A paradoxical presentation of rickets and secondary osteomyelitis of the jaw in Type II autosomal dominant osteopetrosis: Rare case reports

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ABSTRACT

Osteopetrosis is a rare genetic bone disorder arising due to a defect in the differentiation or function of osteoclast which results in a generalized increase in bone mass. Osteomyelitis is one of the most common complications because of decreased bone marrow function and compromised blood supply. Radiologist plays a vital role in diagnosing osteopetrosis. Here, we present two cases of autosomal dominant osteopetrosis Type II (ADO II) with secondary osteomyelitis changes which were reported to our department. One of these two cases presented with secondary osteomyelitis in both maxilla and mandible and features of rickets, which is very rarely seen in ADO II. To the best of our knowledge, the presentation of rickets with ADO is the first of its kind to be reported. In this paper, we describe the clinical and radiological features leading to the diagnosis of ADO in these two patients. Further, a review of the literature regarding ADO is discussed.

Key words: Autosomal dominant osteopetrosis, bone within bone, osteomyelitis, rickets

Osteopetrosis is a term representing a rare genetic bone disorder characterized by widespread osteosclerosis involving most of the bones caused by altered differentiation or function of an osteoclast. Because of the defective osteoclast, normal physiological bone marrow function is compromised resulting in retarded growth, hematopoietic insufficiency, abnormal development, or eruption of teeth. Osteomyelitis is one of the well-recognized complications associated with osteopetrosis. The incidence of Autosomal dominant osteopetrosis Type II (ADO II) is about 1:20,000.[1]

Two cases of ADO II were reported to our Department of Oral Medicine and Radiology. One case presented with a complication of osteomyelitis of both maxilla and mandible. The other case presented with osteomyelitis of mandible only. Osteomyelitis of the maxilla is not a rare finding in osteopetrosis as it is associated with compromised blood supply and diffuse osteosclerosis.[2] This article describes the clinical and radiological features of ADO II. Management and dental considerations relevant to this condition is also discussed.

CASE REPORTS

Case 1

A 20-year-old male reported to our Department of Oral Medicine and Radiology with pain and swelling of 1-month duration in the right side of the face. A history of frequent fracture of long bones and an attempted extraction of 47 (right second mandibular teeth) was reported. The patient had stunted growth with an abnormal gait; signs of anemia and exophthalmos were also noted. Most interestingly, characteristic findings of rickets such as pigeon chest, kyphosis, and knock knees [Figure 1a and b] were also present, which is a rare paradoxical association with

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osteopetrosis. The patient was found to be suffering from such characteristic findings for the past 10 years. Restricted mouth opening, pale mucosa with atrophic glossitis, irregularly arranged malformed permanent teeth were also observed on intraoral evaluation. At the region of fractured tooth segment 47, necrosis of alveolar mucosa and exposed alveolar bone with pus discharge was observed [Figure 1c].

Orthopantomogram (OPG) revealed fractured 47, which was ankylosed to the surrounding bone, incomplete formation and ankylosis of almost all the teeth, multiple impacted permanent teeth with narrowing of inferior alveolar canal. Anatomic structures such as maxillary sinus, nasal fossa, and orbit were difficult to differentiate due to diffuse osteosclerosis [Figure 2a]. Normal bone architecture was absent, and the mandible showed the typical marble bone appearance.

Posteroanterior view of mandible and lateral skull showed abnormally increased radiodensity around the orbit and increased sclerosis of cranial base compared to cranial vault [Figure 2b and c]. X-ray pelvis showed a diffuse increase in radiodensity with the absence of medullary architecture and a poorly healed fracture in right side of the pelvis [Figure 3a]. Hand Wrist radiograph revealed “bone within bone appearance” which is a pathognomonic finding of osteopetrosis [Figure 3b]. X-ray femur showed an abnormal increase in bone mass in the growing end, popularly termed as “Erlenmeyer Flask like deformity” which is a result of defective bone remodeling at the growing end [Figure 3c]. In the X-ray of spine, thickening of endplates of vertebral bone resulting in sandwich vertebrae, also called as “Rugger Jersey Spine” was observed [Figure 3d]. The evaluation of computed tomography (CT) scan of facial bone-axial view revealed an abnormal increase in density of all bones and complete obliteration of both maxillary sinuses. Coronal view revealed reactive bone formation as a hyperdense mass on lateral surface of mandible as a result of chronic osteomyelitis secondary to osteopetrosis [Figure 3e].

