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CASE STUDY

OSTEOPETROSIS: REPORT OF A CASE

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ABSTRACT

Osteopetrosis is a descriptive term that refers to a group of rare, heritable disorders of the skeleton characterized by increased bone density on radiographs. Osteopetrotic conditions vary greatly in their presentation and severity, ranging from neonatal onset with life-threatening complications such as bone marrow failure (*e.g.* classic or "malignant" ARO), to the incidental finding of osteopetrosis on radiographs (*e.g.* osteopoikilosis) (Zornitza Stark and Ravi Savarirayan, 2009). It is caused by the failure of osteoclaststo resorb immature bone. This leads to abnormal bone marrow cavity formation and clinically to the signs and symptoms of bone marrow failure. Impairedbone remodeling causesbony narrowing of the cranial nerve foramina which results in cranial nerve, especially optic nerve, compression. (Wilson and Vellodi, 2000) Classic ARO is characterised by fractures, short stature, compressive neuropathies, hypocalcaemia with attendant tetanic seizures, and life-threatening pancytopaenia. The presence of primary neurodegeneration, mental retardation, skin and immune system involvement, or renal tubular acidosis may point to rarer osteopetrosis variants, whereas onset ofprimarily skeletal manifestations such as fractures and osteomyelitis in late childhood or adolescence is typical of ADO. It is anticipated that further understanding of the molecular pathogenesis of these conditions will reveal newtargets for pharmacotherapy (Zornitza Stark and Ravi Savarirayan, 2009). This paper highlights a rare case of osteopetrosis in an 8 year old boy.

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INTRODUCTION

Osteopetrosis, or marble bone disease, was initially reported by Albers-Schönberg in 1904 as delayed physical development accompanied by bone fragility. It is a pathologically descriptive term referring to a variety of clinical diseases. In humans, the spectrum ranges from mild medical illnesses to severe, lethal conditions. It is genetically determined as either an autosomal dominant benign type or an autosomal recessive malignant type. An intermediate type described by Beighton *et al.* (Hamdan *et al*., 2006) is more prevalent in practice. In the recessive form, the child is severely symptomatic early in life and usually dies of complications of the disease, mainly infections. The dominant type, on the other hand, which is also known as osteopetrosistarda, is more compatible with life. Tips and Lynch (1962) reported no racial or sexual predisposition. A defect in the mechanism of bone remodelling exists and leads to a series of somatic problems in the affected person. Malfunction of osteoclastic activity results in excessive formation of immature bone, thickening of the cortical bones, and narrowing or obliteration of the medullary cavities.

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It is believed that osteoclasts fail to release the necessary lysosomal enzymes for bone resorption into the extracellular space (Priyanka Kant *et al*., 2013). Defects in different genes have been described that lead to a phenotype with osteopetrosis. These defects include mutations in the gene encoding carbonic anhydrase II, the proton pump gene and the chloride channel gene. Recently, the immune response has been incriminated in the pathogenesis of various metabolic bone diseases, including osteopetrosis. Both cytotoxic T lymphocyte associated antigen 4 and programmed death-1, a newly identified immunoregulatory receptor, have been shown to negatively regulate immune responses, and to affect osteoclastogenesis and bone remodelling[6]. The clinical presentation and radiological picture may vary according to the severity of the disease. Bone marrow transplantation has been shown to restore this osteoclastic activity and to alleviate symptoms (Hamdan *et al*., 2006).

Case report

An 8 year old male patientwas referred from VIMS hospital for opinion regarding missing teeth in the upper and lower. Patient was admitted to the hospital for treatment of fractured left arm two weeks back. Patient was apparently normal till 4 years of

