



CHEDIK-HIGASHI SYNDROME: A CASE REPORT

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ABSTRACT

Chediak-Higashi syndrome (CHS) is an extremely rare autosomal recessive immunodeficiency disorder characterized by partial oculocutaneous albinism, frequent pyogenic infections & presence of abnormal large granules in leucocytes & other granule containing cells. Less than 500 cases have been reported worldwide & only a few cases reports from India. Here, we report a case of CHS in a one & half-year-old girl.

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INTRODUCTION

Chediak-Higashi syndrome (CHS) is a rare autosomal recessive disorder characterized by partial oculocutaneous albinism, frequent respiratory system infections, pyogenic infections & intracytoplasmic giant granules in leucocytes.^[1] CHS usually occur soon after birth or in children younger than 5 years. Diagnosis of CHS can be done by finding characteristic giant cytoplasmic granules in all the granule-containing cells of the body particularly the white blood cells of blood & the bone marrow. In the terminal phase, it is characterized by non-malignant lympho-histiocytic infiltration of multiple organs (pseudo-lymphoma). Patient develops severe anemia, bleeding manifestations, organomegaly & overwhelming infections leading to death. Here, we report a case of CHS in a one & half years old baby who presented to us in the accelerated phase of disease. The case is being reported due to its extreme rarity.

CASE REPORT

A one & half year old girl, born of consanguineous marriage presented to us with complaints of high grade fever, cough and difficulty in walking since 2 months. Clinical examination revealed mild pallor, photophobia, hepato-splenomegaly 5 cm, firm, smooth & non-tender and silver gray hair.[fig.1] Past history of the patient was notable for chest infections and high grade fever since birth. She achieved normal developmental milestones. Her family history revealed parents & one elder brother to be normal. X-ray chest showed homogeneous radiopacity involving the middle zone & lower zone of right lung. USG abdomen showed multiple hypo echoic nodules scattered

throughout the splenic parenchyma suggestive of splenic microabscess. Laboratory investigations revealed hemoglobin 8.8gms, total leukocytes count 6200/ul, platelet count 80,000/mm³. The differential leucocyte count P-50, L-44, E-0, M-6. The neutrophils, monocytes & lymphocytes showed coarse granules.[fig.2] Monocytes showed cytoplasmic vacuolations. Red blood cells were normocytic mild hypochromic. Platelets were reduced in number & many giant platelets were seen. Myeloperoxidase stain revealed blue green granules in the neutrophils, lymphocytes and monocytes. As the hematological findings were indicative of CHS, the patient was subjected to further examinations. Microscopic examinations of hair shaft was done which showed small, regularly distributed melanin aggregates in the medulla.[fig.3] parents of the patient refused for skin biopsy to evaluate for abnormal granules in melanosomes. Based on clinical presentation and hematological findings, a diagnosis of accelerated phase of CHS was made. The patient was managed with intravenous antibiotics. She was discharged on request in stable & satisfactory condition with an advice of regular follow-up & was again admitted for swelling in the right hand after 2 months. She was diagnosed to have right hand cellulitis and she died due to septicemia after 4 days of treatment.

DISCUSSION

The Chediak-Higashi Syndrome (CHS) was first described by Bequez (1943), Stainberk (1948), Chediak (1952) & Higashi (1954).^[2] CHS is a disease of infancy & early childhood. Less than 500 cases have been reported worldwide.^[3] There are only few case reports from India.^{[4] [5] [6]} CHS is caused by

mutation in a single gene characterised in 1996 as LYST gene (Lysosome trafficking regulator) localised to 1q 42-43.^[7] The pathologic hallmark of CHS is the presence of massive lysosomal inclusion in the leukocytes, fibroblasts and melanocytes, formed through a combined process of fusion, cytoplasmic injury and phagocytes is due to microtubular defect. Our case showed abnormal granules predominantly in the lymphocytes, neutrophils & monocytes. Increased susceptibility to infection specially skin & respiratory tract is due to defective functions of neutrophils is poor mobilization from bone marrow, decreased deformability resulting in defective chemo taxis and delayed phagolysosomal fusion resulting in impaired bactericidal activity. Our case showed thrombocytopenia, but showed no bleeding manifestations. Besides clinical characteristics, our case was diagnosed with typical microscopic investigation of hairs and clusters of pigments were observed along the hair body. However, due to technical reasons, chromosomal analysis could not be done.



