CASE REPORT

Primary tuberculous osteomyelitis of the mandible in a 3-year-old child

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SUMMARY

A 3-year-old girl child presented with swelling in her right lower jaw that had started 5 days previously. History revealed the child being non-immunised. Initial evaluation revealed proptosis and bony hard swelling over the right body of the mandible. Radiological evaluation including a CT scan indicated expansile osteolytic lesion involving the body-ramus with onion-peel periosteal reaction suggesting osteomyelitis/malignancy. Blood investigations showed raised erythrocyte sedimentation rate and eosinophilia. Family screening for tuberculosis (TB) revealed that the patient, her father and siblings were PPD positive though chest screening and sputum examinations were negative in all of them. Lesion biopsy showed acute/chronic osteomyelitis with eosinophilia, tilting diagnosis towards eosinophilic granuloma/Hand–Schüller–Christian disease. Further investigations for diabetes insipidus, histiocytosis-X, skull–pelvis–femur radiographs, abdominal ultrasonography, ophthalmic consultation and PCR-TB test were negative. Histology, radiography, purified protein derivative (PPD)-positive result and history led to the diagnosis of primary TB of the mandible. Complete resolution occurred following antitubercular therapy. The case report emphasises that diagnosis of TB can sometimes be based on circumstantial evidence and positive response to antitubercular therapy even in view of a negative PCR result.

BACKGROUND

Tuberculosis (TB) is an infectious granulomatous disease with *Mycobacterium tuberculosis*, bovis and atypical mycobacterium being the cause of disease in humans.¹ The primary form of TB affects the lungs whereas the secondary forms affect the extrapulmonary sites.¹ Oral TB is a rare phenomenon with an incidence of 1.4%; Morgagni (1761) first reported on oral TB involving the tongue.² Common sites of oral TB is the tongue with other sites such as the palate, gingiva and floor of mouth are also involved and seen in 5% of total TB cases.^{3–4} Tuberculous osteomyelitis of the mandible is a rare phenomenon observed in <2% of skeletal TB.⁵ Two forms of oral TB occur namely the primary form and the secondary form.

Commonly seen oral lesions are usually a secondary form of tuberculous infection (secondary to primaries in lungs). The source of secondary lesions in oral cavity is due to haematogenous spread or spread of bacilli from one's sputum in infected people. The primary form of oral tuberculous lesion is even rarer. Primary oral tubercular lesions are differentiated from secondary oral tubercular

lesions in that there is no pulmonary involvement making diagnosis very difficult.⁶ Patients always have a classical history related to TB in secondary oral TB which is absent in primary oral TB.

We report an unusual case of primary oral TB involving the mandible in a child. Also, because of absence of classical signs of diagnostics, only a tentative diagnosis of TB could be assumed and later confirmed only after successful treatment with anti-tubercular/anti-Koch's therapy.

CASE PRESENTATION

A 3-year-old girl child was referred to us for evaluation of a swelling involving the right side of the mandible (figure 1). Her guardian reportedly had noticed the swelling just 5 days before. The swelling was abrupt in onset and had not changed much in overall dimensions. There was no associated toothache, pain, fever or swelling anywhere else in the body. History did not reveal any possible contact with Koch's infection. She had no prior medical and family history of treatment for any chronic infective disease. The patient was not immunised since birth. The patient was conscious, cooperative, alert and afebrile. She was thinly built and moderately nourished. The child's height and weight were <1 standard deviate centile based on a standard chart for the local population. Vital signs on the day of examination were within normal limits.

Extraoral swelling was seen in lower one-third of face which was diffuse (mandibular body region), with no tenderness or local rise in temperature. There was bilateral subcentimetric submandibular lymphadenopathy.

Local examination revealed a diffuse swelling over the right body of the mandible which was

Figure 1 Frontal and side profile photographs showing diffuse swelling over the right cheek and body of the mandible with overlying skin normal.

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Figure 2 Intraoral photograph of the mandibular right quadrant and vestibule showing no evidence of caries or swelling/cortical expansion.

bony hard, fixed to the underlying bone, non-tender with mild local rise in temperature. There was slight obliteration of vestibular space in the region of tooth 46. No odontogenic foci of infection were noted (figure 2). Regional teeth showed no tenderness to percussion or pathological mobility.

Intraoral periapical (IOPA) and intraoral occlusal radiographs and orthopantomography (OPG) were advised.

IOPA radiograph showed a crypt of tooth 46 seemingly destroyed in the anteroinferior aspect with the developing tooth drifted distally. Some amount of rarefaction was seen in apices of 85 suggestive of external root resorption. Mandibular occlusal view showed sclerosing osteitis and onion-peel appearance of the mandible.

OPG findings showed an ill-defined radiolucent osteolytic lesion involving the right body and ramus of the mandible,

Figure 3 Intraoral periapical radiograph showing crypt of first permanent molar seemingly destroyed in the anteroinferior region with the developing tooth drifted superiorly.

