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Dental Radiographic Findings of Malignant Osteopetrosis: Report of Four Cases

Osteopetrosis is a rare skeletal disorder that results from a defect in the differentiation and function of osteoclasts.

The lack of normally functioning osteoclasts results in abnormal formation of the primary skeleton and a generalized increase in the bone mass. This disorder is inherited as an autosomal recessive (osteopetrosis congenita) and an autosomal dominant trait (osteopetrosis tarda).

In this article, we report four cases of malignant osteopetrosis and describe the clinical and dental radiographic findings associated with this rare disease.

Keywords: Malignant Osteopetrosis, Panoramic, Dental

Introduction

Osteopetrosis, also known as Albers-Schonberg disease or marble bone disease, is a rare hereditary bone disorder that results from a defect in osteoclasts. Four types of this disease have been described: 1) severe infantile 2) osteopetrosis with renal tubular acidosis, and cerebral calcifications 3) benign 4) intermediate.[1-4] The overall incidence of these conditions is difficult to estimate but autosomal recessive osteopetrosis (ARO) has an incidence of 1 in 250,000 births, and autosomal dominant osteopetrosis (ADO) has an incidence of 1 in 20,000 births.[5] Benign or adult osteopetrosis, the most common type of osteopetrosis, is usually discovered later in life and has a less severe manifestation. The axial skeleton usually shows significant sclerosis, whereas the long bones have minimal or no defects. Approximately 40% of those affected are asymptomatic and marrow failure is rare. Autosomal dominant osteopetrosis is divided into two radiological subtypes. In type I, there is generalized diffuse osteosclerosis affecting mainly the cranial vault, due to mutation in the gene located on chromosome 11q12-13, in the region where a high-bone mass syndrome has been localized. The calvarium is almost normal in type II, but the cranial base is sclerotic. Although both types involve generalized skeletal sclerosis, patients with the type II subtype have a higher risk of fractures.[6,7] Severe infantile or malignant osteopetrosis is present at birth or develops in early childhood. It is an autosomal recessive and severe form of osteopetrosis presumably due to mutations in the TCIRG1 gene which encodes the vacuolar H(+)–ATPase. The failure of normal bone remodeling results in dense, fragile bones that are susceptible to fracture and infection.[4] The development of dentition is severely disturbed in children with malignant osteopetrosis. Dental findings include delayed tooth eruption, impactions, aplasia, unerupted and malformed teeth, enamel hypoplasia, early tooth loss, disturbed dentinogenesis, propensity for tooth decay, defect of periodontal membrane, thickened lamina dura, mandibular protrusion and the presence of odontoma.[8,9]

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Fig. 1. 7-year-old girl with malignant osteopetrosis. Clinical view of the patient shows hypertelorism, frontal bossing, exophtalmus, a broad face and a snubbed nose (case 1).

The treatment of this disease is bone marrow transplantation (BMT).[4] Considering the rarity of this disease, in this article, we demonstrate the clinical pattern and alteration of dental radiography in four cases referred to the Department of Oral and Maxillofacial Radiology of Mashhad University. Two of these patients were from the same family which itself is a rare situation.

Case Presentation

Case 1 and 2: A 6-year-old boy and his 7-year-old sister were referred to our department because their parents complained of uneruption of teeth.

Past medical history: Their parents noticed that their disease appeared a short time after their birth and clinical and laboratory examinations revealed malignant osteopetrosis. Their symptoms included anemia, hepatosplenomegaly, impairment of vision, hearing loss, increased bone density throughout the skeleton, and mental retardation.

Clinical examination: They had a short stature in comparison with their age, and hypertelorism, frontal bossing, exophtalmus, a broad face, and a snubbed nose were evident in their appearance (Fig. 1).

Radiological findings: In the panoramic radiography, both maxilla and mandible were completely radiopaque, in which the maxilla was more sclerotic than the mandible. Almost all the teeth were impacted and unerupted. The panoramic findings in both patients were approximately equal (Fig. 2A&B). We explained to the parents that the teeth are not able to erupt because of their disease, and patients should receive prophylactic dental treatment to maintain the fragile oral health status.

