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Case Report

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CHEDIAK-HIGASHI SYNDROME: A RARE CASE

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ABSTRACT

Chédiak-Higashi syndrome (CHS) is a childhood autosomal recessive disorder of the immune system. It affects multiple systems of the body. Patients exhibit hypopigmentation of skin, eyes, and hair, prolonged bleeding time, recurrent infections, easy bruisability. Mutations have been found in CHS1 gene or LYST and are localised to bands 1q42-43. These mutations lead to abnormal intracellular protein transport. This case report is of a 5 year old male child with progressive distension of the abdomen, breathlessness, fever, pallor and abnormal discoloration of the body and hair since the age of 2 years and diagnosed as a rare disease entity called Chediak-Higashi Syndrome (CHS).

KEYWORDS: Chediak Higashi, Hemophagocytic lympho-histiocytocis, Hematopoietic stem cell transplantation.

INTRODUCTION

Chediak-Higashi Syndrome (CHS) is a rare autosomal recessive disorder, which is characterized by variable degrees of oculo-cutaneous albinism, recurrent infections, a tendency for mild bleeding and late neurologic dysfunction.[1] The disease affects multiple organs and system. Death often occurs early because of infection, bleeding, or development of hemophagocytic lympho - histiocytosis (HLH).

CASE REPORT

A 5 year old female child, born out of second degree consanguineous marriage, presented to the department of Paediatrics with progressive distension of the abdomen, breathlessness, fever, pallor and abnormal discoloration of the body since the age of 2 years. The child also

had history of recurrent gastrointestinal and respiratory infections. Developmental milestones were normal and she was immunized till date. There was no family history of similar complaints.

On Examination – Anthropometry was normal for age. There was mild pallor. There was shiny silvery grey discoloration of the hair and slate grey discoloration of the skin over the face, back, trunk and abdomen with mottled areas of hypopigmentation over the abdomen. Eyes were light brown in color and there was no photo-phobia or nystagmus. The fundus was normal.

Examination of the abdomen revealed mild hepatomegaly with a non-tender liver, smooth surface, sharp border and span of 9 cm. There was massive splenomegaly, palpable 13 cm below the left costal margin. There was evidence of free fluid in the peritoneal cavity (Figure 1) Cardiovascular, respiratory and central nervous systems were normal.
The child was admitted in Paediatrics ward.

Further, the laboratory investigations were carried out : Haemoglobin-6.0 g/dl, a total leukocyte count of 3200 cells/µL, Polymorphs-20, Lymphocytes-76, Eosinophils-0, Monocytes-4 and Erythrocyte Sedimentation Rate 36 mm at end of 1 hour.

Platelet count was 56000 /µL and reticulocyte count was 2.3%. Mean Corpuscular Volume-69.2, Mean Corpuscular Hemoglobin-22, Mean Corpuscular Hemoglobin Concentration-31.8, Red Cell Distribution Width -23.9. The peripheral smear showed abnormal large irregular slate grey granules in neutrophils.

Liver Function Tests, renal function tests, and chest X-ray were within normal limits. Ultrasound abdomen showed hepatosplenomegaly with free fluid in the peritoneal cavity. Liver biopsy showed features suggestive of chronic active hepatitis with lymphohistiocytic infiltration. Bone marrow aspirates demonstrated numerous large eosinophilic cytoplasmic (purple granules), inclusion bodies in cells of myeloid lineage that reacted strongly (positive) for myeloperoxidase. (Figure 2).

Based on the clinical suspicion, which was confirmed with laboratory evaluation and histologic findings, a diagnosis of Chediak-Higashi Syndrome was made.
The child was put on intravenous antibiotics and blood transfusion. During the course of the hospital stay, fever reduced in intensity. She was put on 300 mg of ascorbic acid per day.

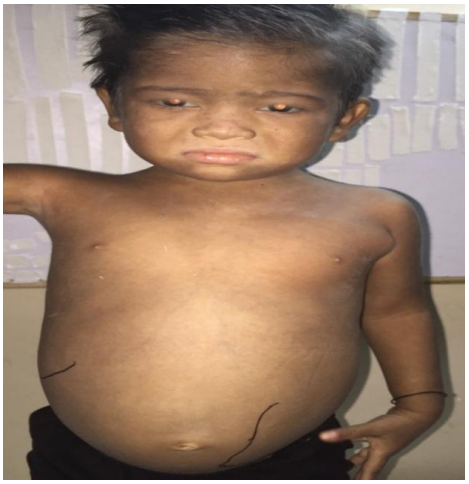

Figure 1- Discoloration of skin and hair with mild hepatomegaly and massive splenomegaly.