Figure 4 Orthopantomography showing ill-defined radiolucent osteolytic lesion involving the right body, inferior alveolar canal, basal bone, ramus of mandible and, extending superiorly up to neck of the condyle and sigmoid notch.

extending superiorly to the neck of the condyle and approximating the deepest portion of the sigmoid notch, distally approximating the superior third of the posterior border of the ramus with distal expansion of the cortex in the region, anteriorly 1 cm from the coronoid notch, inferiorly superimposing the inferior alveolar canal and involving the basal bone in relation to tooth 46, 85 and 84. An onion-peel appearance of the inferior cortex is noted in relation to these teeth with a few ill-defined radiolucencies. Sclerosing osteitis was seen just apical to 85. The crypt of developing 46 was destroyed in the anteroinferior region and is superiorly drifted. There was increased anteroposterior dimension of the ramus as compared to the contralateral side (figures 3–5).

Figure 5 Mandibular occlusal view showing sclerosing osteitis and onion-peel appearance of the mandible.

Figure 6 CT scan axial image showing cystic lesion causing expansion of the right condyle and ramus with cortical breaks both buccally and lingually.

To ascertain the pathology, a CT scan was advised. The CT scan revealed an expansile multilocular cystic lesion in the right ramus and body region with cortical breaks at places. Sequestrum was also noted suggesting osteomyelitis (figures 6–9).

Plane and postcontrast CT MANDible was performed as there was a multilocular cystic lesion involving the coronoid process, ramus and body of the mandible on the right side, causing expansion of the involved bone predominantly along the lateral aspect. The overlying cortex was thinned out with cortical breaks at places. A hyperdense lesion was seen within the cystic lesion suggesting sequestrum. The CT scan findings were most probably suggestive of osteomyelitis.

PROVISIONAL DIAGNOSIS

Based on the history, clinical and radiological examination a provisional diagnosis of tuberculous osteomyelitis of the mandible was given, while differential diagnosis of bone malignancies such as osteosarcoma or Ewing's sarcoma were thought of.

INVESTIGATIONS

Before starting with a systemic evaluation, an incisional biopsy was performed under proper anaesthesia. The histopathological evaluation revealed aggregates of foam cells with plasma cell eosinophils and multinucleated giant cells some with peripheral distribution of nuclei. The overall histopathological features were pointing towards either tuberculous osteomyelitis or Langerhan's cell disease. The immune markers S-100 and CD1a

for Langerhan's cell disease and PCR-TB tests were conducted and both came out negative.

On consultation with the paediatric department, the patient was admitted for evaluation of general health status and for investigations to rule out TB. Evaluation of the health status revealed that the patient had exophthalmoses and was suffering from grade III protein energy malnutrition. Considering that the patient had exophthalmia with lytic jaw lesions with histopathology suggesting Langerhan's disease, a possible triad of eosinophilic granuloma, diabetes insipidus and exophthalmoses also had to be ruled out. Family screening for TB revealed that the patient together with two siblings and father were positive for PPD (each >10 mm/hour) while the chest screening was negative for pulmonary infection. Sputum for acid-fast bacillus (AFB) was negative in all. Routine blood investigations were within normal limits except for leucocytosis, but showed raised erythrocyte sedimentation rate (ESR) (47 mm/hour) and low haemoglobin (8 g/dL). The 24 hour urine output was normal suggesting absence of diabetes insipidus. The abdominal ultrasound scan and skull and pelvic radiographic examinations were normal. Ophthalmology evaluation revealed that the proptosis was physiological but the parents were advised to look for increase in proptosis, congestion of eyes or inability to close eyes in the future. Meanwhile, the incisional biopsy specimen was investigated for immune-marker S-100 and CD1a to rule out eosinophilic granuloma and PCR for TB. Both investigations were negative.

Figure 7 CT scan axial image showing multilocular cystic lesion involving the right ramus with a hyperdense lesion within suggesting a sequestrum.

Figure 8 CT scan axial image showing multilocular cystic lesion involving the right body of the mandible with cortical expansion and breaks buccally.

CONFIRMATORY DIAGNOSIS

Based on the histopathology which revealed osteomyelitis, periosteal reaction and sequestrum were seen on radiographs, CT scan and, the patient being positive for PPD with raised ESR, a final diagnosis of primary tuberculous osteomyelitis of the lower jaw was made.

TREATMENT AND FOLLOW-UP

On consultation with the paediatric and orthopaedic departments, anti-Koch's therapy (AKT) was started (category I: H3R3Z3E3+4H3R3). The patient was advised to continue antitubercular therapy for 1 year. Depending on the response it was considered that the therapy should be continued even after a year, until complete clinical and radiographic resolution of the swelling was observed (figures 10 and 11). Over the course of therapy, the patient gained 3 kg weight and the swelling gradually reduced in dimension. Sequential radiographic evaluations at 4, 8 and 12 months revealed resolution of the lesion,

reduction in the periosteal reaction, healing of the crypt around the developing permanent first molar and normal development of the second premolar crypt.