Hemogram of this patient showed hemoglobin – 6.5 g%, erythrocyte sedimentation rate (ESR) – 70 mm/1 h and microcytic, hypochromic, anisocytosis, reticulocytosis on peripheral smear. Serological investigation revealed hypocalcemia, serum calcium – 6.5 mg/dl (9–11 mg/dl) which can be attributed to the development of rickets. Serum acid phosphatase level was drastically increased (76.5 U/L), another most important diagnostic finding in osteopetrosis. Pus culture showed the presence of Staphylococcus aureus and cefotaxime sensitivity.

With the above findings, final diagnosis of ADO II with secondary osteomyelitis was attained. Local debridement was performed under local anesthesia, and the patient was administered cefotaxime 1 g, Metronidazole 500 mg intravenously and gentamicin 80 mg intramuscularly twice daily for 7 days. The patient was followed up on a weekly basis. Two months later, the patient was reported with secondary osteomyelitic changes in the right maxilla which can be attributed to compromised blood supply of maxilla due to increased osteosclerosis. The patient is under regular follow-up [Figure 4a and b].

Case 2
A 7-year-old female child reported with a chief complaint of pain and swelling of 2 weeks duration in the right side of the face. This patient also reported to have a history of frequent fracture of long bones. There was diffuse swelling on the right side of face with sinus opening and pus discharge in the submental and the right submandibular region [Figure 5a]. Complete absence of teeth in the upper and lower jaw was observed on intraoral examination [Figure 5b and c]. There was necrosis of
alveolar mucosa and the exposed alveolar bone in the right side anterior and posterior region corresponded with the extraoral sinus opening. Features of Rickets were absent in this patient.

OPG revealed a widespread increase in radiodensity with ankylosis and incomplete formation of multiple teeth. The absence of multiple permanent tooth buds was also noted [Figure 6a]. Radiographs of the skull, spine, pelvis, and long bones revealed an increased density of the entire skeleton with cortical thickening, reduced bone marrow spaces and all the characteristic features such as sclerosis of the base of the skull, bone within bone appearance. Rugger jersey spine, Erlenmeyer flask deformity were noted, as in the first patient [Figure 6b-e]. CT axial and coronal view revealed the increased density of all bones with reactive bone formation in lateral surface of body of mandible [Figure 7a and b].

Hemogram of this patient revealed hemoglobin – 7.3 g/dl, ESR – 60 mm/1 h. Serum calcium, serum phosphorus, serum alkaline phosphatase was found to be normal. Serum acid phosphatase level was increased to 11 U/L. Based on these clinical and radiological features; a final diagnosis of ADO II with secondary osteomyelitis was arrived. The patient was administered cefotaxime 50 mg/kg, metronidazole 10 mg/kg intravenously, gentamicin 5 m/kg intramuscularly twice daily for 7 days and local debridement was carried out under local anesthesia. She was also advised to take calcitriol regularly to induce erythropoiesis and prednisolone 10 mg/day under regular monitoring to induce bone resorption.

**DISCUSSION**

In 1904 Heinrich Albers-Schonberg, a German radiologist reported a case of generalized osteosclerosis, and he described the disorder as “Marmor-Knochen Krankheit” (marble bone disease) based on the roentgenographic appearance of the bones. Later Karshner (1920) introduced the term “Osteopetrosis” (petro-stone) because of the petrified nature of the affected bones. Clinical and radiological feature associated with osteopetrosis is mainly because of imbalance in bone remodeling due to defective osteoclast function or differentiation.