Case 3

This patient was a 7-year-old boy who complained of left side mandibular swelling.

Past medical history: Malignant osteopetrosis was previously proved and a history of spleen removal was evident.

Clinical examination: A sinus tract was depicted in the left side of the mandible. Symptoms of inflammation in this region were evident.

His parents pointed out that the patient had a history of tooth extraction one to two months ago and a history of extraoral drainage of the first and second mandibular molar on the left side a few months before this referral. The symptoms that were characteristic in osteopetrosis such as hypertelorism, frontal bossing and exophthalmus were evident in this pa-

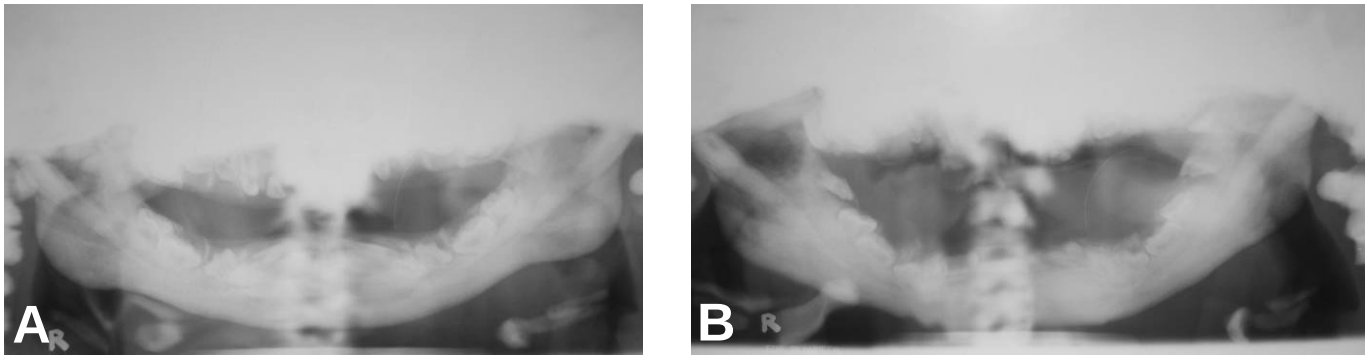

Fig. 2. Dental panoramic radiographs indicating sclerosis of the mandible and the maxilla.
A. 6-year-old boy with malignant osteopetrosis (case 1).
B. His 7-year-old sister (case 2).

tient, but neurologic impairment was not depicted.

Radiographic findings: In the panoramic view, bilateral absence of the first and second mandibular premolar and enlargement of the left mandibular alveolar bone and a few erupted teeth that were almost carious and malformed, were detected. In addition, in this view, loss of the natural pattern of the bone in both jaws that caused increased cortical density of the jaws was revealed. The maxilla was more sclerotic than the mandible. The sinus tract in the left mandible and rarefaction in the periapical region of the first mandibular molar on the left side were depicted (Fig. 3). The patient was referred to a maxillofacial surgeon. The patient underwent antibiotic therapy and the first mandibular molar was extracted. Recovery was uneventful and there was no recurrence of the sinus three months postoperatively.

Case 4

The fourth case was a 7-year-old boy who complained of swelling in the left mandible.

Past medical history: It was proved that this patient has infantile osteopetrosis.

Clinical examination: He had a short stature and frontal bossing, hypertelorism, a snubbed nose, exophtalmus, a broad face, and enlargement of the left mandible were evident (Fig. 4). The skin overlying the left mandible was reddish, inflamed and swelled with a draining sinus tract near the angle of the mandible. None of the neurological impairments, such as hearing loss, deafness, or mental retardation were evident in this case.

