Chediak higashi syndrome: A case report of rare anomaly

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ABSTRACT

Chediak Higashi syndrome (CHS) is a rare autosomal recessive immunodeficiency disorder that arises due to the mutation of a trafficking protein which leads to a decrease in phagocytosis. This results in frequent pyogenic infections, albinism, and peripheral neuropathy. Infections in these patients tend to be very serious and life-threatening. CHS is caused by mutations in a gene LYST on chromosome 1. Here, we report the case of CHS in a 4-year-old boy who presented to us with recurrent fever, splenomegaly, and hypopigmentation. This case is being presented due to its rarity and presentation of pancytopenia without hemophagocytosis.

Keywords: *Albinism, Chediak-Higashi, LYST gene.*

Chediak Higashi syndrome (CHS) is a rare autosomal recessive multisystem disorder characterized by partial oculocutaneous albinism, frequent pyogenic infections, febrile episodes, pigmentation, easy bruisability and abnormally large granules in all granule containing cells [1]. This syndrome affects the immune system and the nervous system. Peripheral neuropathy is often seen as neurologic involvement. Death usually occurs at an early age due to infection or bleeding. CHS is caused by mutations in gene LYST at chromosome locus 1q42.1-q42.2.

CASE REPORT

A 4-year-old boy, born out of non-consanguineous marriage presented to the hospital with a history of generalized body weakness, loss of appetite, fever, and rashes all over the body for2 years. A past history of frequent infections was present. The child had multiple episodes of respiratory and gastrointestinal tract infections in the past 3 years.

Physical Examination revealed severe pallor, silvery grey hair, generalized hypopigmentation and splenomegaly. There was no hepatomegaly, lymphadenopathy and peripheral neuropathy (Fig. 1). Fundus examination revealed pink fundus with elevated disc margins and alternating hypo and hyperpigmented patches. Heterochromia iridis was seen. Nystagmus was present.

A complete blood count showed pancytopenia (hemoglobin of 4.1gm/dl, total WBC count of 1280/cumm with lymphocyte predominance) and platelet count of 28000/ul. Large pink granules in granulocytes and magenta coloured intracytoplasmic inclusions in monocytes were seen in bone marrow aspirate smears (Fig. 2). There was no evidence of haemophagocytosis. Bone marrow biopsy revealed normocellular erythroid preponderant marrow exhibiting trilineage hematopoiesis with prominent large intracytoplasmic granules in granulocytes and monocytes (Fig. 3). A diagnosis of CHS was made based on combined clinical and laboratory findings. The child was treated with antibiotics and steroids.

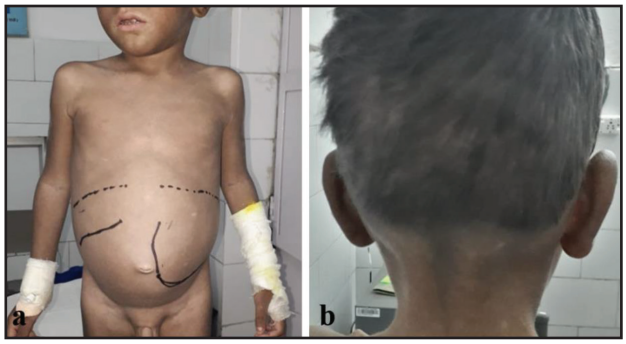

Figure 1: (a) A 4-year-old male child with splenomegaly; (b) silver-grey hair with hypopigmentation.

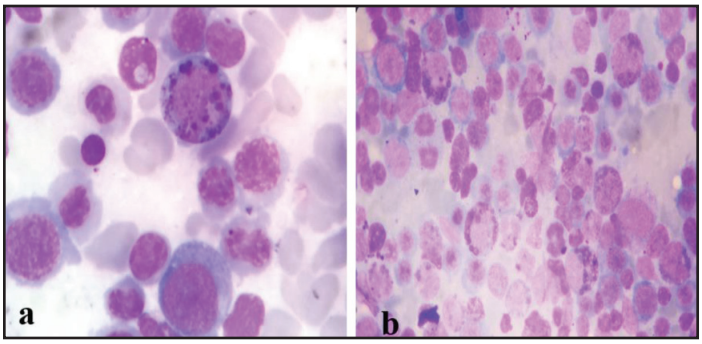

Figure 2: Bone marrow aspirate; 1000x- large pink granules in granulocytes.

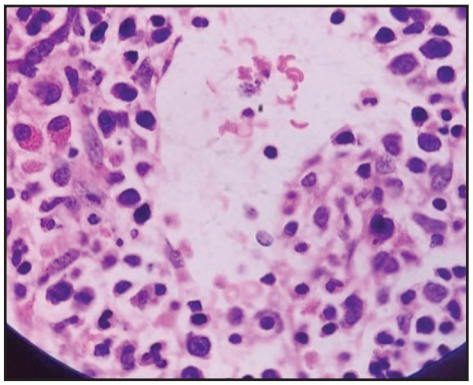

Figure 3: Bone marrow biopsy; 1000x- large intracytoplasmic granules.

DISCUSSION

CHS was first described by Bequez-Cesar in 1943 in 3 siblings having the same clinical features [1]. Chediak, a Cuban hematologist in 1952 and in 1954 Higashi, a Japanese pediatrician found maldistribution of myeloperoxidase in neutrophilic granules of affected patients [1].

Mutations in LYST/ CHS1 gene on chromosome 1q42.1-q42.2 which is important for regulating the biosynthesis of lysosomes result in CHS [2]. Till date, 40 mutations have been identified in this gene. The protein encoded by this gene prevents the fusion of lysosomes with other intracellular membrane vesicles [3].

CHS is a disease of infancy and early childhood. The mean age of onset is 5.85 years; however, most patients die before age 10 years. Our present case was a child aged 4 years old. The clinical features and laboratory findings were consistent with CHS. Clinical features such as silver-grey hair with partial cutaneous albinism, organomegaly were present in our case.

An abnormal truncated protein formed due to missense/ frameshift mutation of CHS1 gene results in defective granule morphogenesis in several tissues.A neutrophil is the most extensively studied affected cell. It has been seen that in addition to giant granules in the cytoplasm, neutrophils are deficient in neutral proteases and Cathepsin G and Elastase. Defective degranulation, decreased bactericidal activity and defective chemotaxis of monocytes cause recurrent infections. The child presented in this case analysis also had recurrent episodes of infection which is the result of a decrease in phagocytosis [4,5]. Ineffective myelopoiesis results in neutropenia in several patients with CHS. Defective T/natural killer cell function results in the development of hemophagocytic lymphohistiocytosis (HLH) in the accelerated phase of CHS and is sometimes precipitated by viral infections e.g. EBV [6].

A stable phase of CHS should be managed by prompt treatment and prevention of infections. Most of the patients undergo an accelerated phase, which is a non-malignant lymphohistiocytic infiltration of multiple organs that occurs in more than 80% of the patients. HLH (accelerated phase) is treated by immunosuppressive drugs followed by allogeneic hematopoietic stem cell transplantation [7].

CONCLUSION

CHS is a disease of infancy and childhood. It affects males and females in equal numbers. There are less than 500 cases of the disease on record. CHS affects all races. A few cases have been reported from India till date. It is recommended that parents and siblings of the patients of CHS should be screened for the presence of giant granules in the leucocytes. Prenatal diagnosis can be done by examination of hair from fetal scalp biopsy specimens. The pathologic hallmark is the presence of lysosomal inclusions in leucocytes. Careful peripheral blood film and bone marrow examination in a child with albinism should be done. Allogenic bone marrow transplant is the only curative treatment.

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