Case Report

Mandibular Osteomyelitis Secondary to Osteopetrosis : A Management Conundrum

Inam Uddin[1], Shrabasti Dey[2], Sweta Sikarwar[3], Shreya Ganguly[3], Aquila Aini Anwar[3]

Osteopetrosis is a rare congenital disorder of the skeletal system characterized by defects in osteoclast function. Presenting with a variety of clinical manifestations, the common features are increased density of bone and reduced marrow spaces caused by increased calcification resulting in sclerosis of bone. Osteomyelitis is a common and serious manifestation of osteopetrosis, seen to occur in about 10% of patients with osteopetrosis and commonly involving the mandible. Osteomyelitis of the mandible secondary to osteopetrosis can present a management conundrum. Defective bone turnover leads to decreased marrow spaces that hamper blood supply to the bone and restrict its healing potential even after debridement of necrotic bone and sequestrectomy for the removal of focus of infection. We present mandibular osteomyelitis in a 13-year-male patient with osteopetrosis which was surgically debrided. His acute infection underwent resolution but the chronic infection continues to persist. This case report highlights the need for preventive therapy and conservative management as the first choice of treatment in osteopetrosis to avoid the need for aggressive treatment and further complications as a consequence of impaired healing of bone.

[*J Indian Med Assoc* 2024; **122(4):** 80-3]

Key words **: Osteomyelitis, Osteopetrosis, Dental Complications, Mandibular Osteomyelitis.**

Osteopetrosis, also known as marble bone disease, osteosclerosis fragilis generalisata or Albers-Schönberg disease, is 'a group of rare, heritable disorders of the skeleton characterised by increased bone density on radiographs'as defined by the World Health Organisation (WHO) in International Classification of Diseases-11 (ICD-11)[1,2].

In 1904, Albers Schönberg, a German radiologist, reported the disease that we know today as 'osteopetrosis', a term coined by Karshner in 1926[1,3-8]. Various genetic defects responsible for a single phenotype cause the group of diseases collectively termed osteopetrosis[9]. Despite the heterogeneity of genetic defects, osteopetrosis may be transmitted as Autosomal Recessive Osteopetrosis (ARO) and Autosomal Dominant Osteopetrosis (ADO). ARO, also known as malignant osteopetrosis, presents in infancy and has a poor prognosis. Obliteration of marrow spaces leads to severe anaemia while extramedullary haematopoiesis is responsible for hepatosplenomegaly in these patients. The benign variant of osteopetrosis, Autosomal Dominant Osteopetrosis (ADO) designated as Albers-Schönberg disease, presents in the third or fourth decade of life and is associated with fewer symptoms[1,5,10]. ADO can be further classified into two varieties differentiated based on clinical and radiological signs – ADO type I and ADO type II. ADO type I is the sole variant of osteopetrosis that is not associated with an increase in the rate of fracture. On the other hand, ADO type II presents with long bone fractures associated with or without trauma in 78% of patients[9]. ADO typically presents with many orofacial findings such as malformed, unerupted and delayed eruption of teeth, multiple carious teeth and osteomyelitis[5,9,11]. Osteomyelitis is the most severe complication of ADO. An intermediate variety has also been reported which manifests with varying degrees of bony sclerosis, pathological fractures and anaemia[9].

Osteopetrosis has an overall incidence ranging from approximately 1 in 1,00,000 to 5,00,000[4,7]. Although osteopetrotic conditions present a great variety in their severity and expression of molecular lesions as well as clinical features, a single pathogenic nexus in the osteoclast is shared by all known forms[6]. The causative factor in humans for this group of disorders has been identified as mutations in at least 10 genes that lead to failure of osteoclast differentiation or function. These mutations involve the proton pump gene, the chloride channel gene or the gene encoding for carbonic anhydrase II[1,9]. However, the underlying genetic abnormality is not known in around 30% of patients[1,7,8]. Decreased bone resorption by osteoclasts resulting in sclerotic bone, either due to poor quantity of osteoclasts (osteoclast poor type due to a reduction or absence of

Editor's Comment :

- Mandibular osteomyelitis in a patient with osteopetrosis can be a challenge to treat and cure due to the unique anatomical considerations. Palliative treatment may be the best possible option for the patient without having to resort to extreme modalities that are either inaccessible to the masses or cause a deterioration in the Quality of Life. Increased awareness coupled with preventive care is the silver bullet to managing mandibular osteomyelitis secondary to osteopetrosis.

