Infantile Osteopetrosis- A Case Series

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Abstract

Osteopetrosis comprises of clinically and genetically heterogeneous group of conditions that share the hallmark of increased bone density on radiographs. We present 3 male babies of osteopetrosis who presented with fever and paleness and organomegaly at 4 months, 11 months and 30 months of age respectively. The blood picture showed pancytopenia in all the three cases and they had failure to thrive and pallor.

Key words: Failure to thrive, Organomegaly, Osteopetrosis, pancytopenia, Pallor.

Introduction:

The term osteopetrosis is derived from the Greek 'osteo' meaning bone and 'petros', stone. Osteopetrosis is also known as 'marble bone disease' and 'Albers-Schönberg disease', after the german radiologist credited with the first description of the condition in 1904.[1]

Osteopetrosis is a rare autosomal recessive disorder with incidence of 1 in 250,000 births and autosomal variant osteopetrosis has an incidence of 5:100,000 births.[1]

Osteopetrosis can present with varying range of severity from asymptomatic to fatal in infancy.

The increase in bone density can paradoxically weaken the bone, resulting in a predisposition to fractures and osteomyelitis. The longitudinal growth of bones is impaired, resulting in short stature. Macrocephaly and frontal bossing develop within the first year, resulting in a typical facial appearance. The expanding bone can narrow nerve foramina, resulting in blindness, deafness, and facial palsy.[2]

Children with autosomal recessive osteopetrosis are at risk of developing hypocalcaemia, with attendant tetanic seizures and tooth eruption defects and severe dental caries are also common. The most severe complication of autosomal recessive osteopetrosis is bone marrow suppression. The abnormal expansion of bone interferes with medullary haematopoiesis, resulting in life-threatening pancytopaenia, and secondary expansion of extramedullary haematopoiesis.[1,2]

Cases:

Case 1: A 4 months old male born to 2nd degree consanguineous married couples by normal vaginal delivery with uneventful postnatal period now presented with history of excessive crying, not gaining adequate weight, not following objects and on and off fever since 2 months.

On examination child had excessive irritability, severe pallor, hepatomegaly (3.5cm-4cm below right costal margin), moderate splenomegaly and no light perception on ophthalmic examination.

Investigations: Hemoglobin-6.1 gm%, total leukocyte count-33,100 cells/cu.mm, platelet count-16,000 cells/cu.mm, peripheral smear study- Leucocytosis and reactive lymphocytosis and thrombocytopenia. reticulocyte count-9%, Vit-B12-451pg/ml, folic acid->20.00ng/ml, serum ferritin-213.9ng/ml, serum calcium-7.5mg/dl

USG abdomen showed hepatosplenomegaly and infantogram showed generalised skeletal sclerosis, absent cortico-medullary differentiation & fundus examination showed marked choroidal sclerosis, disc pallor with clear margins and dull foveal reflex.

Case 2: A 30 month old male child born to a 2nd degree consangious married couples by normal vaginal delivery with history of sibling death at 1 year of age due to unknown etiology. The child presented to us with history of recurrent fever since 1 month. The child also had ear discharge and paleness.