age. Parents noticed increased size of head as compared to body at the age of 4years and 6 months. Gradual distension of abdomen on the left side was noted by the parents which was hard to touch. Occasionally patient complained of dull aching pain in the abdomen which was not related to eating or defecating. There were no aggravating or relieving factors. Patient also complained of tiredness and easy fatigue on carrying out daily activities with pain in the limbs when pressed upon. There was history of fever one to two times a month. Each episode lasts for 4-5 days. The patient achieved normal mental milestones. Primary dentition was normal till the age of 6 years. Few primary teeth exfoliated after the age of 6 and permanent teeth had not erupted at the time of examination No history of blood transfusion, or convulsions and weight was not adequate for the patient's age. Patient interacted normally with other people and was able to perform his daily activities with some help. Gradually his vision was affected and patient was unable to focus on any object. Vision was blurred but hearing was normal. There was history of pathological fracture in left arm one month back Patient gave a history of jaundice at the age of 5 years which was treated with ayurvedic medicines. Parents had 2nd degree consanguineous marriage. Fathers age was 34 years and mothers age 31 years at the time of patients birth. No h/o similar complaints or repeated fractures in the family and antenatal, birth and post natal history were normal. On extra oral examination severe pallor was noted. The patient was not able to fix at objects, horizontal nystagmus was present with hypertelorism and sclera above the cornea was visible. There was frontal bossing of the skull with depressed nasal bridge (Fig.1). On intraoral examination seven deciduous teeth were present which appeared normal. No abnormalities were seen in gingival, tongue, hard palate and soft palate.

Radiographic features

Orthopantomogram shows increased density of the maxilla, mandible and the nasal bones. The trabeculae appear thickened and there is obliteration of marrow space. There is loss of corticomedullary differentiation and medullary spaces. Outline of inferior alveolar canal cannot be delineated. Multiple retained deciduous teeth and impacted permanent teeth can be seen (Fig.2). Sclerosis of base of skull with thickening of the outer and inner diploe was seen in the lateral skull radiograph. Radiograph also revealed loss of mandibular angle (Fig.3). In skull Antero-postero view marked sclerosis of the cranial vault was seen. There was generalized thickening of the skull bones with dense frontal and nasal bones. Frontal sinus outline cannot be appreciated (Fig.4). Chest radiograph showed generalized increase in density of the bones with mild cardiomegaly (Fig. 5). Lumbar spine lateral view showed sandwich appearance of veretebrae (Fig.6). Hand wrist radiograph showed bullet shaped phalanges with dense metaphyseal bands (Fig.7). Femur – knee joint radiograph shows loss of corticomedullary differentiation with loss of medullary spaces. Erlyn-Mayer flask shaped appearance of the femur can be appreciated. (Fig.8). Radiograph of humerus shows modelling deformities of proximal end of humerus with loss of cortex and medulla with evidence of pathological fracture at the proximal end (Fig.9). Haematological investigations revealed low Hb (7.4 gm/dl), Serum calcium (8.3 mg/dl) and Serum albumin (3.4 gm/dl). Serum calcium and potassium were within normal limits. Peripheral smear revealed a picture of Microcytic hypochromic anemia with thrombocytopenia.Patient was advised prosthetic rehabilitation of upper and lower jaw. Tab prednisolone 0.7mg/kg/day was advised for first 10 days of every month with Calcitriol sachet with milk once a week for 8 weeks and referred to higher center for bone marrow stem cell transplantation.

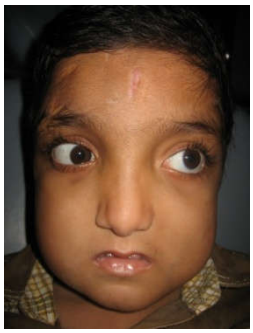

Fig. 1. Frontal view showing hypertelorim, frontal bossing of the skull and depressed nasal bridge

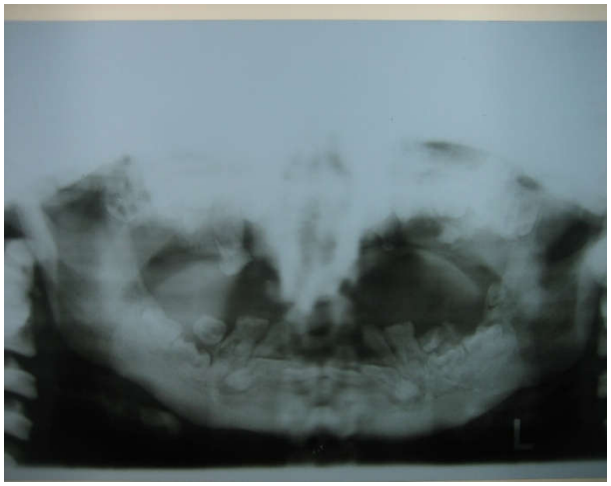

Fig. 2. OPG showing loss of corticomedullary differentiation with loss of medullary spaces