Department of Oral and Maxillofacial Surgery, Dr R Ahmed Dental College & Hospital, Kolkata 700014
[1]MDS, Assistant Professor
[2]BDS, Postgraduate Trainee and Corresponding Author
[3]BDS, Postgraduate Trainee

Received on : 08/03/2023
Accepted on : 13/11/2023

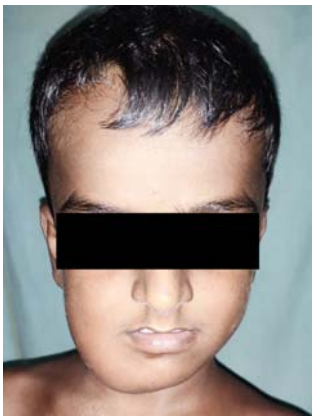

Fig 1 — Extraoral swelling of right mandible

Fig 2 — Intraoral pus discharge from right alveolar segment

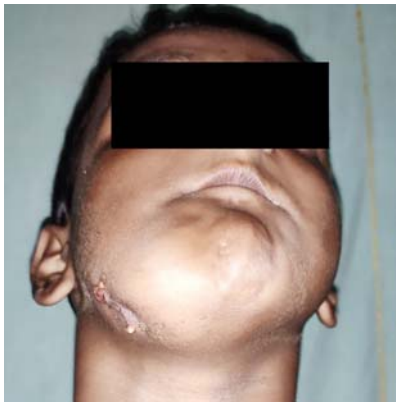

Fig 3 — Extraoral discharging sinus

osteoclast precursors) or due to functional defects (osteoclast rich type - where osteoclasts are normal or increased in number but are unable to form the ruffle border necessary for bone resorption), is the characterizing feature of this disorder. The mutations that are known to date cause defects in ionic charge regulation across the cell membrane of osteoclasts, in osteoclastic proteins necessary for resorption lacunae acidification and the subsequent resorption of the inorganic matrix component of bone. Certain cases also exhibit mutations in genes encoding the cell surface receptor RANK or RANKL that further interferes with osteoclastogenesis[7]. These mutations lead to the development of bones that, as a result of bony sclerosis and modelling defects, are overly dense, typically brittle, and exhibit poor mechanical properties making them prone to fracture.

Case Presentation

A 13-year-old male patient was referred to our department for evaluation and treatment of a swelling of the right mandible (Fig 1) associated with persistent pus discharge intraorally (Fig 2) as well as extraorally (Fig 3). The patient reported a history of swelling of the right mandible since the last one and a half years that was insidious in onset and gradually increasing in size. He also reported undergoing extraction of a tooth present in the lower right jaw the previous month which was followed by the development of a persistent discharging sinus, communicating both intraorally and extraorally.

On general examination, the patient was seen to have partial blindness which he reported to be progressive in nature. He also presented with limb length discrepancy, lordosis, (Fig 4) scoliosis and pectus excavatum (Fig 5). Patient was of normal intelligence. Extraorally, the patient presented with frontal bossing. He exhibited gross facial asymmetry due to the presence of a solitary, ill-defined swelling present in relation to the right side of the mandible with the expansion of buccal and lingual cortices. The swelling was firm in consistency, tender on palpation and the overlying skin was not fixed to the underlying swelling. A pus-discharging sinus was present on the right side of the mandible which exuded yellowish creamy pus since the extraction had been performed. On intraoral examination, the patient presented with partial anodontia, the presence of a malformed tooth – a peg-shaped lateral incisor in his upper right quadrant and an ill-defined firm swelling present in the lower right posterior alveolar segment that was associated with pus discharge. Past medical history revealed pathological long bone (femur) fracture after trivial trauma. There was no reported history of prolonged fever, loss of weight, jaundice, haematemesis, haemoptysis, haematological disorder in the family, nor any history of previous tubercular infection. Patient was born of a non-consanguineous marriage. Patient has a younger sibling who is a 5-year-old female.None of the family members had history of fractures or any significant history of a similar condition.