DISCUSSION

Following advancements in chemotherapeutic agents and improvement in healthcare, there is reduction in number of cases of TB; however, recently TB is re-emerging because of reasons such as (1) increased epidemicity of HIV infection, (2) discontinuation of drugs by the patients before complete remission, (3) involvement of multidrug resistant bacteria and (4) lack of enough public health efforts to completely eliminate TB.⁷

As per the WHO Global Report-2011, in 2010, 8.8 million incident cases were established with 1.1 million deaths among HIV negative cases and an additional 0.35 million deaths among people who were HIV positive. India is second most populous country and has more new TB cases annually than any country. In 2009, 2 million cases were estimated in India out of the estimated global annual incidence of 9.4 million cases of TB, thus adding one-fifth of total global burden.⁸

In particular as HIV has become a pandemic, cases of TB has seen a resurgence as TB is one of the most commonest secondary infection following immunodeficiency in these patients. With paediatric HIV cases also increasing globally, the burden to prevent the disease is increasing.⁹ The patient was tested for HIV to check for any association but test result was negative.

Figure 9 Sequestrum within the expansile lesion in the right ramus.

Figure 10 Facial view showing good resolution 12 months after anti-Koch's therapy.

Figure 11 Radiographic view 12 months after anti-Koch's therapy showing signs of resolution and reduction in periosteal reaction, healing of crypt around developing permanent first molar and normal development of second premolar crypt.

The primary form of TB usually involves the lung through inhalational route, and later spreads to lymph nodes. Usually the initial lesions heal; however, in certain individuals the tubercle bacilli may remain dormant. Following any immune suppression, the bacilli may get reactivated and spread to other parts of body through the haematogenous route causing multiorgan involvement (miliary TB). These lesions are referred to as secondary form of TB. Secondary forms of TB are always accompanied or easily diagnosed due to presence of primary lesions in the lung or its associated lymph nodes.^{3 4}

Oral TB is very rare as low as 1.4%. Oral TB that is commonly seen in patients is a secondary form of TB, where the bacilli present in expectorated sputum from the patient can involve the oral cavity or the upper gastrointestinal/respiratory tract. Secondary TB is more common in adults or geriatric cases. The lesions of primary oral TB generally occur in younger patients.^{3 4 8} TB in the young has dissimilar characteristics from those of the secondary form of TB seen in adults. In present case we report primary TB of the oral cavity as there was no presence of lung lesion as chest screening and sputum analysis for AFB were both negative.

Oral TB is a rare lesion because of following reasons (1) the presence of intact stratified squamous epithelium resists the penetration of tubercle bacilli into the connective tissues, (2) rinsing action of saliva, (3) presence of antimicrobial factors in saliva, (4) presence of salivary enzymes, (5) local pH alteration causing unfavourable environment for bacterial multiplication and (6) competition from oral saprophytes for colonisation. However, certain systemic factors that favour chances of oral infection in TB include: (1) lowered host resistance, (2) increased virulence of organism, (3) local trauma and (4) pre-existing conditions such as leukoplakia, periapical granuloma, cysts, abscesses, periodontitis, extracted sockets and jaw fractures.^{6 10} In this case, the child neither had any of the oral problems which can act as nidus for penetration/localisation of bacilli nor primaries in the lungs for haematogenous spread; hence, the source of bacilli into bone can only be speculated.

One of the commonest areas of involvement is the tongue although there is involvement of other tissues such as gingiva, palate, maxillary and mandibular bone, temporomandibular joint and salivary glands.^{4 6 11} Theoretically involvement of the mandible is extremely rare as it contains less cancellous bone. However, the mandible is more commonly involved than maxillary, with alveolus and angle of mandible being the commonly involved areas.^{12 13}

Oral TB as reported by authors differ in presentations varying from superficial ulcers, patches, indurated soft tissue masses, granulomas, secondary displacement of tooth buds or non-specific involvement of jaws.¹⁰ TB of the jaws can cause gradual

necrosis of the local osseous tissue and might progress to involve whole jaw. Presentation of tuberculous involvement of jaws varies from periodontitis with horizontal bone loss, apical osteitis and widespread destructive lesions which may be misinterpreted for routine dental abscesses. Sequestration may also be noticed. Pathological fracture of bone is also reported.¹⁴ In the present case we could see sequestration and unilocular destructive bony lesion that has elicited a periosteal reaction with cortical expansion.