Radiographic findings: In the panoramic view, generalized radiopacity concurrent with the sinus tract in the left mandible, near the angle of the mandible was evident (Fig. 5A) and probably bone expansion was related to the periosteal reaction in the right side in which the lamination pattern was lost (Fig. 5B). Dental decay, delayed eruption of succedaneous teeth and retention of primary teeth, defect in periodontal ligament and missing roots in the mandibular molar were revealed. Approximately all the teeth were impacted (Fig. 5C).The patient was referred to a maxillofacial surgeon and was put on antibiotic therapy and drainage of the abscess. The mandibular molar was extracted. There was no evidence of sinus formation six months postoperatively, but the patient had deafness.

Discussion

Malignant osteopetrosis is a rare hereditary bone disorder that results from dysfunction or lack of osteoclasts. It is an autosomal recessive form of osteopetrosis. Encroachment of the bone marrow space leads to extramedullary hematopoiesis and hypersplenism, resulting in anemia, severe thrombocytopenia, leukoerythroblastosis and progressive hepatosplenoemegaly.[8] These patients are susceptible to infection as a result of granulocytopenia.[10]

Bony encroachment of the cranial nerve foramina leads to cranial nerve palsies and optic atrophy with blindness and deafness. Their bones are susceptible to fracture. Most patients fail to grow and death occurs at an early age, as a result of severe chronic anemia, bleeding and/or infection.[9] Although the radiographs

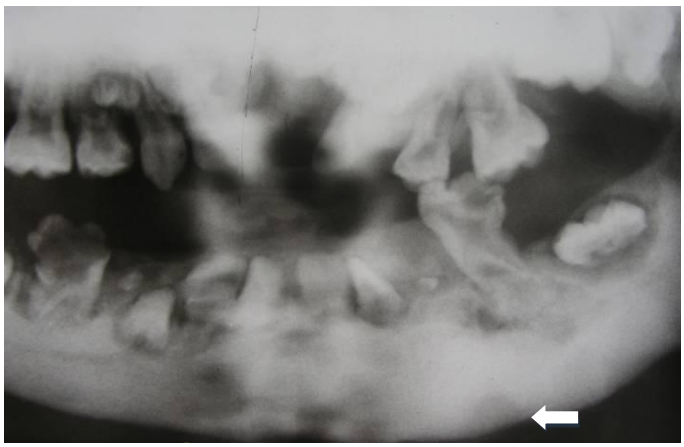

Fig. 3. 7-year-old boy with malignant osteopetrosis. Dental panoramic radiograph shows bone sclerosis, arrow indicating a sinus tract in the left mandible (case 3).

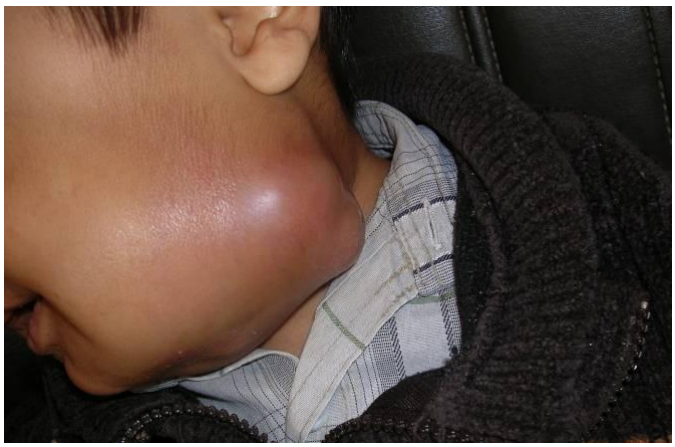

Fig. 4. 7-year-old boy with malignant osteopetrosis. Clinical view of the patient indicating swelling, redness and a sinus tract in the left mandible (case 4).

