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Case Report

Osteopetrosis presenting as Leukoerythroblastosis in 4 month old patient: A case report

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ABSTRACT

Osteopetrosis, is also known as marble bone disease or the Albers Schonberg disease. It is an extremely rare inherited disease. The disease results due to defective resorption of bone by the osteoclasts. This causes bone mass to increase accompanied by decreased hematopoietic tissue, causing extramedullary hematopoiesis. The clinical and radiological assessment plays an important role in diagnosis of infantile osteopetrosis. Clinical symptoms range from asymptomatic adults to life threatening condition in infants. We report a 4-month-old female patient with infantile osteopetrosis presenting with leukoerythroblastic blood picture and hepatosplenomegaly. This case highlights the importance of hematological findings, radiographic and genetic analysis for diagnosis of osteopetrosis.

1. Introduction

Osteopetrosis is also known as “Albers-Schonberg disease” or “marble bone disease”. It is a rare autosomal recessive disorder in which there are defects in osteoclastic function, resulting in failure of removal of bony trabeculae and decreased marrow space.[1] This disease genetically and clinically presents with increased bone density. Clinical symptoms range from asymptomatic adults to life threatening condition in infants. Incidence of autosomal recessive osteopetrosis is estimated to be about 1 in 250,000 births while the dominant form has an incidence of 1 in 20,000 births.[2,3]

Leukoerythroblastic blood picture is characterized by presence of immature white cells like metamyelocytes, myelocytes and nucleated red cells. This is observed in myelofibrosis, metastasis and in hemolytic anemia.[4]

We report a 4 month old female patient with osteopetrosis presenting with leukoerythroblastic blood picture and hepatosplenomegaly. Patient underwent all laboratory & imaging investigations at our centre.

2. Case Report

We report a case of 4- month old female infant, born at term to non- consanguinous parents, who presented to a private clinic with complaints of cough, cold & persistent bulging of the anterior fontanelle. Her developmental milestones were mildly delayed. Her weight and height were 3.85 kilograms and 57 cms respectively. The child was immunized for age. There was no family history of similar illness.

On examination, the infant had pallor and frontal bossing with mild hepatosplenomegaly, both palpable 5 cms below the respective costal margins. The rest of the systems were within normal limits.

Laboratory studies demonstrated an elevated LDH of 1387 units/L (normal range 163-452 units/L). A complete blood count performed at that time showed anemia

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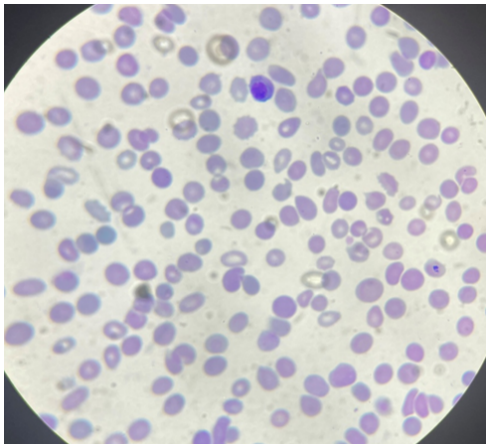

Fig. 1: (power 100x): Peripheral smear showing Nucleated RBC's with polychromasia

