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MALIGNANT INFANTILE OSTEOPETROSIS

Paediatrics

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ABSTRACT

Osteopetrosis is a disorder involving defective bone resorption [1]. Two main forms of osteopetrosis have been delineated: a severe autosomal recessive form with an incidence of 1 in 250,000 births and a mild autosomal dominant form with an incidence of 1 in 20,000 births [1]. Intrinsic disturbances of osteoclast function due to mutations in genes encoding osteoclast-specific subunits of the vacuolar proton pump are found in most patients [1]. Here we report a 3 year 10 months old female child with chief complaints of Fever since 4 days followed by Nasal bleed since 1 day prior to admission.

KEYWORDS

Infantile malignant Osteopetrosis, fatal, genetic, marble bone disease, hepatosplenomegaly.

INTRODUCTION:

Osteopetrosis is a rare congenital genetic disease characterized by increased bone density due to impaired bone resorption by osteoclasts [3]. It is classified into three forms: Infantile malignant autosomal recessive (AR) osteopetrosis, intermediate (AR) osteopetrosis and autosomal dominant (AD) osteopetrosis. The autosomal dominant form (AD) of osteopetrosis is usually asymptomatic. It is diagnosed incidentally or may exhibit mild symptoms in later life, but is compatible with long term survival[2]. Autosomal recessive (AR) malignant infantile osteopetrosis (MIOP), is uncommon however, it is a severe fatal disorder. Incidence of Incidence of AR form is 1 in 250,000 births and if untreated has a fatal outcome [1]. This condition is most commonly diagnosed soon after birth or within 1st year of life with severe symptoms of abnormal bone remodeling, including significant hematologic abnormalities with bone marrow failure and extramedullary hematopoiesis, resulting in hepatosplenomegaly, a characteristic macrocephaly with frontal bossing, exophthalmos, bonefractures, and failure to thrive[3].

CASE REPORT:

A 3 year 10 months old female child born to 3rd degree consanguineous couple residing at Tanuku presented to us with complaining of Fever since 4 days followed by Nasal bleed since 1 day prior to admission.

Fig 1: picture showing frontal bossing of child

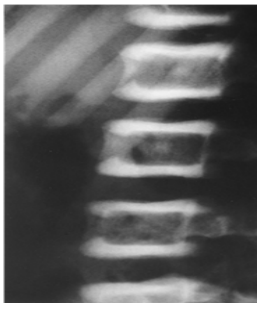

Fig 2: x-ray lateral spine showing endplate sclerosis of vertebrae – sandwich appearance

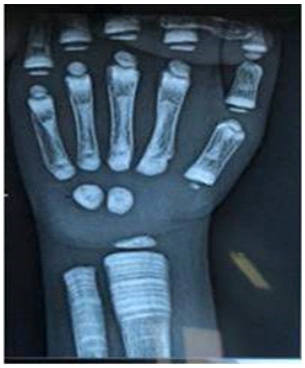

Fig 3: x-ray Left wrist showing sclerosis with loss of medullary space and giving bone with in bone appearance in metacarpals

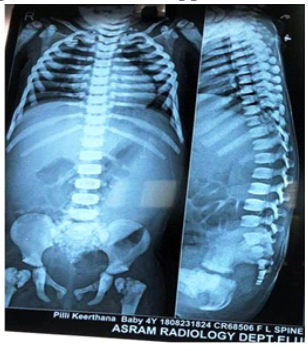

Fig 4:X-ray chest AP and spine lateral view showing diffuse sclerosis involving all visualized bones.

- **Past H/O:** Child had recurrent episodes of epistaxis since nine months of age. Child was not on regular follow up. Mother noticed progressive pallor and child was requiring 1 blood transfusion for every 2 months.
- **Anthropometry:** Falls under Grade 2 PEM according to IAP classification.
- **General examination:** child had pallor, skull- frontal bossing present, oral cavity – malocclusion of teeth present along with dental caries of upper and lower lateral incisors.
- **Systemic examination:** Abdomen is grossly distended with visible veins. Hepatomegaly present with liver span of 9cm, smooth surface, non tender and firm in consistency. Grade V splenomegaly present which is firm in consistency. No evidence of

free fluid in the abdomen noted. CVS: S1 & S2 heard, Grade 3 ejection systolic murmur heard over pulmonary area. Other systems were found to be normal. Suspecting hemolytic disorder following investigations were sent.

- **Investigations:** Hb- 4.1 gm/dl, Total counts- 1400 cells/mm^3, Platelets- 13,000 cells/mm^3, Reticulocyte count- 1%. Peripheral smear has shown anisocytosis, poikilocytosis, polychromatophilia, nucleated RBCs without any blast cells. LFT, RFT, ABG, Sr. Calcium and coagulation profile were within normal limits. Hb electrophoresis was normal. Sickling test, Osmotic fragility test and Direct coombs test were found to be negative. **Bone marrow examination:** cortical bone with intervening marrow showing haemopoeitic foci in trabecular spaces and appear widened with irregular thickness suggested skeletal survey of bone pathology. X ray left wrist has shown sclerotic bones with loss of medullary space giving bone with in bone appearance in metacarpal bones. X ray spine lateral view shows endplate sclerosis of vertebrae – sandwich appearance.
- **Differential diagnosis:** 1. Congenital haemolytic anemia with hypersplenism, 2. Myeloproliferative disorders – juvenile myelomonocytic leukemia, 3. Pyknodysostosis & 4. Osteopetrosis with renal tubular acidosis.

DISCUSSION:

MIOP is a AR form which if untreated has a fatal outcome[4]. The diagnosis of MIOP is based on typical clinical and haematological parameters and charectiristic radiological changes of increased bone density. The characteristic radiological feature is generalised sclerosis of bone.

In this present case, child presented to us with recurrent epistaxis, failure to thrive, pancytopenia and hepatosplenomegaly. The haematological manifestations are due to obliteration of marrow cavity leading to leuko-erythroblastic bone marrow. Cells of promyeloid series may be found due to ineffective marrow function, which was found in our case. Hepatosplenomegaly develops because of extramedullary hematopoiesis. Hypersplenism may lead to thrombocytopenia, who may present with bleeding symptoms similar to present case. Anemia and thrombocytopenia is a constant feature in most of the studies[2]. Severe forms are detected in infancy or earlier because of macrocephaly, hepatosplenomegaly, deafness, blindness and severe anemia. Dental problems, pathological fractures, psychomotor delay are common. The characteristic radiologiacal feature of osteopetrosis is generalised sclerosis of bone [2]. Untreated patients mostly die during infancy and rarely survive beyond second decade. Children surviving beyond 2 years have normal intelligence despite hearing and vision loss. We have conservatively managed the child. Hematopoietic stem cell transplantation is the definitive therapy and should be done before development of secondary complications.

COCLUSION:

Although diagnosis of MIOP is easy and depends mainly on radiographic examination, its 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, an otherwise fatal disease.

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