CASE REPORT

MALIGNANT INFANTILE OSTEOPETROSIS- A RARE CAUSE OF ANEMIA WITH LEUCOERYTHROBLASTIC BLOOD PICTURE

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ABSTRACT: Osteopetrosis is a rare hereditary metabolic disease with myriad of hematological, otolaryngological, neurological and radiological presentations. Infantile malignant autosomal recessive osteopetrosis is a severe bone disease with a fatal outcome generally within the first decade of life. A brief review of classical case of autosomal recessive malignant infantile osteopetrosis is presented here.

KEY WORDS: Malignant infantile osteopetrosis, anemia, leucoerythroblastic blood picture.

INTRODUCTION: Osteopetrosis is a rare sclerosing inherited dysplasia of bone caused by the deficient function of osteoclasts. At first the disease was divided into the severe infantile recessive and the more benign autosomal dominant types. The Autosomal recessive variety also known as congenital or infantile or malignant Osteopetrosis occurs in infancy and has a rapid downhill course due to severe bone marrow failure. The underlying pathophysiological mechanism in all types of OP is failure of the osteoclasts to reabsorb bone, leading to thickened sclerotic bone with poor mechanical properties. It results from a deficit in bone resorption caused by osteoclast malfunction or formation and is associated with a number of severe clinical manifestations, including macrocephaly, cranial nerve dysfunction such as deafness and blindness, hepatosplenomegaly, and severe bone marrow failure beginning in early infancy or in fetal life. Rickets, osteomyelitis, pathological fractures are frequently observed findings in infantile variety of osteopetrosis, while it was conspicuous by its absence in our case.

CASE REPORT: A 3 month old girl baby 1st born of 3rd degree consanguineous parentage presented with, progressive pallor, failure to thrive (baby weighed 2.3 kg while birth weight was 2.5kg), stridors, noisy breathing and abdominal distention. Mother also gave the history that the baby does not have eye contact, does not turn to sound of rattle or toys. On examination baby had macrocephaly, wide open anterior fontanelle, proptosis, hypognathism, severe pallor and massive firm hepatosplenomegaly. Fundus examination revealed bilateral optic atrophy, hearing evaluation suggestive of mixed conductive and sensorineural hearing loss. Peripheral smear revealed normocytic normochromic anemia, thrombocytopenia, leucoerythroblastic blood picture, x-rays of skull and long bones showed increased density with bone in bone appearance. Hypocalcemia was also noted in our case though there was no obvious rickets clinically or radiographically. Bone marrow aspirate was dilute and showed only minimal cellularity. Bone marrow biopsy showed a variably cellular marrow. Severe compromise of marrow spaces was seen with thickened bony trabeculae. There was moderate degree of disorganization of bony trabeculae accompanied by fibrosis of bone marrow spaces. Erythroid series showed normoblastic maturation. Myeloid series showed all stages of maturation, with dyspoiesis. Megakaryocytes were inadequate with focal...
clustering. Markedly thickened bony trabeculae were seen with regular cement lines. Deposition of calcific debris in the cartilaginous matrix was noted. No osteoclast activity was seen.

Genetic counseling was offered to the parents and need for bone marrow transplantation explained which was not possible due to financial constraints. The baby required repeated blood transfusions on subsequent follow up and died at the age of 7 months due to severe pneumonia and sepsis.

DISCUSSION: Osteopetrosis is a disease of unknown etiology. It is a genetically heterogeneous disorder classified as autosomal recessive and autosomal dominant type OP3. The underlying pathophysiological mechanism in all types of OP is failure of the osteoclasts to reabsorb bone, leading to thickened sclerotic bone with poor mechanical properties. Recently mutations have been identified in the ATP 6 (ICIR G1 gene) encoding the a3 subunit of the vascular proton pump, which mediate acidification of the bone osteoclast interface. This defect is estimated to occur in half of the case of AR OP. A defect in the CIC-7 chloride channel has been demonstrated in minority of both AR and AD OP. Parental consanguinity has been frequently observed by investigators from Saudi Arabia which was observed in our case3. Normocytic anaemia is caused either by hypoproliferation of haemopoietic tissue or increased destruction of red cells3. Cells of promyeloid series may be seen due to ineffective marrow function as was seen in our case. Recurrent infections are common due to defective immune system. The encroachment on the bone marrow leads to a compensatory intra and extramedullary hematopoiesis – and hence the resultant hepatosplenomegaly. Deafness and blindness are generally thought to represent effects of pressure on cranial nerves exerted by the overgrowth of bone, but the possibility of a primary defect in sensory cells has also been raised4. Deafness of conductive type may be presenting features. It may be due to poor drainage of middle ear secretions due to eustachian tube dysfunction. With progressive disease, there is immobility of malleus and incus due to epitympanic encroachment, obliteration of oval and round windows and ossification of ligaments1. Hypocalcemia6, rickets a paradoxical association is also reported in few of the case reports5. The diagnosis remains radiographic, supported by computed tomography (CT), if necessary2. Bone marrow biopsy supports the diagnosis. The current recommended treatment of OP is based on its variety. In AR OP BMT is recommended along with high dose calcitriol, recombinant human gamma interferon 3.

REFERENCES:

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