![Figure 5: Extraoral image (a) diffuse swelling in the right side of face. Intraoral image (b and c) anodontia in maxilla and mandible](image)

![Figure 6: Orthopantomogram (a) diffuse sclerosis and absence of tooth bud for permanent teeth. X-ray spine (b) rugger jersey spine. X-ray long bones (c) erlenmeyer flask like deformity at the growing end. Posteroanterior view (d) diffuse sclerosis around orbit and base of the skull. X-ray pelvis (e) diffuse sclerosis](image)

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**Indian Journal of Dental Research, 27(6), 2016**

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Osteopetrosis usually manifest in three forms: Autosomal recessive osteopetrosis (ARO), ADO and X-linked osteopetrosis.\(^1\) ARO form is a life-threatening condition where the mortality of patient is high, manifesting within first few months of life and the patient may die before the age of 6 due to recurrent infection and septicemia. Genetic mutation of genes such as CLCN7, TCIRG1, CA II is responsible for the development of osteopetrosis, of which CLCN7 gene mutation can be associated with all forms of osteopetrosis.\(^1,2\)

ADO is further subdivided into two types based on clinical and radiological features: ADO Type I and ADO Type II. In Type I ADO, sclerosis of the cranial vault, cranial nerve compressions, low fracture incidence, and normal serum acid phosphatase level are common. In Type II ADO, base of the skull is mainly involved. High incidence of fracture and osteomyelitis are common complications. Rarely cranial nerve compression occurs. Radiological features such as Rugger jersey spine, sandwich vertebrae, and bone within bone appearance are commonly associated with the Type II form. Type II ADO is called as “Albers Schonberg disease.” Hence, both the cases reported in this article come under ADO II because of typical clinical and radiological features as mentioned earlier.\(^3\)

Dental features associated with ADO II are anodontia or oligodontia, delayed eruption of deciduous and permanent teeth due to defective resorption, malformation of teeth, hypoplasia of enamel and dentin, multiple dental caries, hypoplastic or complete absence of pneumatization of maxillary sinuses and presence of odontomes. Osteopetrosis with rickets is a rare paradoxical association.\(^4,5\) To the best of our knowledge, this rare presentation of rickets with ADO is first of its kind to be reported. Few cases of rickets with osteopetrosis were reported in infantile form but not with ADO II form.\(^6\) The association of rickets with osteopetrosis is proposed to be because of dysfunctional osteoclasts which are unable to maintain serum calcium and phosphorus levels to mineralize the newly formed chondroid and osteoid even with positive total body calcium. More than 99% of total body calcium is shut off in the bone leading to decrease in the serum calcium which is often exacerbated by inadequate dietary intake of calcium leading to rickets.\(^7\) Usually, the term Rickets is used to describe the disorder in children, whereas “osteomalacia” is used when it occurs in adults. However, the history of the first patient revealed that these clinical appearances were found to be the long-term effects of rickets. Hence, the term osteomalacia is not used. Low calcium intake in older toddlers and children before the fusion of epiphyseal plate may lead to increased catabolism of Vitamin D, resulting in Vitamin D deficiency and then rickets. Serum calcium level was 6.5 mg/dl, which may be mainly attributed to the development of features of rickets.

Diagnosis of osteopetrosis is mainly based on clinical and radiological features, especially radiological presentation provides a better understanding and proper diagnosis. Apart from OPG and other intraoral radiographs, complete skeletal survey and CT scan are mandatory for accurate diagnosis and differentiating the various forms of osteopetrosis. Hematological findings in ADO II are usually within normal range, though it may not be diagnostic but helpful in understanding secondary features like anemia. Microcytic hypochromic anemia in the first case could be because of nutritional deficiency. Serum calcium, phosphorus, and alkaline phosphatase levels in the ADO II form are also usually within normal limits, but tartrate-resistant acid phosphatase levels are diagnostic, increased invariably and useful for predicting the clinical severity of the disease.\(^8\) In both the cases, Acid phosphatase level was increased, especially in the first case which showed a marked increase. As radiographic findings itself are diagnostic, bone marrow biopsy or histopathology are not mandatory. Genetic testing can be used to confirm the diagnosis and differentiate between different subtypes of osteopetrosis, but it was not carried out in our cases, which is one of the limitations of this study.

