



OSTEOPETROSIS -- A CASE REPORT

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ABSTRACT Osteopetrosis is a very uncommon genetic disorder with characteristic features of increased bone density due to impaired bone resorption by osteoclasts. This leads to increased bone density. It is classified into three forms: Infantile malignant autosomal recessive (AR) Osteopetrosis, intermediate (AR) Osteopetrosis and autosomal dominant (AD) Osteopetrosis. Incidence of infantile malignant AR is 1/2, 00,000 and if untreated has a fatal outcome. The condition is commonly diagnosed in infancy with symptoms of significant hematological abnormalities and bone marrow failure, hepatosplenomegaly, macrocephaly with frontal bossing and bone fractures. As malignant infantile form of Osteopetrosis is very rare, we are reporting a case of Malignant Infantile Osteopetrosis who presented to us with convulsions and a bulging fontanel, anemia and melaena at eight months of age.

KEYWORDS :

INTRODUCTION

We are presenting a very rare case of Osteopetrosis in a two months old infant who presented to our center. Osteopetrosis is a rare congenital genetic disorder characterized by increased bone density due to impaired bone resorption by osteoclasts. The autosomal dominant (AD) form of Osteopetrosis is usually asymptomatic and is diagnosed incidentally. It may exhibit mild symptoms in late childhood or adult life, but is compatible with long term survival.(2) The autosomal recessive (AR) or malignant infantile Osteopetrosis (MIOP) is a very severe and fatal disorder with an average incidence of 1:200,000-1:300,000.(1) This disease is caused by defector mutation in gene, and in a study 14 out of 20 MIOP patients had gene mutations.(1) This condition is most commonly diagnosed soon after birth or within first year of life with severe symptoms of abnormal bone remodeling, including significant hematologic abnormalities with bone marrow failure and extramedullary hematopoiesis. There may be hepatosplenomegaly, a characteristic macrocephaly with frontal bossing, exophthalmus, bone fractures, and failure to thrive.(1,3)

Case Note

02 months old male baby, presented with poor social smile and absent eye contact increasing pallor, abdominal enlargement and seizures. This infant was a full term normal delivery in a hospital without any antenatal, intranatal or postnatal complications. He was the product of a non consanguineous marriage. On examination he had large head with frontal bossing, a bulging fontanel (Fig-6) and significant pallor. The weight was 4.5 kgs, OFC-39 cms, length 54 cms. There was evidence of exophthalmus. The liver was enlarged to 3.5 cms and spleen 3 cms. Hb 6 gm%, TLC-3500 cells/cumm, Platelet count was 55000 cells/cumm, alkaline phosphatase was 450 U/L. Examination of fundus revealed bilateral optic atrophy. Various X-rays revealed sclerotic changes (Figs 1-3). MRI brain revealed diffuse mild bilateral cerebral atrophy involving frontal and temporal lobes (Fig-4)

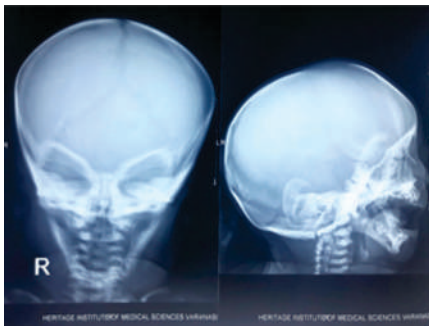


Fig.1.X-rays showing sclerotic changes in most of the bones, slight bulging anterior fontanel



Fig .2..X ray wrist showing mild generalized increased density of bones , mild fraying of distal radius and ulna with lucent horizontal bands bone age of the patient > 4 month to < 1 year



Fig .3. X- ray B/L knee showing generalized increased density, flaring of metaphysical ends of femur ,tibia , fibula with lucent horizontal bands



Fig 4. X- ray Dorso Lumbar Spine AP and Lat view - ill defined

horizontal bands, generalized increased bone density , with maintained joint spaces . splaying and widening of posterior ends of ribs seen with widening of medial ends of both clavicles.

