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Osteopetrosis a Rare Cause of Anemia - Case Report

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Abstract

Malignant Infantile Osteopetrosis (MIOP) is a rare genetic disorder due to abnormal osteoclast activity. We report a case of two year old girl, diagnosed as MIOP while investigating the cause of anemia with hepatosplenomegaly and hydrocephalus. Her medical history revealed non consanguineous parents. Systemic examination showed severe anemia, hepatosplenomegaly, growth failure, and rickets. Skeleton radiographs detected generalized dense bone. Cerebral CT scan revealed hydrocephalus. MIOP was suspected based on clinical, radiological and haematological findings. MIOP should be kept in mind as a rare cause of anemia. Early diagnosis and timely hematopoietic stem cell transplantation are the only curative approach for an otherwise fatal disease.

Keywords- *Osteopetrosis, hepatosplenomegaly, hydrocephalus*

INTRODUCTION

Malignant infantile osteopetrosis (MIOP) is a rare genetic disorder in which defective bone absorption by osteoclasts leads to excessive bone deposition , which replaces haematopoietic cells in the medullary cavity and also increases the incidence of fractures due to bone fragility. The reduction in haematopoietic cells causes haematological abnormalities including thrombocytopenia, anaemia, susceptibility to infections and extramedullary haematopoiesis. Neurological manifestations of osteopetrosis occur due to narrowing of osseous foramina. We

report a case of MIOP with hydrocephalus and rickets.

CASE REPORT

A Two year old girl was admitted with complaints of fever, cough and increased crying since 4 days. She also had abdominal distention since last 6 months. She was a first product of non consanguineous marriage. Her weight was 6.7 Kg, height was 68 cm (both <5 centile NCHS) but her head circumference was 50 cm (>97percentile NCHS).She had mild developmental delay and nystagmus in both eyes. On examination she had severe pallor, tachycardia, tachypnoea with subcostal and intercostals indrawing. Anterior fontanel was open (3 by 3 cm) & pulsatile. She had signs of rickets (pectus carinatum,Harrison sulcus and rickety rosary).She had firm,nontender ,smooth liver extending 4 cm below right costal margin and a firm spleen 8 cm below left costal margin. She had bilateral crepitations & soft systolic murmer.

Her investigations revealed Haemoglobin of 2.9 gm%, Total leukocyte count was 25,100/mm^3 with differential count of polymorphs 40%,lymphocytes,46%,eosinophils2%,monocytes 12%.Her platelet count was severely depleted 13,000/mm^3.Retic count was 2.8%.The blood smear was suggestive of severe hypochromic microcytic anaemia with few macrocytes & grossly reduced platelets. Other investigations revealed Serum calcium8.1mg%,Serum phosphorous 4.7mg%,Serum alkaline phosphatase 640 IU/L. Liver and kidney function tests were normal. CT scan brain showed hydrocephalus with generalized brain atrophy. Fundoscopy revealed early optic atrophy.

Skeletal survey revealed generalized increase in bone density with characteristic ‘bone in bone appearance’ in the long bone, chest and the base of the skull. (Fig 1-4). Rickety rosary was observed in the chest but the ends of the long bones did not show any cupping or fraying. (Fig 3,4).Hence the diagnosis of osteopetrosis with lower respiratory tract infection and rickets was made.The child received packed cell transfusion and broad spectrum antibiotics. Parents were explained about the prognosis and the nature of the disease.

Within 2 months of discharge she got admitted with tachycardia, tachypnoea & marked pallor. She had developed pronounced frontal bossing,cheeck prominence and the organomegaly had increased. Liver had increased to 6 cm below costal margin & spleen to 11 cm below costal margin. She was, given packed cell transfusion and was started on prednisolone, Vitamin D, calciumorally and was asked to follow up regularly. She died 4 months after discharge due to pneumonia at her native place.