may be characteristic, a through history and clinical examination are also important in the diagnosis of osteopetrosis. Radiographically, osteopetrosis presents as an increased density of the entire skeleton, which is homogeneous. The entire bone may be mildly enlarged. The long bones show increased cortical thickening and decreased marrow space and become club shaped. The skull also shows increased radiodensity of the base and widening of the diploe. The pelvis and scapula may show endobone formation. The vertebra also shows the effects of increased density at the end plate, which causes a sandwich-like appearance of the spine that is also termed "rugger jersey" spine. Other features include metaphyseal widening, calvarial "hair on end" appearance and underdevelopment of paranasal sinuses.[6,7] The mandible is less often involved than other bones.[11] Bone pain is the most common symptom and osteomyelitis is a serious complication of the disease that occurs most often in the mandible and occasionally in the maxilla, scapula and extremities.[10]

Dental findings include delayed eruption due to bony ankylosis, absence of alveolar bone resorption, early tooth loss that may be a result of a defect in the periodontal ligament, missing teeth, malformed roots and crowns, missing roots, partial anodontia, hypoplasia, dental decay, abnormal pulp chamber, presence of odontoma, thickening of lamina dura, disturbed dentinogenesis and mandibular protrusion.[4,9,11-13] Due to these findings tooth removal should be limited as it may induce bone fracture and osteomyelitis.[7,12] Early bone marrow transplant (BMT) is the only treatment for congenital osteopetrosis and it induces normalization of osteoclast function, allowing normal bone hemostasis to be established, which is a prerequisite for normal dental development, and eruption of teeth can be reconstitute.[9] Important differential diagnosis includes other sclerosing bone dysplasias such as sclerosteosis, infantile cortical hyperostosis, pyknodysostosis, craniometaphyseal dysplasia, diaphyseal dysplasia, melorheostosis, and Engelmann's disease. Osteosclerosis from fluoride poisoning and secondary hyperparathyroidism from renal disease may also produce a general sclerotic appearance. All these