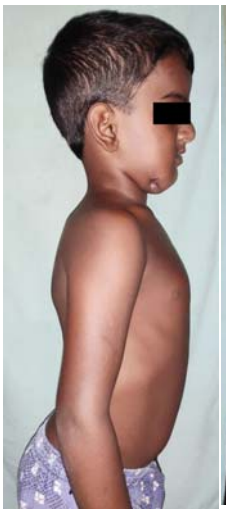

Fig 4 — Lordosis

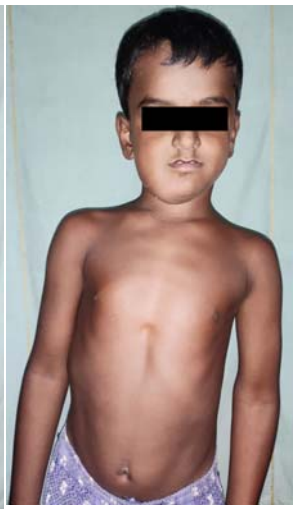

Fig 5 — Scoliosis and pectus excavatum

Cone Beam Computed Tomography (CBCT) of the face revealed increased radiodensity of the maxilla and mandible (Fig 6). Radiolucent foci associated with an expansion of the buccal cortex demonstrated evidence of sequestrum in the right side of the mandible suggestive of chronic osteomyelitis (Fig 7). Multiple tooth like structures were seen to be present in both the jaws which had roots indistinguishable from the surrounding bone. Other radiographic investigations revealed the presence of a

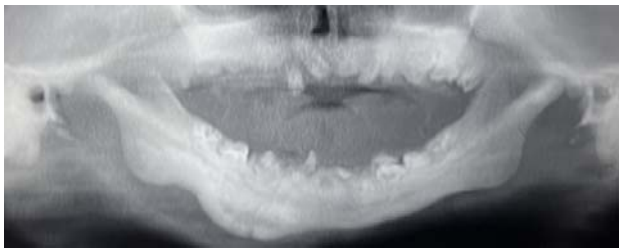

Fig 6 — Increased radiodensity of maxilla and mandible

generalized increase in bone density, small and under-pneumatized sinuses, evidence of previous femur fracture, and funnel-like appearance of long bones (Erlenmeyer flask deformity) with transverse banding (Fig 8).

Biochemical and Haematological Investigations Revealed the following :

Hb 10 g/dL, haematocrit 30%, total leucocyte count of 5.6 x 103/µL with polymorphs 48%, lymphocytes 16%, eosinophil 2%, MCV 88.24fl, MCH 29.41pg, MCHC 33.33 g/dL, Erythrocyte Sedimentation Rate 45 mm (first hour), normal platelet count and coagulation profile and without apparent evidence of extramedullary haematopoesis. Serum albumin was 4.2 g/dL, calcium 8.4 mg/dL, phosphorus 3.2 mg/dL, alkaline phosphatase 236 IU/L.

Biopsy was not performed for this patient as radiological investigations were diagnostic for osteopetrosis[8,12]. The swelling in the mandible which was suspected to be osteomyelitis was managed by thorough surgical debridement of necrotic bone and sequestrum till the exposure of fresh bone exhibiting healthy bleeding (Fig 9) followed by primary closure extraorally as well as intraorally. Bacterial culture was performed with antibiotic sensitivity testing which was followed by antibiotic therapy with gentamicin for 3 days and linezolid for 14 days, followed by clindamycin for another 7 days. The wound was also subjected to daily irrigation using povidone iodine solution.

The debrided bone, upon undergoing histopatho-logical examination, was diagnosed as chronic osteomyelitis, secondary to the extraction of a primary tooth on the right side of the mandible due to osteopetrosis.

The patient is currently under 6 months of follow-up. There has been complete resolution of the acute infection which has resulted in the cessation of pus discharge and tenderness without resolution of chronic osteomyelitis (Fig 10). The patient reported with intraoral wound dehiscence one month postoperatively exposing underlying necrotic bone (Fig 11). The intraoral wound has since then been managed with regular application of a gauze pack impregnated with Bismuth-Iodoform-Paraffin Paste (BIPP). A second debridement was also carried out three months postoperatively to remove the newly formed necrotic bone but there has been recurrent necrosis of the healthy bone that was exposed upon debridement once again. Secondary healing of the intraoral wound by the formation of granulation tissue has not occurred as the underlying bone is necrotic in nature. The patient has currently been advised to remain under follow-up and maintain strict oral hygiene measures along with the regular application of BIPP-impregnated gauze to facilitate healing as best as possible.