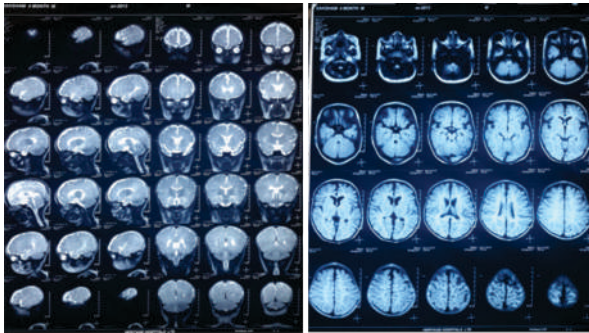


Fig 5. MRI brain showing features of diffuse mild bilateral cerebral atrophy involving frontal and temporal lobes



FIG. 6. Showing frontal bossing and exophthalmu

DISCUSSION

Malignant Infantile Osteopetrosis (MIOP) is an autosomal recessive disorder which if treated or untreated has a fatal outcome in India and most of the south east Asian and African countries. Results are slightly better in the developed countries.(3.) The diagnosis of MIOP is based on clinical and hematological parameters and characteristic radiological changes of increased bone density. The characteristic radiological feature of Osteopetrosis is generalized sclerosis of bone.(2) Our patient had classical characteristics of Malignant Infantile Osteopetrosis (MIOP) and increased bone density was found in all the bones.

Most of these babies present during infancy. (1,3) The age at the time of diagnosis was between 03 months and 18 months in a study by Phadke et al.(2) The mean age at the time of diagnosis was 3.9 months (range 15 days to 9.5 months) in a study by Mazzolari et al.(1) Out of 08 children 07 were diagnosed after 06 months of age in a study from India.(3) Usually, MIOP presents with anemia, thrombocytopenia, hepatosplenomegaly, visual impairment due to optic atrophy, and deafness within a year of life.(1,2,4) Most of the clinical features are due to bony overgrowth of the marrow space and compression of optic and auditory nerve.(1).The commonest clinical presentation has been due to optic nerve compression in various studies, which was there in our case also.(1,4) Even Phadke et al. observed optic atrophy as the common finding in their cases.(3) Another common presentation was pallor and listlessness in another study. (2) Our patient presented with anemia , hepatosplenomegaly ,seizures and a bulging fontanel at 2 months but without vision defects. Subsequently he also developed vision defect.

The risk of developing a visual defect in the first year of life is about 75% and surgical decompression of optic nerve may restore vision.(2) The hematological manifestations in MIOP are due to obliteration of marrow cavity leading to leukoerythroblastic bone marrow.(2). Hepatosplenomegaly develops because of extramedullary hematopoiesis. Hypersplenism may lead to thrombocytopenia and bleeding. Anemia along with thrombocytopenia is a constant feature in most of the studies.(2,3) The risk of developing hematological impairment in the first year of life is about 75% and its onset within 3 months of life is indicative of a poor outcome.(4) Increased risk of

infections occur because of unrecognized immunologic abnormalities in patients with MIOP.(1) Alkaline phosphatase levels may or may not be elevated.(2,3) In a study by Srinivasan et al. Symptomatic hypocalcaemia was observed in the first month of life in 8 infants with MIOP,(6) but our patient had normal calcium levels. In a study by Phadke et al. none of them had hypocalcaemia and only one had alkaline phosphatase levels >1500 U/L.(2)

Management with parathormone, calcitrol, interferon gamma and prednisone therapy has been found to be inconsistent and variable.(1,2) An accurate diagnosis is essential in view of availability of curative treatment (Bone marrow transplant) and for genetic counseling as the risk of recurrence in siblings is 25%.(1,2)Most of the children die during infancy or early child hood without curative treatment by bone marrow transplantation.(3)This is a reality in most of the developing countries. Early diagnosis is crucial if the bone marrow transplantation has to be done.

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