A MALIGNANT INFANTILE PSTEOPETROSIS: TWO CASE REPORTS

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ABSTRACT

Osteopetrosis designated by Karshner (1926) formerly known as ‘Marble Bones’ by Albers-Schonberg is a rare hereditary, generalized disorder of bone characterized by a significant increase in the density of the skeletal tissues and failure of tubulization, with persistence of calcified cartilage.

The present article documents two cases showing features of osteopetrosis in conventional radiography, in a 2-year-old child and a 4 year child came within an interval of 1 year to Maharajah’s Institute of Medical Sciences, Vizianagram, Andhra Pradesh, India.

Keywords: Osteopetrosis, Marble Bones, Bone disorder

INTRODUCTION

Osteopetrosis or Albers-schonberg disease, is a rare hereditary, generalized bone disorder that results from defective osteoclasts and overgrowth of bone. The bones become thick and sclerotic without any aid towards its strength. Consequent impaired bone resorption and endochondral formation replaces haematopoietic cells in the medullary cavity, and also increases the incidence of fractures due to bone fragility. The reduction in haematopoietic cells can also cause haematological abnormalities including thrombocytopenia, anaemia, susceptibility to infections and extramedullary haematopoiesis. Neurological manifestations of osteopetrosis can also occur due to narrowing of osseous foramina.

Overall incidence of osteopetrosis is estimated to be 1 case per 100,000-500,000 population. However, the actual incidence is uncertain.

CASE REPORT 1

Our first case is a 4 years old male child brought to pediatrics outpatient department of our hospital, with complaints of fever, nasal congestion since 4 days and failure to thrive. There is history of recurrent URTI and LRTI since infancy with h/o febrile convulsions and HRAD.

Family history: He was born of consanguineous marriage. Antenatal history is G3P2L2A1. 1st pregnancy ended in abortion, the 2nd child is alive and is suffering from grade III PEM and splenomegaly and the 3rd Child,(our case) is a term child with birth weight of 2.5kg delivered by LSCS.

O/E: The patient was short statured (his length and weight are below 3rd percentile) and his cranial perimeters were between 75th and 90th percentile.

Patient was pale with mild icterus and abdominal distension. Frontal bossing, parietal bossing and low set ears were noted. Blood investigations revealed severe anaemia and thrombocytopenia. Hb-4.8g/dl, PLT-35,000/cu.mm,TLC-8,100/cu.mm and S.BILIRUBIN-2mg/dl. Serum calcium was normal. On USG: There is moderate hepatosplenomegaly and cholelithiasis (3mm size).

Radiograph of chest was done to rule out chest infection (figure1a).

On Radiograph, generalized increase in bone density was noted and then a skeletal survey was done which showed.

Skull AP view: sclerosis of the orbits and sphenoid bones resulting in “Harlequin mask appearance”. Skull lateral view: increased thickness of skull base with prominent sella and posterior clinoid.(figure1b)

X ray thoracolumbar spine AP/Lateral vertebral endplate sclerosis resulting in “sandwich vertebrae “appearance (figure1c)

Pelvis and lower limbs radiograph: Generalized increased bone density, bowlegs and ”Erlenmeyer flask deformity” (clublike long bones with flaring of ends) (figure 1d)

CASE REPORT 2

Second case is a 2year old female child presented with fever, respiratory distress, progressive blindness, failure to thrive, hepatosplenomegaly and generalized lymphadenopathy. General examination revealed pallor and frontal bossing.
Fundus examination revealed bilateral optic atrophy. On investigations she had anemia with hemoglobin 7.0 gm%, TLC - 4000, PCV 20%, and platelet count of 40,000. Peripheral smear suggestive of microcytic hypochromic cells with reduced platelets.