Diagnosis of TB should be undertaken at earliest in children as it can lead to severe morbidity due to multiorgan involvement. Diagnosis is usually made based on history, clinical presentation, radiography, sputum analysis, histopathology and serological investigations.¹⁵

Radiologically, there is no specific appearance of TB involvement of jaws. However, few authors have reported findings such as blurring of bone details, diffuse radiolucency of the cortical plate and even mixed radiolucent/opaque appearances. The normal presentation is indistinguishable from any other pyogenic organism causing non-specific osteomyelitis sometimes associated with periosteal reaction. In the present case, extra oral radiography showed ill-defined, smooth osteolytic radiolucent multilocular lesion with onion-peel periosteal reaction over the inferior cortex; intraoral radiography showed crypt of first permanent molar destroyed in the anteroinferior region with the developing tooth drifted superiorly and a CT scan revealed an expansile multilocular cystic lesion with cortical breaks at places and sequestration at places; all of the signs which are routine to non-specific osteomyelitis; and none specifically indicative of tuberculous osteomyelitis.^{6 10 12}

Culture sensitivity, histology and serological testing are gold standards for the detection of TB. However, Dimitrakopoulos *et al*¹⁶ reported primary TB of the oral cavity showing negative smears and culture for AFB from the oral lesion and the sputum, but confirmed diagnosis based on history and histological only on the examination which showed giant cells and epithelioid cells with the absence of classical caseation.

Radiography showed an onion-peel appearance, osteosarcoma or Ewing's sarcoma was to be ruled out. Fine-needle aspiration cytology (FNAC) can distinguish Ewing's sarcoma which shows round cells containing demarcated nuclear outlines and ill-defined borders.¹⁷ FNAC is a useful tool and the first choice of investigation in India because of cost involved in tests such as PCR is high. Newer diagnostic tests such as PCR are emerging for diagnosis of TB in children. In present case PCR-TB test was negative.

According to the current authors diagnosis of primary oral TB especially in children is very difficult because of following reasons:

- ▶ Absence of classical history because the primary lesion is localised to the bone.
- ▶ There was no pathognomonic bony picture but there was presence of non-specific radiological changes depending on the amount of osseous destruction.
- ▶ Sputum analysis was negative due to the absence of primary lung lesion.
- ▶ Histology picture was non-specific because of the absence of classical caseation in the oral lesion.
- ▶ Paucibacillary or absence of tubercle bacilli in lesions led to negative reports in Ziehl-Neelsen staining or serum culture sensitivity.
- ▶ We had difficulty in conducting specific PCR tests due to absence PCR equipment in all centres and the costs involved.

- ▶ There was absence of organisms in blood cultures as children are subjected to episodic antibiotics that would have decreased the amount of organisms in blood making bacteriological corroboration difficult.
- ▶ Rarity of lesion led to low index of suspicion causing misdiagnosis as non-specific osteomyelitis.

Antitubercular treatment was started on the basis of a mix of following factors-

1. Radiological findings though non-specific but were still consistent with findings as reported by several authors.^{6 10 12} Radiographical findings were one of the criteria but not the single criteria for starting the antitubercular therapy.
2. Haematological findings such as raised ESR,^{18 19} leucocytosis (eisonophilia), positive PPD among patients, parents and siblings.
3. Prevalence in India was considered before starting treatment.⁸ Patients might have come in contact with a undiagnosed carrier.^{20 21}
4. Histopathology (histopathological evaluation revealed aggregates of foam cells with plasma cells eosinophils and multinucleated giant cells some with peripheral distribution of nuclei).
5. Child suffering from protein energy malnutrition usually associated with chronic inflammatory disease such as TB.
6. Proper history from parents regarding immunisation revealed that the child did not receive proper vaccination schedule as per Indian standards.

Though PCR-TB test was negative, history of non-immunisation, histology, radiography and a PPD-positive result led to the tentative diagnosis of primary TB of the mandible. Complete resolution occurred following antitubercular therapy. The case report emphasises that diagnosis of TB can sometimes be based on circumstantial evidence and give positive response to antitubercular therapy.

Learning points

- ▶ Secondary forms of oral tuberculosis (TB) are always accompanied or easily diagnosed due to presence of primary lesions in the lung or its associated lymph nodes, whereas primary forms of oral TB do not have primaries in the lung.
- ▶ Oral TB as reported by authors differ in presentations varying from superficial ulcers, patches, indurated soft tissue masses, granulomas, secondary displacement of tooth buds or non-specific involvement of the jaws.
- ▶ Diagnosis of TB should be undertaken at the earliest in children as it can lead to severe morbidity due to multiorgan involvement. Diagnosis is usually made based on history, clinical presentation, radiography, sputum analysis, histopathology and serological investigations.

CONCLUSION

Primary TB of the mandible is a rare phenomenon; however, rarity of the lesion should not be a reason to detect the presence of disease.

Competing interests None declared.

Patient consent Obtained.

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