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Infantile Osteopetrosis: A case Report in Yemen

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Abstract

Malignant infantile osteopetrosis, is a rare genetic osteosclerosing type of skeletal dysplasia that typically presents in infancy and is characterized by a unique radiographic appearance of generalized hyperostosis - excessive growth of bone, which has a special predilection to involve the medullary portion with relative sparing of the cortices. The clinical presentation varies widely based on the type of osteopetrosis and ranges in severity from asymptomatic to a fatal course. In this paper we report a 3 years old Yemeni male child with infantile osterpetrosis presented with fever, hepatosplenomegaly, and growth retardation**.**

Key words: Osteopetrosis, osteoclast, Yemeni child.

1-Introduction

Osteopetrosis is a clinical syndrome characterized by the failure of osteoclasts to resorb bone. As a consequence, bone modeling and remodeling are impaired [1]. The defect in bone turnover characteristically results in skeletal fragility despite increased bone mass, and it may also cause hematopoietic insufficiency, disturbed tooth eruption, nerve entrapment syndromes, and growth impairment[2,3]. The actual incidence is unknown but it is estimated to be 1 case per 100,000–500,000 population (Stark and Savarirayan, 2009)[4]. Osteopetrosis was first described in 1904, by German radiologist Albers-Schönberg who in 1904 described a 26-year-old man with generalized sclerosis of the skeleton with multiple fractures[2]. In human, 3 distinct clinical forms of the disease_ infantile, intermediate, and adult onset_ are identified based on age and clinical features[3]. The clinical manifestations are varies related to the underlying defect in osteoclastic activity

and increased bone density. Children exhibit characteristic phenotypic features such as macrocephaly, broad face, and frontal bossing. Bone fractures occur because the bones are dense but fragile, and failure to thrive occur. Neurological manifestations occur due to overgrowth and narrowing of cranial foramina which leads to nerve compression most frequently optic, auditory and facial nerves resulting in blindness, hearing loss, and facial palsy; sometimes patients develop hydrocephalus. Continued bone formation and thickening interfere with medullary hematopoiesis which leads to bone marrow failure and compensatory extramedullary hematopoiesis occurs in various organs such as the spleen and liver, eventually resulting in hepatosplenomegaly, anemia, thrombocytopenia, granulocytopenia, and recurrent infections[5,6]. The mainstay of diagnosis is clinical and largely depends on the radiographic appearance of the skeleton[4]. The radiological features of osteopetrosis show a characteristic sign of increased bone density and bone on bone appearance, help in establishing the diagnosis[7]. Hematopoietic stem cells transplantation (HSCT) from human leukocyte antigen (HLA) identical donors is the only treatment that has been proven to change the course of the disease [8].

2. Case Presentation

A 3-year old boy was admitted for growth retardation and recurrent fever. He was born at term after an uneventful pregnancy from consanguineous parents. Parents reported delayed developmental millstones, dentition; and growth retardation as compared to a child at the same age. Easy skin bruising was also reported but no history of blood transfusion. Visual contact was also said to be poor since birth.

Physical examination at presentation revealed a pale child with, proportionate short stature (Hight= 82cm and wieght= 11kg) and large head (head circumference at the 25th percentile) (figure 1). Head and neck examination revealed dolicocephalic skull, proptosis with alternating convergent squint, flattened malar eminence [Figure 1&2]. Hepatosplenomegaly was present with a liver at 4 cm below the costal margin. Developmental milestones were significantly delayed.

Laboratory and radiological findings

Laboratory work-up showed anemia and thrombocytopenia (Hb= 7.8 g/dl, white blood cell count was 8.8 cells/mm3, platelet count was 79/mm3). Parathyroid hormone is Elevated [PTH= 265pg/ml (normal range= 14-65pg/ml)].

Skeletal radiographs revealed a generalized increase in bone density, increased sclerosis of both femurs with metaphyseal flaring, (Figures 3). Abdominal ultrasound showed hepatosplenomegaly with a spleen of 12.6 cm of diameter.