Discussion

The vascularity of bone is the most critical factor for the healing of bone. Patients with osteopetrosis present with varying degrees of bony sclerosis leading to poor blood supply to the bone. Consequently, the bone is more susceptible to infection and exhibits a delayed healing process despite removal of the source of infection, leading to an unfavourable outcome such as avascular

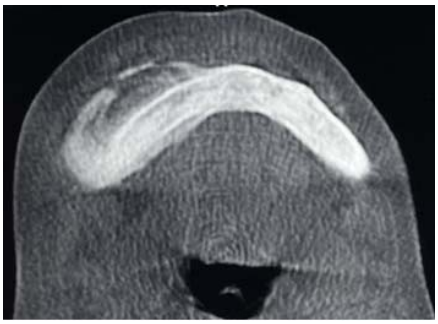

Fig 7 — Expansion of buccal cortex with radiolucent foci suggestive of sequestrum

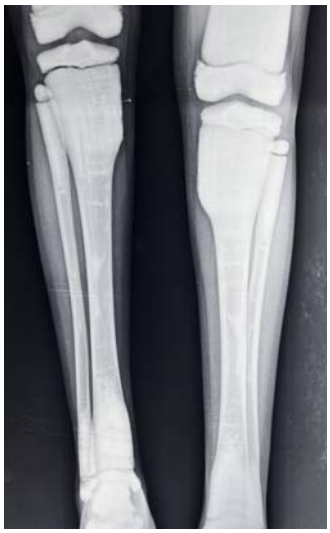

Fig 8 — Erlenmeyer flask deformity of long bones of lower limb

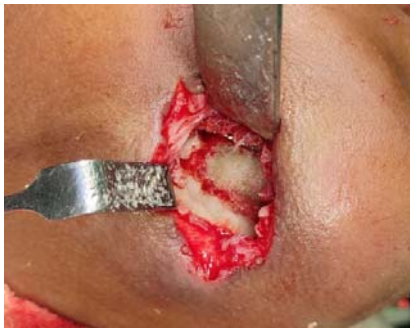

Fig 9 — Necrotic bone and sequestrum debrided till exposure of fresh bone

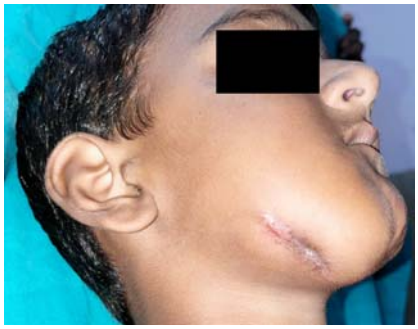

Fig 10 — Resolution of extraoral sinus

Fig 11 — Intraoral wound dehiscence with necrotic bone exposure

necrosis and infection after extraction of a carious tooth[9].

The maxilla rarely presents as a site for osteomyelitis as it has a rich blood supply and thin cortical plates[9,11]. The commonest site for osteomyelitis is the mandible, usually associated with dental extractions or surgical exposure of the pathological bone. Patients with osteopetrosis commonly present to the general dental practitioner with grossly carious teeth[9]. Tooth extraction or pulpal necrosis are the common causes of osteomyelitis in osteopetrosis. Extraction in these cases leads to the creation of a wound that has to undergo healing in an area of poor blood supply. Accompanying anaemia and neutropenia may lend it an even more severe form with a protracted course. Mandibular osteomyelitis, seen in 10% of osteopetrosis cases, presents a grave management conundrum. Lack of adequate blood supply to the mandible due to constriction of the inferior alveolar canal housing the neurovascular bundle and the marrow spaces is the leading cause of the increased rate of infection[9]. Management of the infection is challenging due to the poor vasculature as well as the progressive obliteration of marrow space in surrounding areas. Bony sequestrum and draining fistulae are common findings of osteomyelitis secondary to osteopetrosis[9].

Treatment regimens include bacterial culture for antibiotic sensitivity testing, thorough surgical debridement and primary closure (if possible), followed by prolonged high-dose systemic antibiotics[5,9]. Surgical debridement to remove the sequestrum and surrounding necrotic bone may act only as palliative care as the bone inherently lacks the capacity to heal the surgically created wound during debridement. The overlying soft tissue healing may also be hampered due to the presence of underlying necrotic bone causing wound dehiscence following primary closure.

Hyperbaric oxygen has also been used for the treatment of chronic osteomyelitis for its actions of increased osteoclastic resorption of the necrotic bone, enhanced leucocytic killing, neovascularisation, collagen production, fibroblastic division and enhanced permeation of certain antibiotics (aminoglycosides) across bacterial cell walls within the necrotic tissue[5,9]. Osteoclasts, being 100 times more metabolically active are highly dependent on oxygen for their function leading to the success of hyperbaric oxygen therapy as reported in the literature[9]. However, it has a restricted role due to its limited infrastructural presence and the high associated cost making it inaccessible in many areas and amongst certain demographics of patients.