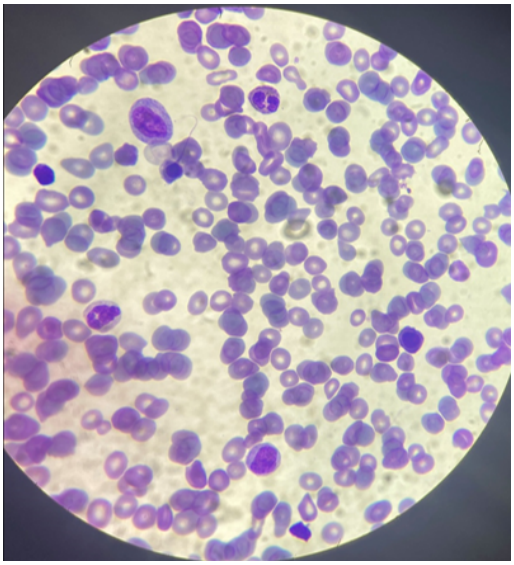

Fig. 2: (power 100x): Peripheral smear showing left shift upto promyelocytes

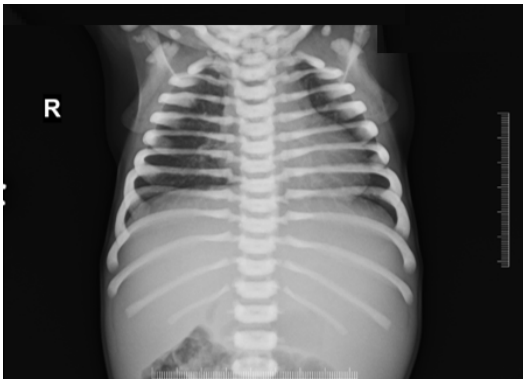

Fig. 3: X-ray chest AP view showing increased density of bones, resembling marble appearance with vertebral bodies showing classical sandwich appearance.

(haemoglobin; 7.1gm %), Leucocytosis (WBC count; 27.56x 10^3/ cu.mm) and thrombocytopenia (platelet:40x 10^3/cu.mm). The peripheral blood smear showed RBC's with moderate anisopoikilocytosis with both microcytic hypochromic and macrocytic RBC's. Polychromasia and 20 nucleated red cells/100 WBC's were seen (Figure 1). Leukocytosis was seen with left shift upto promyelocytes (Figure 2). However, the patient did not show any signs of sepsis.

Ultrasonography revealed mild hepatosplenomegaly. X-ray chest showed increased density of bones, with marble like appearance and vertebral bodies showing classical sandwich like appearance suggestive of osteopetrosis. ($).

3. Discussion

Osteopetrosis is a disease of unknown etiology and overall incidence is difficult to estimate. Autosomal dominant osteopetrosis (Albers- Schonberg disease) has incidence of 5:1,00,000 births.[5] It manifests in late childhood or adolescence, and displays the classical radiographic sign of "sandwich vertebrae" where there are dense bands of sclerosis found parallel to the vertebral endplates. The major complications affect the skeleton, causing fractures, scoliosis, osteoarthritis of the hip and osteomyelitis.[6]

Autosomal recessive osteopetrosis, also called congenital or infantile osteopetrosis has an overall incidence of about 1 in 250,000 births.[7] The basic pathophysiological causein both the types is failure of bone resorption by osteoclasts due to which the bones become thickened and sclerotic.

Autosomal recessive osteopetrosis (ARO)is also known as malignant infantile osteopetrosis or infantile malignant osteopetrosis (IMO). Infantile osteopetrosis, as the name suggests, starts showing symptoms in infancy. The patients may present with cytopenias, leucoerythroblastosis, and extramedullary hematopoiesis. Patients who present with early hematologic impairment, along with visual impairment have very poor prognosis. The increase in bone density paradoxically weakens the bone, causing increased risk to fractures and osteomyelitis. Signs of macrocephaly and frontal bossing become evident within first year, resulting in a typical facies. The skull changes cause cloanal stenosis and hydrocephalus, resulting in blindness, deafness and facial palsy.[8] Bone marrow suppression is the most severe complication of ARO. Medullary haematopoiesis is impaired due to bone expansion and causes pancytopenia which can be life threatening and also leads to extramedullary haematopoiesis. Nearly 50% of the cases of infantile autosomal recessive osteopetrosis have a mutation in the TCIRG1 gene. Diagnosis is principally based on clinical and radiological findings and confirmed by genetic analysis.[9] But as our patient was of poor socioeconomic status, the genetic analysis could not be done and was also lost for follow up.

4. Conclusion

Osteopetrosis is a rare cause of anemia caused by replacement of hematopoietic tissue by fibrous tissue. Marrow failure leads to hepatic and splenic extramedullary hematopoiesis resulting in hepatosplenomegaly. Patients who demonstrate hematologic impairment in early stages have a very poor prognosis.[3] The diagnosis is usually evident by clinical and radiological assessment showing typical marble bone appearance. Genetic testing is done for confirmation and prognostication and to differentiate between different types of osteopetrosis, but is expensive and not readily available. Treatment options include stimulating the osteoclast function or replacing the osteoclasts by stem cell transplantation.

5. Conflict of Interest

None.

6. Source of Funding

None.

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