On systemic examination child had hepatosplenomegaly with liver span of 8cm and

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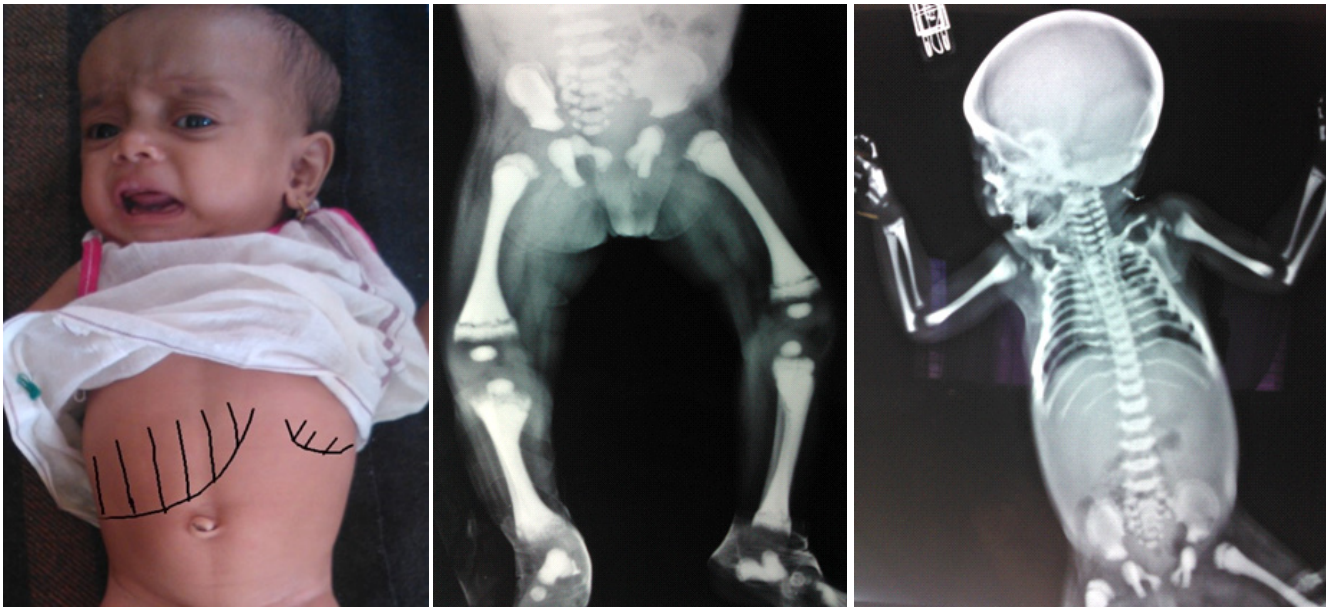
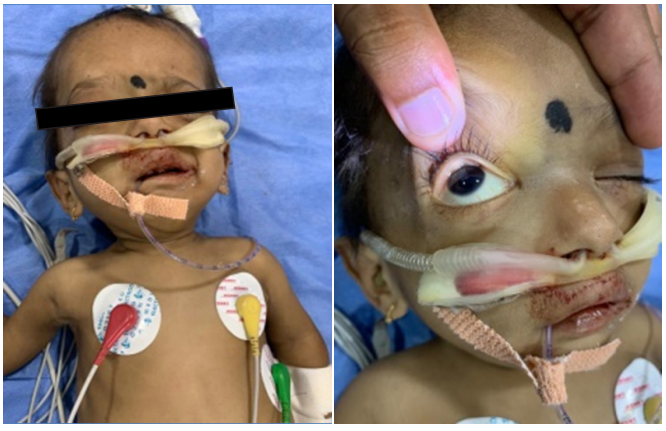


spleen 9 cm. The child had frontal bossing, height 66cm (<3rd percentile), weight 6kg (<3rd percentile), head circumference 48 cm(3rd-50th percentile).

On lab investigations child had pancytopenia and classical radiological "bone within bone" appearance was seen and was diagnosed as osteopetrosis. The child was referred to higher center on day 3 of admission.

Investigations: Hemoglobulin-2.9gm%, total leukocyte count-22100cells/cu. mm, platelet-46000 cells/cumm, c-reactive protein-20mg/L, sodium-138 mEq/L, potassium-2.9 mEq/L, chloride-103 mEq/L, creatinine-0.6 mg/dL, urea-17.1 mg/dL, lactate dehydrogenase-662U/L, calcium-7mg/dL, reticulocyte count 2.6%, peripheral smear study-dimorphic anemia with neutrophilic leucocytosis and thrombocytopenia, urine routine-normal, blood culture-citrobacter ferundi.



Case 3: Here is a 11 month old male child born to a 2nd degree consanguineous married couples by normal vaginal delivery presented to us with fever and respiratory distress. The child previously had admission at 5 months of age for fever, cough and cold. The child had history of recurrent fever. On clinical examination child had hepatosplenomegaly. Blood report showed pancytopenia. The hemoglobin electrophoresis was normal and then bone marrow biopsy was done which showed bloody tap without bone marrow particles. The infantogram was done which was suggestive of osteopetrosis and parents were counseled for genetic testing and referred to higher center.

Discussion:

Osteopetrosis is a family of bone diseases characterized by osteoclast failure and impaired bone resorption. It has three forms: autosomal recessive, autosomal dominant and X-linked inheritance. Autosomal recessive osteopetrosis has the most severe course.[1]

Infantile osteopetrosis is present at birth or develops within the first month. Abnormal bone formation and fibrous tissue replace the bone marrow and hematopoesis decreases. Extramedullary hematopoesis occurs resulting in leukoerythroblastic anemia and thrombocytopenia. Liver and spleen enlarge progressively. Hemolysis due to hypersplenism worsen the anemia and thrombocytopenia.[1,2]

Radiologic finding show increased bone density with defective metaphyseal remodeling. "bone within bone" appearance is characteristic and diagnostic.[2]

Stem cell transplantation (SCT) is the only curative

therapy, should be performed as soon as the diagnosis is made before the irreversible neurological impairement occur. Appropriate medication includes vitamin D, corticosteroids, interferon and erythropoietin. Palliative treatment is bone marrow transplantation with 5 year survival for HLA identical Bone marrow transplant is 79%.[2,3]

Conclusion: Oeteopetrosis should be considered in infancy in children with pancytopenia, hepatosplenomegaly, sibling death with radiological findings. Early diagnosis and early intervention with stem cell transplantation before neurological impairment are life saving.

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