Radiograph of chest was done to rule out chest infection. X-rays showed the thick bones with increased bone density arousing suspicion for osteopetrosis hence skeletal survey was conducted which showed

Skull AP/Lateral - Extensive sclerosis of the skull (figure2f,g)

Thoraco-lumbar spine-sandwich vertebrae/rugger jersey spine i.e. alternating sclerotic and radiolucent transverse metaphyseal lines representing fluctuating course of disease (a,b)

Phalanges-bone within bone i.e., inner layer of cortical new bone within an existing bone (figure2d,e)

Leg-long bones showing Erlenmeyer flask deformity, splayed metaphysis, club like shape with flared ends.(figure 2c)

![Figure 1a: Chest x ray PA view showing generalized increase in bone density.](image1)

![Figure 1b: Skull AP: Sclerosis of the orbits and sphenoid bones (Harlequin mask appearance). Skull Lateral: Increased thickness of skull base with prominent sella and posterior clinoid.](image2)
Figure 1c: Thoracolumbar spine AP/Lateral: vertebral endplate sclerosis (sandwich vertebrae appearance).

Figure 1d: Pelvis and lower limbs radiograph: Generalized increased bone density, bowlegs and "Erlenmeyer flask deformity" (clublike long bones with flaring of ends)
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.\(^5\)

There are four subtypes of OP

a. Malignant or Infantile OP
b. Benign or adult OP
c. Intermediate OP
d. Carbon anhydrase type II (CAII) deficiency.  

a. Infantile autosomal recessive; Malignant infantile osteopetrosis (MIOP) is the autosomal recessively inherited form of this disease that generally begins in utero. It presents at birth or within the first year of life and is associated with increased severity compared to the autosomal dominant form.

b. Benign Adult Autosomal Dominant Osteopetrosis
Autosomal dominant form can be further divided into:

Type 1: Marked thickening of the sclerotic skull vault, but with an almost normal spine.

Type 2. A sclerotic skull base and a ‘Rugger Jersey’ spine. Patient with type 2 have a high risk of fracture than those with type 1.

c. An intermediate form with recessive inheritance.

d. A syndrome of carbonic anhydrase 2 deficiency associated with renal tubular acidosis.

Radiographic Findings
Taking skeletal survey leads to a good diagnosis but on the cost of heavy radiation to the patient. Skull radiograph can show sclerosis predominantly involving base of skull, calvaria often spared, hair-on-end appearance of cranial vault can also be evident. Jaw -crater-like lytic lesion, unerupted teeth and lack of corticomedullary differentiation. Phalanges-Pyknodysostosis, showing bone in bone appearance. Sandwich Vertebra-appearance of vertebra in osteopetrosis due to increased density of endplates,alternating sclerotic and radiolucent transverse metaphyseal lines; Long bones- Longitudinal metaphyseal striations, Obliteration of mastoid air cells,paranasal sinuses,basal foramina by osteosclerosis.

The disease has been treated with Haematopoietic Stem Cell Transplantation (HSCT), which in most cases improves but does not to fully rescue the phenotype. This approach has mostly been used to treat Autosomal Recessive variant, with >50% of successful engraftment and several undesired effects, including the progression of neural failure with vision deterioration. Some attempts have been made to cure CAII deficiency (defined as Intermediate Autosomal Osteopetrosis ) with HSCT with similar outcome. The results of pharmacological treatments with corticosteroids, vitamin D/calcium supplementation, PTH or gamma-interferon are inconsistent and generally cannot substitute for HSCT, with a very few exceptions. Treatment of Autosomal Recessive Osteopetrosis is generally based on empiric approaches. No guidelines are available so far for therapy and usually patients are treated symptomatically.

The conservative treatment of patients with OP is not the primary subject of this protocol and patients should be managed in a multi-disciplinary setting according to their clinical. These guidelines will focus on HSCT with particular respect to its indication, conditioning and follow up. HSCT using HLA-identical donors has an acceptable outcome (73% five-year disease-free survival). The success rate of HSCT from experienced centres using alternative sources as T-cell depleted hematopoietic stem cells from HLA-haploidentical family donors or cord blood from unrelated donors has improved markedly in recent years.

CONCLUSION
Benign and adult form shows normal life expectancy, whereas infantile autosomal recessive form tends to be still birth, survival beyond middle life is highly unlikely due to recurrent infection ,massive hemorrhage and terminal leukaemia. Conventional radiographic examination, often give complete picture of the disease. Early diagnosis and timely HSCT is the only curative treatment approach for MIOP

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