Osteopetrotic bone is significantly harder than normal bone resulting in greater risk of pathological fractures and secondary osteomyelitis. Osteomyelitis of the jaws rarely affects maxilla because of the rich blood supply. However, in osteopetrosis, because of compromised blood supply and due to the defective bone marrow function, osteomyelitis of maxilla can also occur.\(^9\) In the first case, osteomyelitis of the mandible was the result of traumatic extraction of 47, which was performed without any radiographic examination and 2 months later the patient reported with osteomyelitis of maxilla. In the second case, osteomyelitis of the mandible was because of the physiological shedding of deciduous teeth as reported.

Management of ADO is preferably conservative. Surgical intervention along with high dose systemic antibiotic is
effective for the management of osteomyelitis associated with osteopetrosis. Systemic steroids may be helpful to induce bone resorption but not for long-term. Other alternatives include calcitriol, gamma interferon, and erythropoietin. Low calcium diet is always recommended in osteopetrosis patients, but when it is complicated with rickets, calcium-rich diet is advisable.

Maintenance of good oral hygiene is also important as it may preclude infection and secondary osteomyelitis. Extraction in osteopetrotic patient should be carried out with utmost precaution as fracture of teeth or bone are more frequent if untoward force is given. Conservative management should always be considered as compared to invasive procedures. Implants are contraindicated as osseointegration in osteopetrotic bone is questionable.\[10\]

CONCLUSION

Osteopetrosis is a rare entity and often radiological features may provide a better diagnostic value. As oral physician, we may encounter cases of ADO, hence a sound knowledge of clinical and radiographic features will be helpful in early diagnosis and proper dental management. As these patients are more prone for infection especially osteomyelitis, utmost precaution should be taken while treating these patients with any kind of invasive procedures. ADO superimposed with rickets is a very rare presentation. Skeletal Roentgenograms and serological investigations play an important role in the diagnosis of both osteopetrosis and rickets.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Del Fattore A, Cappariello A, Teti A. Genetics, pathogenesis and complications of osteopetrosis. Bone 2008;42:19-29.
2. Tolar J, Teitelbaum SL, Orchard PJ. Mechanisms of disease: Osteopetrosis. N Engl J Med 2004;351:2839-49.
3. Tohidi E, Bagherpour A. Clinicoradiological findings of benign osteopetrosis: Report of two new cases. J Dent Res Dent Clin Dent Prospects 2012;6:152-7.
4. Vázquez E, López-Arcas JM, Navarro I, Pingarrón L, Cebrián JL. Maxillomandibular osteomyelitis in osteopetrosis. Report of a case and review of the literature. Oral Maxillofac Surg 2009;13:105-8.
5. Andersen PE Jr., Bollerslev J. Heterogeneity of autosomal dominant osteopetrosis. Radiology 1987;164:223-5.
6. Luzzi V, Consoli G, Daryanani V, Santoro G, Sfasciotti GL, Polimeni A. Malignant infantile osteopetrosis: Dental effects in paediatric patients. Case reports. Eur J Paediatr Dent 2006;7:39-44.
7. Umesh K, Rajesh J. Osteopetrorickets- Osteopetrosis with rickets, a rare paradoxical association. Internet J Pediatr Neonatol 2008;10:1-4.
8. Kolawole TM, Hawass ND, Patel PJ, Mahdi AH. Osteopetrosis: Some unusual radiological features with a short review. Eur J Radiol 1988;8:89-95.
9. Alatalo SL, Ivaska KK, Waguespack SG, Econs MJ, Väänänen HK, Halleen JM. Osteoclast-derived serum tartrate-resistant acid phosphatase 5b in Albers-Schonberg disease (type II autosomal dominant osteopetrosis). Clin Chem 2004;50:883-90.
10. Jayachandran S, Mohamed Riyaz SS, Kayal L. Benign osteopetrosis with secondary osteomyelitic changes in the mandible. A report of two rare cases. J Indian Acad Oral Med Radiol 2009;21:25.