Medical management of osteomyelitis secondary to osteopetrosis has been reported with varying success in literature. Restriction of calcium intake, parathyroid hormone, steroids, high-dose calcitriol therapy and recombinant human interferon gamma-1b are some of the interventions used for the modulation of osteoclasts. Recently, bone marrow transplantation has also been performed successfully for the treatment of malignant osteopetrosis[7-9].

Conclusion

The definitive treatment of osteomyelitis secondary to osteopetrosis is unfortunately an enigma without the complete removal of the affected mandible or maxilla. Preventive care such as maintenance of good oral hygiene should be encouraged. Carious teeth should preferably be treated endodontically rather than opting for extraction. Any surgical procedure should be the last resort to prevent the promotion of osteomyelitis resulting from the periosteal stripping of bone which may render even asymptomatic bone to become necrotic. Surgical debridement, when absolutely necessary, should be performed in a conservative fashion with restricted flap elevation and periosteal stripping. Palliative treatment is the method of choice in most cases to avoid the promotion of the disease process and manage the patient's discomfort. Increased awareness could play a crucial role in the early diagnosis of osteopetrosis and the identification of its proclivity to cause osteomyelitis can avoid inappropriate treatments, unnecessary surgical intervention and further complications.

References

1 Stark Z, Savarirayan R — Osteopetrosis. *Orphanet J Rare Dis* 2009; **4:** 5. doi: 10.1186/1750-1172-4-5. PMID: 19232111; PMCID: PMC2654865.

2 Available from: https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/1498426606

3 Karshner RG — Osteopetrosis. *AJR* 1926; **16:** 405-19.

4 Lam DK, Sándor GK, Holmes HI, Carmichael RP, Clokie CM — Marble bone disease: a review of osteopetrosis and its oral health implications for dentists. *J Can Dent Assoc* 2007; **73(9):** 839-43. PMID: 18028760.

5 Makarem A, Lotfi N, Danesh-Sani SA, Nazifi S — Osteopetrosis: Oral and Maxillofacial Manifestations. *Int J Head Neck Surg* 2012; **3(2):** 115-7.

6 Mahmoud Adel AH, Abdullah AA, Eissa F — Infantile osteopetrosis, craniosynostosis, and Chiari malformation type I with novel OSTEM1 mutation. *J Pediatr Neurosci* 2013; **8(1):** 34-7. doi: 10.4103/1817-1745.111420. PMID: 23772242; PMCID: PMC3680893.

7 Neville BW, Damm DD, Allen CM, Chi A — Bone Pathology. In: Oral and Maxillofacial Pathology. First South Asia Edition. New Delhi: Reed Elsevier India Pvt Ltd 2015. 574-6.

8 Sivapathasundaram B, editor. Bone and Joints Diseases. In: Shafer's Textbook of Oral Pathology. 8th Edition. New Delhi: Elsevier, Inc; 2016. 460-2.

9 García CM, García MA, García RG, Gil FM — Osteomyelitis of the Mandible in a Patient with Osteopetrosis. Case Report and Review of the Literature. *J Maxillofac Oral Surg* 2013; **12(1):** 94-9. doi: 10.1007/s12663-011-0196-y. Epub 2011 Apr 20. PMID: 24431821; PMCID: PMC3589508.

10 Beighton P, Horan F, Hamersma H — A review of the osteopetroses. *Postgrad Med J* 1977; **53:** 507-16.

11 Wu CC, Econs MJ, DiMeglio LA, Insogna KL, Levine MA, Orchard PJ, *et al* — Diagnosis and Management of Osteopetrosis: Consensus Guidelines From the Osteopetrosis Working Group. *J Clin Endocrinol Metab* 2017; **102(9):** 3111-23. doi: 10.1210/jc.2017-01127.

12 Wu CC, Econs MJ, DiMeglio LA, Insogna KL, Levine MA, Orchard PJ, *et al* — Diagnosis and Management of Osteopetrosis:Consensus Guidelines From the OsteopetrosisWorking Group. *J Clin Endocrinol Metab* 2017; **102(9):** 3111-23. doi: 10.1210/jc.2017-01127.