculosis isoniazid monotherapy for 9 months is suggested in 90% of patients (Grover and Takkar 2008).

CONCLUSIONS

Tuberculosis, though the most common infectious disease among the developing low socio economic status population, its varying presentation is quite challenging for the physician to identify and treat at the earliest possible. Hence, regular updates and adequate knowledge on its presentation and the development of advanced technologies to diagnose this disease is essential for all the physicians. Diagnosis of extra pulmonary tuber was hampered due to the absence of a history of TB exposure in the majority of cases, and to a lower sensitivity of TST.

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Conflic of Interest. None.

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