Fig 1 Silver gray hair

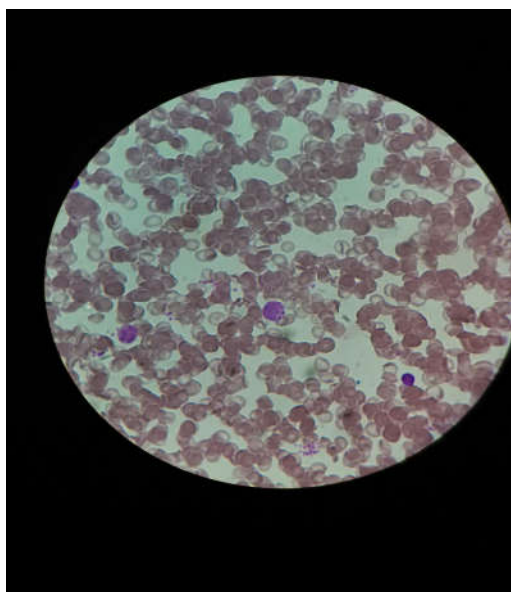


Fig2 The neutrophils, monocytes & lymphocytes showed coarse granules.

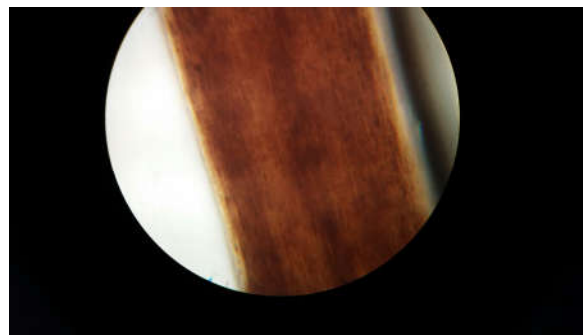


Fig3 Microscopic examinations of hair shaft was done which showed small, regularly distributed melanin aggregates in the medulla

Disease precedes in two periods as stable and accelerated. In stable period, clinical situation is milder. A majority (85%) of patients with CHS develop an accelerated phase of the disease characterised by fever, jaundice, hepatosplenomegaly, lymphadenopathy, pancytopenia, coagulopathy, neurological abnormalities, and diffuse mononuclear cell infiltrates into the organs.^[8] Originally thought to be a malignancy resembling lymphoma, the accelerated phase is now known to be Hemophagocytic lymphohistiocytosis characterized by multiorgan inflammation.^[9] CHS should be differentiated from pseudo CHS where abnormal granules are seen only in granulocytic cells in some cases of acute myeloid leukemia.^[10] Granules abnormality is never seen in other types of WBCs in pseudo-CHS. Other two extremely rare syndrome i.e. Griscelli syndrome (GS) and Elejalde syndrome (ES) also clinically mimic.^{[11] [12]} Both are characterized by skin hypopigmentation, silver gray hair, central nervous system dysfunction in infancy and childhood and very large unevenly distributed granules of melanin in the hair shaft and skin. But the presence of giant abnormal granules in all types of WBCs eg. Granulocytes, lymphocytes and monocytes is the single most important differentiating feature of CHS from these two syndromes which characteristically lack them. Allogenic bone marrow transplant has been proposed as the only possible curative treatment, when done early before the onset of accelerated phase.^[13] Once the accelerated phase occurs, the syndrome is fatal within 30 months. This emphasizes the need for early identification of the disease by careful examination of the peripheral smear for presence of giant granules in the leucocytes, so that bone marrow transplantation can be suggested at the earliest.

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