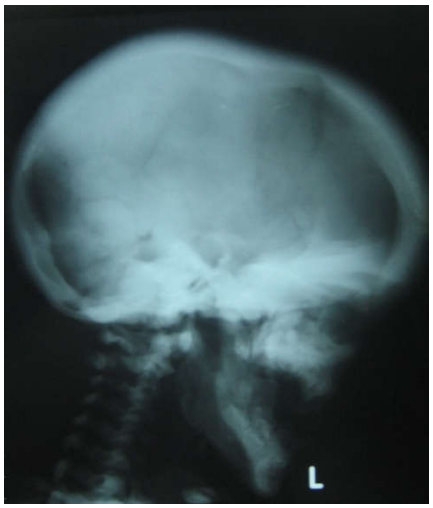

Fig. 3. Lateral skull view showing sclerosis of base of skull. Thickening of the outer and inner diploe .Loss of mandibular angle

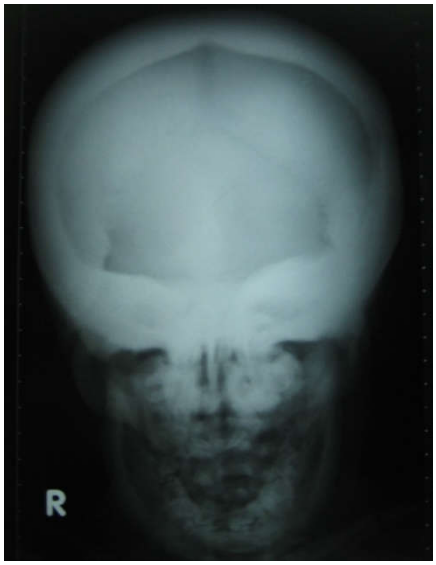

Fig. 4. Sclerosis of base of skull with thickening of the outer and inner diploe was seen in the lateral skull radiograph

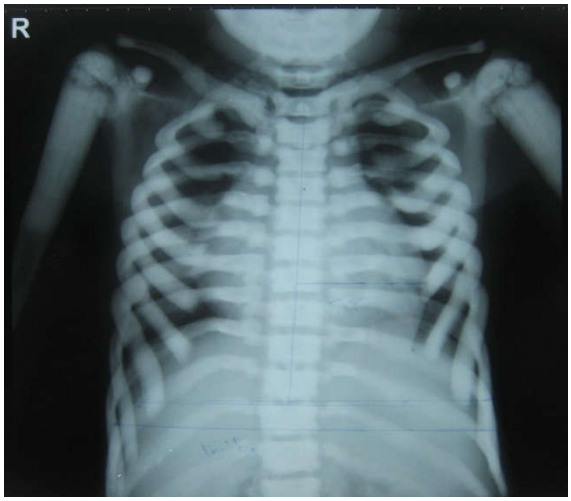

Fig.5. Chest radiograph showed generalized increase in density of the bones with mild cardiomegaly