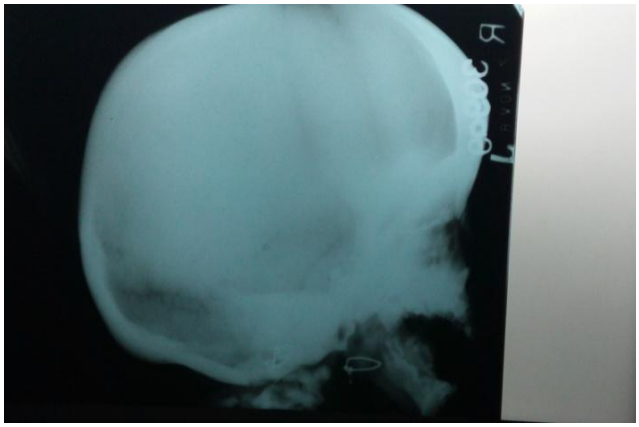

Figure 1: Lateral skull radiograph. Note increased thickness of skull base

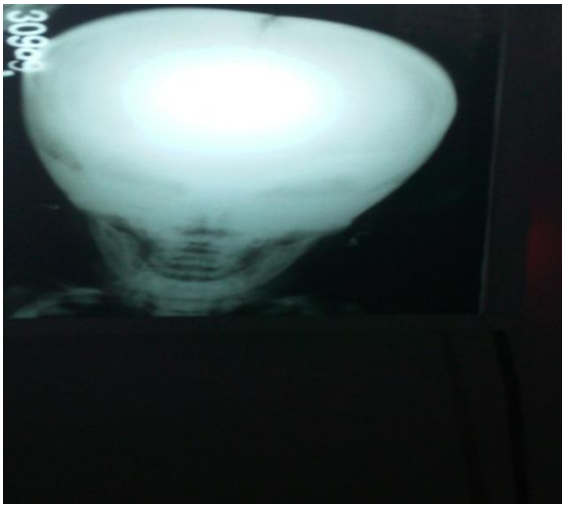

Figure 2: Facial skull radiograph. Note sclerosis of the orbits and sphenoid bones resulting in "Harlequin mask appearance''

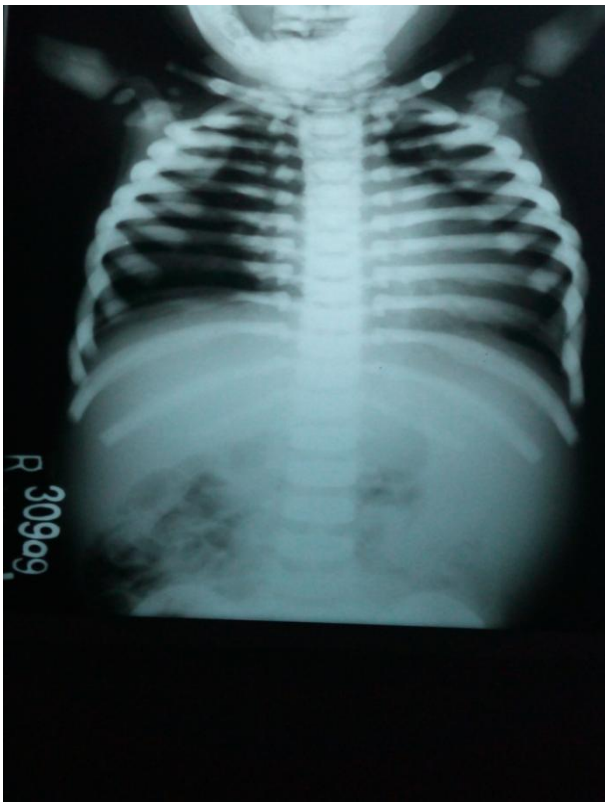

Figure 3: Generalised increase in the bone density andrachitic rosary

DISCUSSION

Osteopetrosis (OP) 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. There are four subtypes of OP (a) malignant or infantile OP, (b) Benign or adult OP, (c) intermediate OP, and (d) carbon anhydrase type II (CAII) deficiency [1,2].