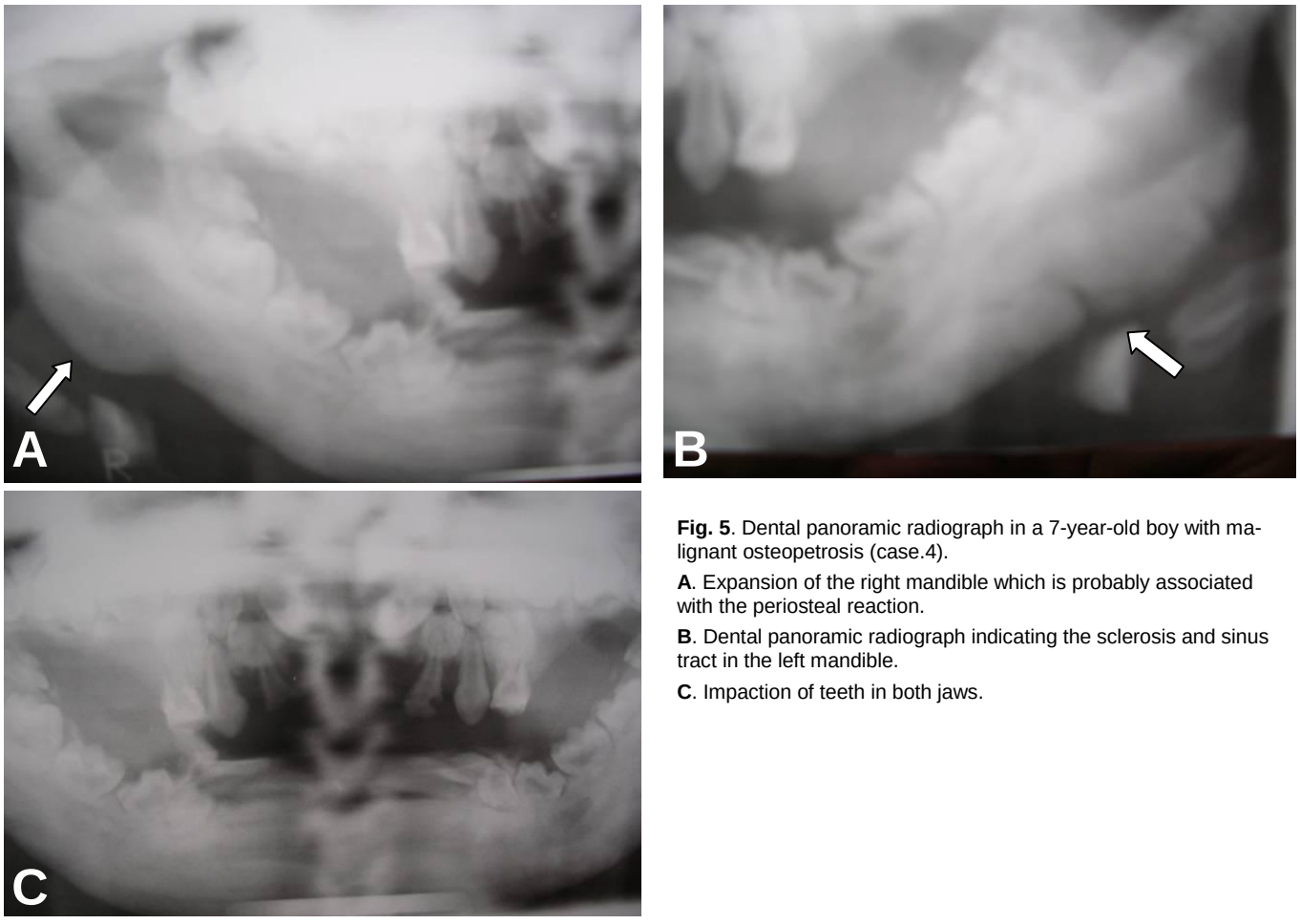

Fig. 5. Dental panoramic radiograph in a 7-year-old boy with malignant osteopetrosis (case.4).

A. Expansion of the right mandible which is probably associated with the periosteal reaction.

B. Dental panoramic radiograph indicating the sclerosis and sinus tract in the left mandible.

C. Impaction of teeth in both jaws.

entities have characteristic clinical, biochemical and /or radiological findings, which help to differentiate them from osteopetrosis.[4] Regarding all cases in this report, diagnosis of malignant osteopetrosis was previously proved. In this present article, our findings are similar to characteristics previously reported in the literature about patients with malignant osteopetrosis. These four cases show clinical findings that were compatible with those described in the literature which include short stature, frontal bossing, hypertelorism, exophthalmus, broad face, and a snubbed nose. These findings were evident in all four cases.[4,11] Neurological abnormalities such as hearing loss, deafness and mental retardation were evident in the first two cases. In the fourth case these defects were seen six months after the first visit. The radiographic findings including an overall sclerotic appearance in the jaw, and obliteration of medullary cavities, in which the maxilla was more sclerotic than the mandible are compatible with those described in the literature. This increased bone density, initially presented as thickening of lamina dura, obscures the roots.[4,9-11] Although it has been reported that the mandible is less frequently involved than other bones,[11] it was affected in all cases of our study which was similar to findings of Filho et al.[8]

The dental findings of absent and impacted teeth, malformed roots and crowns, hypoplastic teeth, missing roots and dental decays correspond with those reported by several authors.[4,9,11-13]

Infection and sinus tract formation was evident in case 3 and 4. One interesting finding in our report was the detection of two cases in the same family (a sister and a brother), in which clinical and radiological findings were similar and another interesting finding was the involvement of both the maxilla and the mandible in all cases. In conclusion, special attention should be paid to patients with osteopetrosis due to their fragile bone status, resulting from defects in osteoclast function and consequent impaired wound healing. These patients should receive increased attention and prophylactic dental treatment to maintain their fragile oral health status. Continuous and vigorous preventive measures should be maintained. To ensure management of serious adverse effects that may rise from oral surgery, the dentist should refer patients with osteopetrosis to a specialist for even the simplest extraction or other surgical dental procedures. However, every effort should be made to avoid extractions in this high-risk group of patients because it may result in jaw fracture.

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