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Case Report

Chediak Higashi Syndrome masquerading as acute leukemia / storage disorder - A rare case report

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ABSTRACT

Chediak higashi Syndrome (CHS) is a rare autosomal recessive multisystem disorder with a defect in granule morphogenesis with giant lysosomes in leucocyte and other cells. CHS is a rare disease, approximately 200 cases have been reported so far. It was described in detail by Chediak in 1952 and Higashi in 1954.

1½ year old male child presented with multiple hypopigment patches on lower extremities, light colored hair, Hepatosplenomegaly and generalised Lymphadenopathy.

PBS shows giant prominent liliac to purple granules in neutrophils, band forms, few lymphocytes and monocytes. Bone marrow is hypercellular showing giant prominent gray blue to purple heterogeneous granules often multiple seen in many myeloid precursors, Neutrophils, few lymphocytes and monocytes. Occasional lymphocytes shows single giant liliac inclusions. Erythropoiesis, myeloid series and Megakaryocytes are mildly increased. Hemophagocytosis noted.

CHS is characterised by partial oculocutaneous albinism, frequent fatal bacterial infections, bleeding diathesis and peripheral + Cranial nerve palsies. This disorder further culminates into accelerated phase (Lymphoproliferative Syndrome) progressing into pancytopenia. CHS is due to single gene mutation in LYST (CHS) gene localized to 1q chromosome. The diagnostic hallmark of CHS is presence of giant purple to blue violet inclusions in leucocytes. In this study granules are more prominent in Bone marrow than in PBS correlating well with previous studies.

Approximately 85% of the cases, of CHS culminates into Accelerated phase showing Lymphohistiocytic infiltration progressing to pancytopenia and death due to infection. The very rare nature of this disease and its grave prognosis merits its reporting.

Keywords: Oculocutaneous Albinism, Lymphohistiocytic histiocytes, Hemphagocytosis

INTRODUCTION

Synonyms: "Begnez Cesar's Syndrome", oculocutaneous albinism with leucocytes defect & Chediak Steinbrinck syndrome.

Chediak higashi Syndrome (CHS) is a rare autosomal recessive multisystem disorder with a defect in granule morphogenesis with giant lysosomes in leucocyte and other cells.[1]

CHS is a rare disease, approximately 200 cases have been reported so far. It has been first described by Beguez – Cesar in 1943[1] then Steinbrinck in 1948[1], Chediak in 1952[2] and Higashi in 1954.[2,3]

CHS is characterised by partial oculocutaneous albinism, frequent fatal bacterial infections, bleeding diathesis and peripheral + Cranial nerve palsies. This disorder further culminates into accelerated phase (Lymphoproliferative Syndrome) progressing into

pancytopenia[1]. Molecular Defect is (CHS[1]) Lyst gene mutation which codes for lysosomal tracking protein.

The diagnostic hallmark in CHS is Giant purple- blue violet inclusions in neutrophils, myeloid precursors, Lymphocytes and monocytes. These are Azurophilic & specific granules.

CASE REPORT

1½ year old male patient presented with generalized lymphadenopathy, massive, hepatosplenomegaly. On physical examination child had multiple hypopigment patches on lower extremities, light colored hair and generalised Lymphadenopathy.

Bilateral crepitations were noted. Abdominal examination shows Lymphadenpathy, massive hepatomegaly (10 cms) & Splenomegaly.

Lab investigations

PT- 70, PTT- 120, INR= 6.3, WBC- 4,700, HGB -5.8 & Plt- 66 Cr-38.2 LDH – 950 Triglycerides - 3.69 Serium Ferrittin – 19024 ALT & AST are Increased.

Peripheral smear shows giant prominent liliac to purple granules in neutrophils, band forms, lymphocytes and monocytes. Bone Marrow Aspiration is hypercellular showing giant prominent gray blue to purple heterogeneous granules often multiple seen in many myeloid precursors, Neutrophils, few lympocytes and monocytes. Erythropoiesis, myeloid series and Megakaryocytes are mildly increased. Hemophagocytosis noted.

Comment: Chediak – Higashi syndrome.

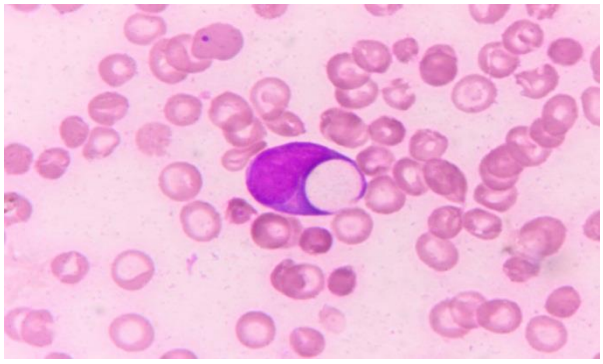

Figure 1: 100 x 10X; MGG Stain – large prominent liliac to reddish purple Intracytoplasmic Granule.