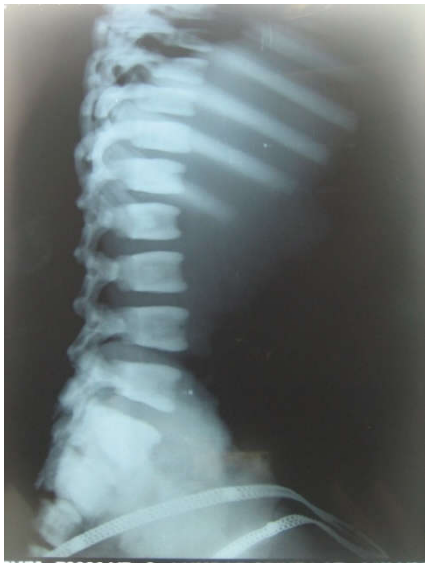

Fig. 6. Lumbar spine lateral view shows sandwich appearance of vertebra

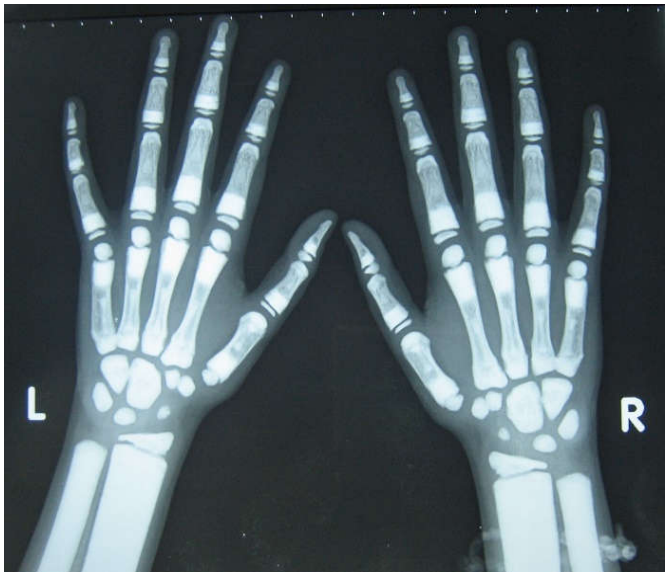

Fig. 7. Hand wrist radiograph showed bullet shaped phalanges with dense metaphyseal bands

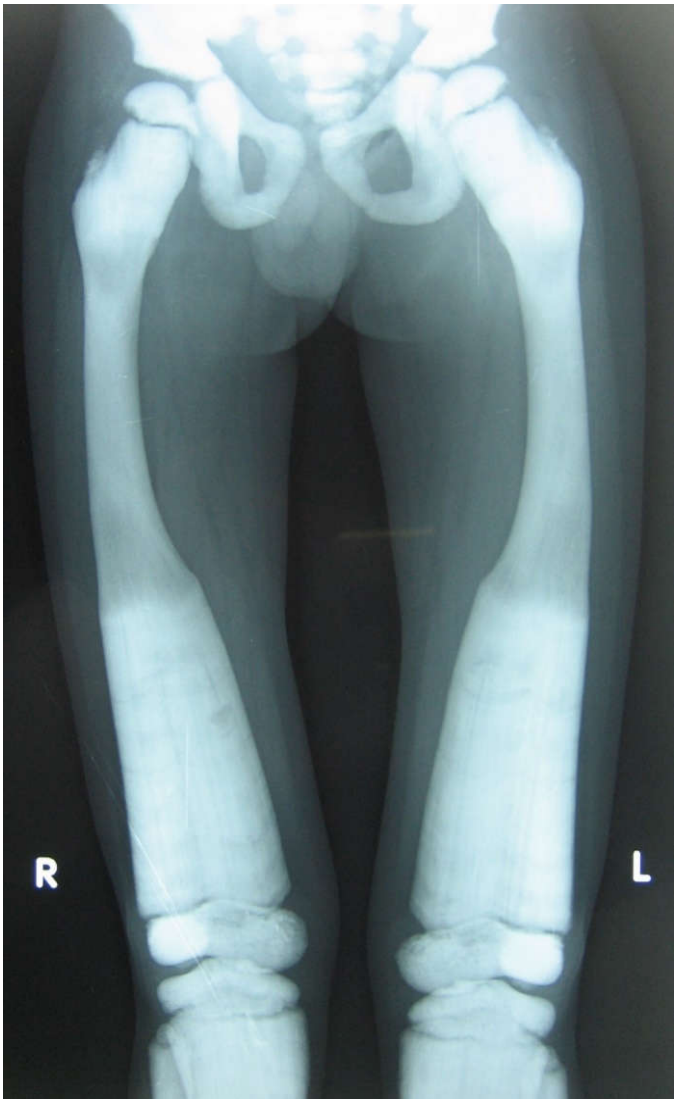

Fig. 8. Femur – knee joint radiograph shows generalized increased bone density.Loss of corticomedullary differentiation with loss of medullary spaces. Erlen-meyer flask appearance