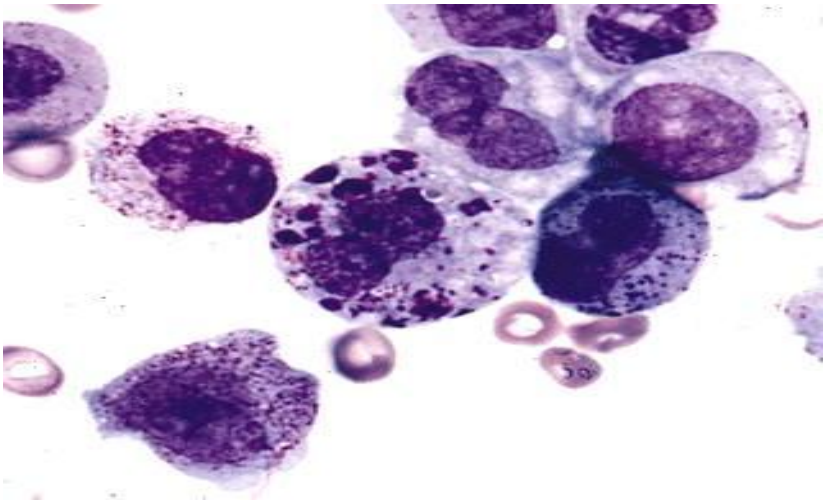

Figure2 showing purple granules in bone marrow examination.

DISCUSSION

Chediak-Higashi Syndrome (CHS) is a rare autosomal recessive disorder. The genetic defect resulting in CHS was identified in 1996[2, 3, 4], and was mapped to human chromosome 1q42–44. The human gene, CHS1, was originally called LYST for lysosomal trafficking regulator gene.[6, 7]

In this disorder, giant cytoplasmic organelles, such as inclusion bodies, lysosomes, or melanosomes are present in virtually all granulated cells. Furthermore, the exocytic pathway of secretory lysosomes is defective and plasma membrane repair mechanisms are impaired.[9] Patients with CHS frequently exhibit hypopigmentation,[5, 6] enhanced susceptibility to bruising, recurrent infections, and peripheral neuropathy.

Patients are affected by frequent and severe pyogenic infections secondary to the abnormal functions of poly-morphonuclear leukocytes.

The 'accelerated phase' of CHS is the most life-threatening clinical feature of CHS, affecting about 85% of CHS patients within the first decade.[1] This manifestation is characteristic of 'childhood' form of the disease and is characterized by massive hepatosplenomegaly. Affected children are more susceptible to gram positive and gram negative bacteria and fungi with *Staphylococcus Aureus* being the most common offending organism and there is inability to contain and control Epstein Barr Virus infections, which leads to feature stimulating virus associated haemophagocytic syndrome. This proliferation is associated with recurrent bacterial and viral infections resulting in death. Hemophagocytic lympho-histiocytosis (HLH) develops in 50 –85% of patients, and is fatal if not treated. This disorder was first reported by Beguez Cesar, a Cuban pediatrician, in 1943.[1]

The basic pathophysiologic mechanism underlying HLH is inappropriate cytotoxic activity[10], leading to impaired down-regulation of immune responses and the sustained activation and proliferation of cytotoxic T lymphocytes and Natural Killer cells.[11, 12] Activated lymphocytes and macrophages secrete high levels of pro- and anti-inflammatory cytokines and chemokines, giving rise to the characteristic clinical and laboratory findings. Histopathology reveals lymphoproliferative infiltration of the bone marrow and reticulo-endothelial system.

The backbone of treatment for CHS focuses on three main areas: supportive management of disease derived complications, treatment of the "accelerated phase" or HLH (hemophagocytic lympho-histiocytosis (HLH)[7], and HSCT (Hematopoietic stem cell transplantation) Management includes early disease identification and diagnosis. While these patients can safely receive all killed or inactivated vaccines, live vaccines are contra-indicated. The duration of antimicrobial therapy to treat common infections should ideally be two to three times longer than standard recommendations.[8]

Patients may exhibit an increased bleeding tendency owing to platelet dysfunction caused by delta storage pool deficiency. Preventive measures include avoidance of drugs that interfere with platelet functions such as aspirin, other non-steroidal anti-inflammatory agents, or serotonin reuptake inhibitors. Intramuscular injections are prohibited.

1) The therapy of HLH involves a two-pronged approach aiming to suppress the exaggerated immune response through the use of immunosuppressive agents and a long-term strategy attempting to definitively correct the underlying genetic defect by allogeneic HSCT as early as possible[9], when an acceptable donor is available.

2) Hematopoietic stem cell transplantation– Allogenic HSCT appears to be the most successful treatment, if performed prior to the accelerated phase in the early-onset form of CHS, for prevention of life-threatening infections and HLH.

CONCLUSION

A timely diagnosis is imperative and the disorder can be easily screened for with a simple, quick, and non-invasive careful examination of a peripheral blood smear. Early treatment of children with CHS is of paramount importance.

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