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 [1,3,6]. Our patient had the symptoms since the age of eighteen months. It has an incidence of 1 in 250.000 births, with a particularly high incidence reported in Costa Rica (3.4:100000) [3]. The increase in bone mass leads to phenotypic features such as macrocephaly and frontal bossing. The abnormal expansion of bone

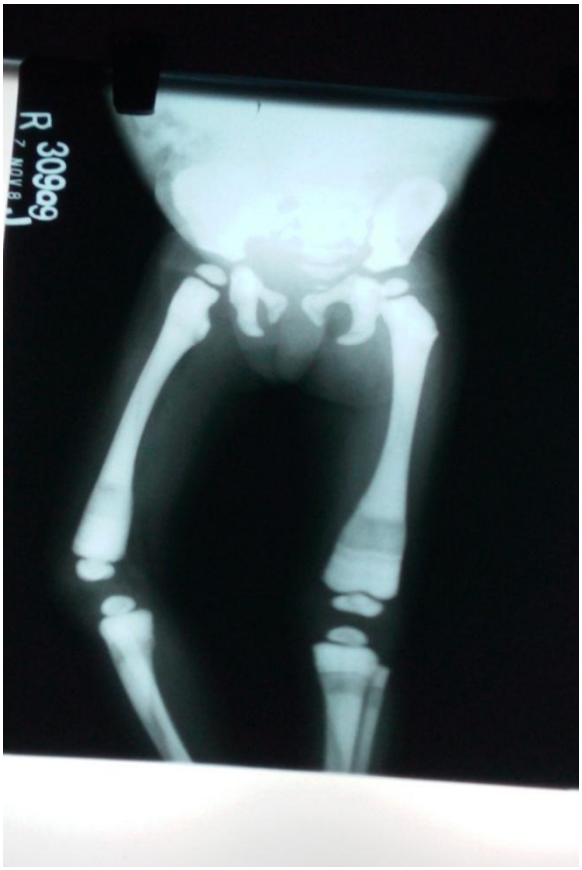

Figure 4: Note metaphyseal modelling defects, Erlenmyer flask deformity of the femur and characteristic lucent bands

Which interferes with medullary haematopoiesis, resulting in life-threatening anemia, thrombocytopenia, increased susceptibility to infections, and secondary expansion of extramedullary haematopoiesis sites such as the liver and spleen [2,5]. Visual impairment, nasal obstruction,tooth eruption defects are also common. The longitudinal growth of bones is impaired with a short stature and predisposition to fractures and osteomyelitis. Our reported case showed all these characters except bony fractures and osteomyelitis [1, 2, 3].

Parental concern regarding the child's vision is the most common presenting complaint [2, 4].Our patient had bilateral optic atrophy with nystagmus. The most commonly observed neurological manifestations of osteopetrosis are secondary to obstruction of the foramina through which the cranial nerves, spinal cord and major blood vessels transverse the skull, resulting in blindness, hearing loss, facial palsy and hydrocephalus [1,2,3]. Our child had hydrocephalus with generalized cerebral atrophy.

hypocalcemia MIOP are at risk of developing hypocalcemia, with attendant tetanic seizures and secondary hyperparathyroidism[6]. Rickets is a common and paradoxical feature of MIOP and results from the inability of osteoclasts to maintain a normal calcium-phosphorus balance in the extracellular fluid. Despite a markedly positive total body calcium balance, rickets arises when the serum calcium x phosphorus product is insufficient to mineralize newly formed chondroid and osteoid.The above patient showed Calcium to phosphorous ratio < 40 and clinical features of rickets. [7,8].(Fig 3)

Characteristic radiographic findings in osteopetrosis include a marked increase in bone density with defective metaphyseal remodelling and a ″bone within a bone″ appearance [1, 3]. (Fig 3,4).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 [1]. The skeletal survey and CT scan of our patient was specific for radiologic findings of osteopetrosis.

Management of patients with osteopetrosis requires a comprehensive approach to characteristic clinical problems including haematological and metabolic abnormalities, recurrent infections, bone complications and neurological sequel [1]. At present, Hematopoietic stem cell transplantation (HSCT) offers the only chance of cure for MIOP; it should be performed early before the irreversible neurologic impairment. In our case, mutation analysis and HSCT was not performed given its high cost.

CONCLUSION

Though rare, infantile osteopetrosis should be considered in differential diagnosis in an infant presenting with anemia with hepatosplenomegaly. Early and prompt diagnosis can be made by simple skeletal radiography. Prenatal screening of the subsequent pregnancies may be considered.

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