DISCUSSION

CHS is rare AR disorder with a defect in granule morphogenesis with giant lysosomes in leucocytes mainly in neutrophils and other myeloid series cells, and less commonly in Lymphocytes, monocytes and rarely in erythroid series cell.[1]

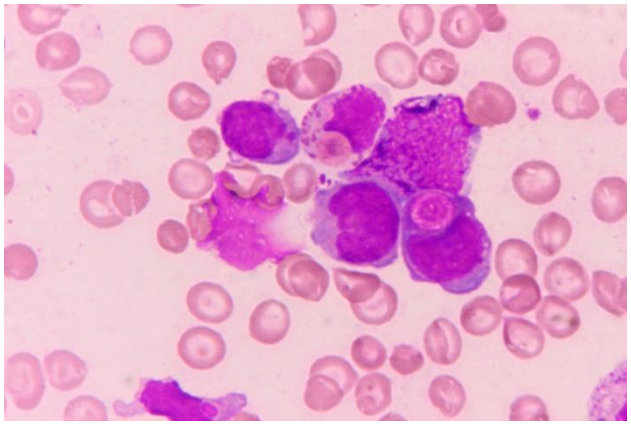

Figure 2: 100 x 10X; MGG Single large and Multiple small Purplish Intracytoplasmic Granules.

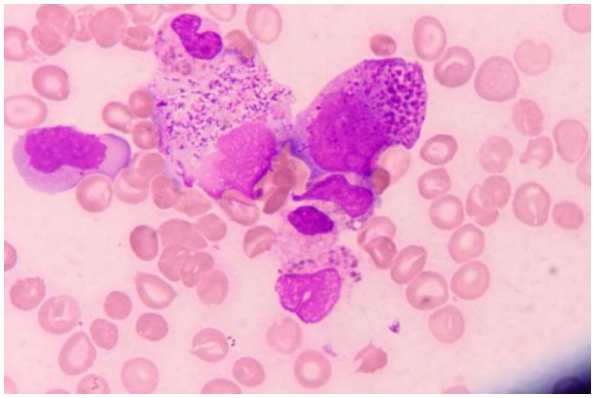

Figure 3: 100 x 10X; MGG – Multiple small purple intracytoplasmic Granules.

CHS was first described by Bequez-cesar[11] in 1943 in 3 siblings presenting with similar clinical features. Steinbrink, chediak[8,9] a Cuban in 1952 and Higashi a Japanese in 1954.[10] In 1955 Sato Coined the eponym Chediak Higashi sydrome[12]

CHS is characterised by partial oculocutaneous albinism, frequent fatal bacterial infections, bleeding diathesis and peripheral + Cranial nerve palsies. This disorder further culminates into accelerated phase (Lymphoproliferative Syndrome) progressing into pancytopenia.[1]

Molecular genetics: CHS is due to single gene mutation in LYST (CHS[1]) gene localized to 1q chromosome. These gene codes for Lysosomal tracking protein which regulates microtubule mediated, Lysosomal fusion[6] this leads to accumulation of giant lysosomal granules in variety of cells like leucocytes, melanocytes, keratinocytes, This leads to defective phagocytosis and chemotaxis. Also there is platelet storage pool defect.

The Clinical Features are the Cream to slate gray coloured skin with silvery hairy and recurrent bacterial infections (Staphylococcus). Oculocutaneous Albinism is one of the prominent features. Patient may have photophobia and Strabismus.

When Central Nervous System & Peripheral Nervous System is involved it may progress to Accelerated phase which is characterised by Lymphohistiocytic proliferation of cells in liver, Spleen, lymph node & Bone marrow leading to Massive hepatosplenomegaly and bleeding diathesis. This progress to pancytopenia leading to serve life threatening infections. Approximately 85% of patient develops Accelerated phase till second decade and succumb to death.

Here in this case also Patient was aged 1½ years & typically presents with generalised Lymphodenopathy, Massive Hepatosplenomegaly, albinism on Lower limb, PT, PPT is typically high which is due to storage pool disease. It was clinically diagnosed as Acute Leukemia/ Storage disease.

The diagnostic hallmark of CHS is presence of giant purple to blue violet inclusions in leucocytes [12.] In this study granules are more prominent in Bone marrow than in PBS correlating well with previous studies. The leucocytes shows prominent heterogeneous liliac to purple giant inclusion like granules often multiple in number in BM and PBS. These inclusions were very similar to granules mentioned in other studies.[3,5] There was no Lymphohistiocytic infiltration in this case. The patient often has agranulocytosis with Absolute neutrophil count (ANC) = 500 – 2000/ mm^3. These are because abnormal myeloid precursors are destroyed before leaving bone marrow.[1] In this case also ANC was around 1000/mm.

These granules are deficient in antimicrobial activity (Cathepsin and Elastase), Delayed degranulation and impaired chemotaxis.

In this study giant inclusion where noted in neutrophils, other myeloid cells, lymphocytes monocytes and were more prominent in BM.[2]

CONCLUSION

Approximately 85% of the cases of CHS culminates into Accelerated phase showing Lymphohistiocytic infiltration progressing to pancytopenia and death due to infection.

The very rare nature of this disease and its grave prognosis merits its reporting.

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