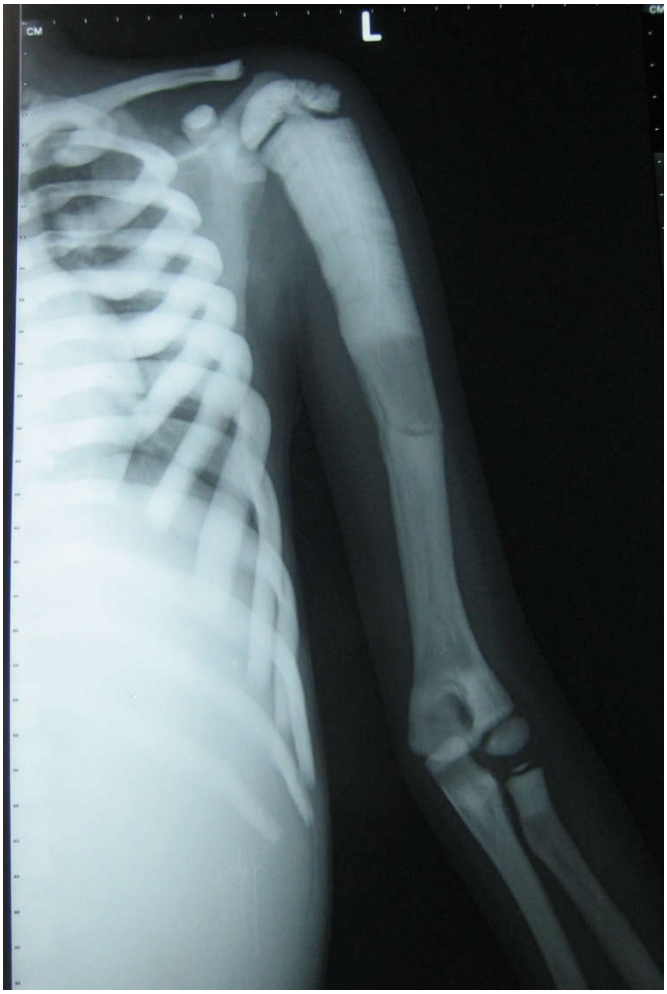

Fig. 9. Radiograph of humerus shows modelling deformities of proximal end of humerus with loss of cortex and medulla with evidence of pathological fracture at the proximal end

DISCUSSION

Bone turnover is a phenomenon that is highly regulated, resulting from the balance process of boneformation by osteoblasts and bone resorption by osteoclasts. Consequently, bone density is dependent on the relative activity of these two types of cells (Elahe Tohidi and Ali Bagherpour, 2012).The basic defect in osteopetrosis is probably a failure of normal osteoclast function, since the number of osteoclasts present is oftenincreased; however, because of their failure, bone is not resorbed. The causes of osteoclast failure are unclear, but may involve abnormalities in the osteoclast stem cell or its microenvironment, osteoblast precursor cells or the mature heterokaryon, or bone matrix (Sekerci*et al*., 2012).The aetiology of osteopetrosisis purely due to defects in the osteoclasts which can be of two types—osteoclast-rich and osteoclast-poor forms. In the former, the osteoclasts are eithernormal or increased in number but are unable to form the ruffle border which is indispensable for resorbing bone. In the osteoclast-poor form, there is a reduction in the number of osteoclasts which could be due to reduced number or absence of osteoclast progenitor/ precursor cells. The defect is with osteoclast ogenesissignalling, hence the progenitor cells do not progress into mature osteoclasts. The ability of mature osteoclasts to resorb bone is also reduced due to mutations in RANKL genes. Lack of bone resorption explains the pathogenesis of haematological and neural failure and of bone fragility (Sharma *et al*., 2013). Anderson *et al.* and others described two sub-types of benign autosomal dominant osteopetrosis (ADO) on the basis of radiological and clinical differences, including ADO Type I and ADO type II. Approximately 40% of patients with the adult form of osteopetrosis are symptom-free, regardless of type. Bone pain is common to both types. Bone marrow failure does not occur in benign osteopetrosis (Sekerci *et al*., 2012). In ADO Type I, the fracture rate is low because of the increased bone strength compared with normal. Radiographs reveal sclerosis of the skull, which mainly affects the cranial vault, with increased thickness of the vault. Cranial nerve compression is common in type I. In contrast to ADO II, the acid phosphatase levels are normal (Elahe Tohidi and Ali Bagherpour, 2012). Infantile malignant osteopetrosis exists at birth or appears within the first months of early childhood. Osteopetrosis patients at birth or early infancy usually have a severe form of the disease and present with a diffusely sclerotic skeleton. The diagnosis of osteopetrosisis, therefore, based on a history of numerous fractures and radiologic findings indicative of osteosclerosis, although the radiologic features are usually sufficient tomake a definitive diagnosis (Sekerci *et al*., 2012). Osteomyelitis is the common clinical manifestation in patients with autosomal dominant osteopetrosis type II. Waguespack *et al*. reported osteomyelitis of the femur inindividuals after surgical repair of the fracture. B´enichou *et al*. reported osteomyelitis in 11% of the patients. Ourcase had no signs and symptoms of osteomyelitis affecting any of the bones (Tips and Lynch, 1962). The dental changes reported to be associated with OP include disturbance of tooth eruption due to impaired alveolar bone resorption of osteoclasts, hypodontia, malformed teeth, multiple caries, enamel dysplasia, abnormal pulp chambers, and hypercementosis. The increased bone density, initially presented as thickening of lamina dura, obscures the roots. Multiple dental caries, pulpoperiapical lesions, hypoplastic maxillary sinuses and the loss of contrast between the inferior cortical border and the cancellous portion of the bone were seen in both of our cases, consistent with those reported by several authors (Elahe Tohidi and Ali Bagherpour, 2012).