Histopathological findings

Bone marrow aspiration was dry tap and shows hypocellularity of all cell lines.

Correlating the radiographic features with the clinical and para-clinical features, the case was diagnosed as infantile osteopetrosis. Palliative care was implemented. Bone marrow transplantation was not done due to unavailability and cost.

3. Discussion:

Osteopetrosis is clinically a highly heterogeneous group of conditions that share the hallmark of increased bone density on radiographs due to abnormalities in osteoclast differentiation or function[9]. There are four subtypes of OP (malignant or infantile OP, Benign or adult OP, intermediate OP, and carbon anhydrase type II (CAII) deficiency[10]. Hematologic manifestations related to bone marrow suppression and subsequent pancytopenia are a major source of morbidity and mortality. Additionally extramedullary hematopoiesis can result in liver and spleen dysfunction[11]. Cranial nerve dysfunction and neurologic complications are usually associated with infantile osteopetrosis[11].

Expansion of the skull bone leads to macrocephaly, delayed motor milestones and poor dentition can occur[11].Characteristic radiographic findings in osteopetrosis include a marked increase in bone density with defective metaphyseal remodeling, and a ″ bone within a bone″ appearance [4,12]. Alternating sclerotic and lucent bands can give the vertebrae a ′ sandwich′ appearance[12]. Computerized tomography scan can be used for diagnosis and to determine the effect of the treatment. It is also used to assess auditory and optic canal [13]. The clinical presentations and skeletal radiologic findings of our patient was specific for osteopetrosis. The most effective treatment for this disease has been bone marrow transplantation because the osteoclasts are from hematopoietic cell origin.

4. Conclusion:

Infantile malignant OP is a lethal disease. Although diagnosis of MIOP is easy and depends mainly on radiographic examination, it's often delayed due to rarity of the disease and lack of clinical suspicion. Early diagnosis and timely HSCT is the only curative treatment approach for MIOP.