Treatment of severe infantile malignant osteopetrosis is either bone marrow transplant or haematopoietic stem cell transplant. Treatment with calcitriol to stimulate dormant osteoclast has been tried with mixed success. Other therapies including interferon and corticosteroids have been reported. Management of this condition depends on the type and clinical severity of the disease. The aggressive infantile malignant ARO still carries a significant mortality rate. Late onset osteopetrosis of ADO type II may not be fatal but still leaves a significant morbidity for the patient (Sharma *et al*., 2013).

Conclusion

Despite recent advances in the understanding of the pathogenesis of osteopetrotic conditions, the genetic basis of approximately 30% of cases remains to be elucidated. It is hoped that ongoing research into osteoclast physiology will result in novel therapeutic targets. Bone marrow transplantation

is the only treatment that has been proven to significantly alter the course of disease. While successful recipients may continue to have minor orthopaedic and dental problems and their vision rarely significantly improves, their haemopoietic potential is restored and the long term prognosis is favourable.

REFERENCES

Bonapace *et al*. 2014. Identification of two novel mutations on CLCN7 gene in a patient with malignant ostopetrosis. *Italian Journal of Pediatrics*, 40:90.

Elahe Tohidi1, Ali Bagherpour. 2012. Clinicoradiological findings of Benign Osteopetrosis: Report of Two New Cases. *JODDD*, Vol. 6, No. 4.

HamdanALH, MM Nabulsi, FT Farhat, RK Haidar, NS Fuleihan. 2006. When bone becomes marble: Head and neck manifestations of osteopetrosis. *Paediatr Child Health*, 11(1):37-40.

Priyanka Kant, Neelkamal Sharda, Rahul R. Bhowate. 2013. Clinical and Radiological Findings of Autosomal Dominant Osteopetrosis Type II: A Case ReportCase Reports in Dentistry, 1-8.

Sekerci *et al*. 2012. Infantile Malignant Osteopetrosis: Report of 2 Cases with Osteomyelitis of the Jaws. *Journal of Dentistry for Children*, 79:2.

Sharma SS, *et al*. 2013. BMJ Case Reports, doi:10.1136/bcr-2012-007487.

Tips RL, Lynch HT. 1962. Malignant congenital osteopetrosis resulting from a consanguineousmarriage. *ActaPaediatr*., 51: 585–8.

Wilson, C J.2000. A Vellodi. Autosomal recessive osteopetrosis: diagnosis, management, and outcome. *Arch Dis Child*, 83:449–452.

Zornitza Stark1, Ravi Savarirayan. 2009. Osteopetrosis. *Orphanet Journal of Rare Diseases*, 4:5.

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