Figure 1: Macrocephaly with squint

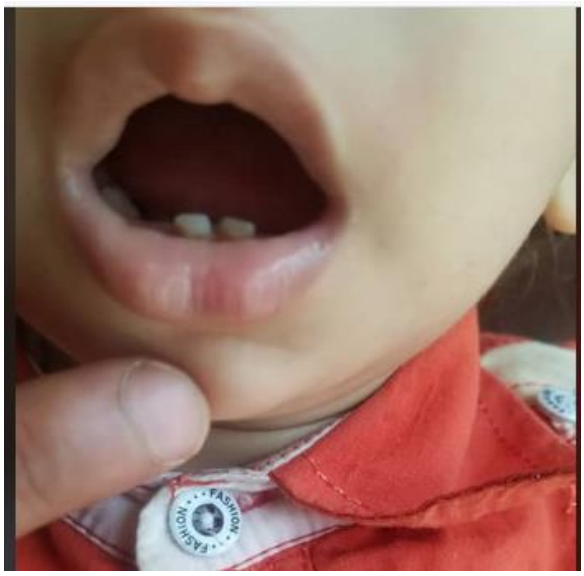

Figure 2: Poor teeth eruption

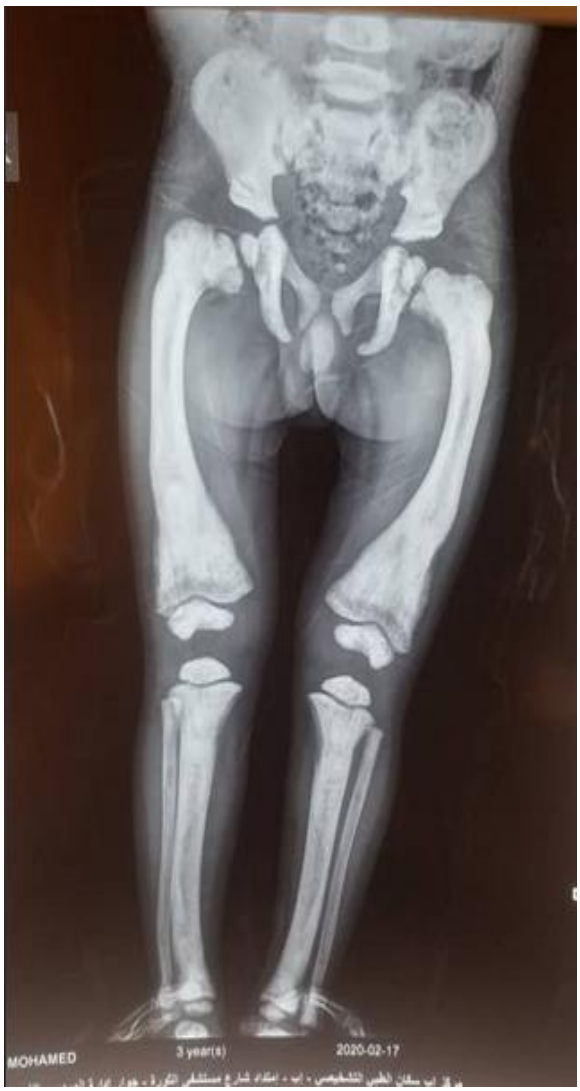

Figure 3: Homogeneous increased density of bone with little Differentiation

between cortex and medulla in long bones and pelvis

5. References:

1. Bubshait D K, Himdy Z E, Fadaaq O, et al. (January 21, 2020) Malignant Infantile Osteopetrosis: A Case Report. Cureus 12(1): e6725. doi:10.7759/cureus.6725.
2. Goswami R: Primer on the metabolic bone diseases and disorders of mineral metabolism. Indian J Med Res. 2016, 144:489-490. 10.4103/0971-5916.198664.
3. Tamer AE, Ezzat E, Ismaiel S, Solaf M. E, Mohamed FK. A case of infantile osteopetrosis: The radioclinical features with literature update. Bone Reports 4 (2016) 11–16.
4. Stark, Z., Savarirayan, R., 2009. Osteopetrosis. Orphanet J. Rare Dis. 4, 5. http://dx.doi.org/10.1186/1750-1172-4-5.
5. Lam DK, Sándor GKB, Holmes HI, Carmichael RP, Clokie CML: Marble bone disease: a review of osteopetrosis and its oral health implications for dentists. J Can Dent Assoc. 2007, 73:839-842.
6. Kalekar T, Sehrawat V: Autosomal recessive infantile osteopetrosis: case report with radiological review. Int J Res Med Sci. 2017, 5:10.18203/2320-6012.ijrms20172490.
7. Sit, C., Agrawal, K., Fogelman, I., Gnanasegaran, G., 2015.
14. Osteopetrosis: radiological & radionuclide imaging. Indian J. Nucl. Med. 30 (1), 55–58. http://dx.doi.org/10.4103/0972-3919.147544.
8. Wilson CJ, Vellodi A: Autosomal recessive osteopetrosis: diagnosis, management, and outcome. Arch Dis Child. 2000, 83:449-452. 10.1136/adc.83.5.449
9. Zornitza Stark, Ravi Savarirayan. Osteopetrosis. Orphanet Journal of Rare Diseases. 2009; 4 (1): 5. PubMed | Google Scholar
10. David KL, George KB, Howard IH, et al. Marble bone disease: a review of osteopetrosis and its oral health implications for dentists. Journal of the Canadian Dental Association. 2007; 73(9): 839-844. PubMed | Google Scholar
11. Orchard PJ, Fasth AL, Le Rademacher J, et al (2015). "Hematopoietic stem cell transplantation for infantile osteopetrosis". *Blood*. 126:270–6. DOI: 10.1182/blood-2015-01-625541. PMC 4497967 PMID 26012570
12. Cherry S, Kanhaiyalal A, Ignac F, Gopinath Gnanasegaran. Osteopetrosis: Radiological & Radionuclide Imaging. Indian J Nucl Med. 2015 Jan-Mar; 30(1): 55–58
13. Shapiro Frederic. Osteopetrosis: current clinical considerations. Clinical orthopaedics and related research. 1993; 294: 34-44. PubMed | Google Scholar