University Journal of Medicine and Medical Specialities

ISSN 2455- 2852 2019, Vol. 4(5)

A rare cause of Partial Albinism - GRISCELLI SYNDROME

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Abstract : It is a rare autosomal recessive disease named after Claude Griscelli Prunieras . He described the Griscelli syndrome or partial albinism in 1978. So far only 65 cases were reported all over the world. Age group affected 4months-4years, No sex predilection. Incidence less than 1 to 1,00,000. This child presented with abdominal distension and hypopigmented hair with normal mental Development. There was no similar illness in the family. Differential diagnosis of griscelli syndrome, chediak higashi syndrome and elejalde syndrome were made. Hair shaft examination clinched the diagnosis. Skin biopsy was also done which also helped in the diagnosis. Mutational analysis can be done but it was not done this case.

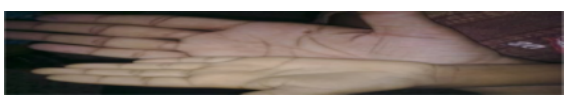
Keyword : Griscelli Syndrome, Melanosomes,Hemophagocytosis,Chediak Higashi,Elejalde Syndrome

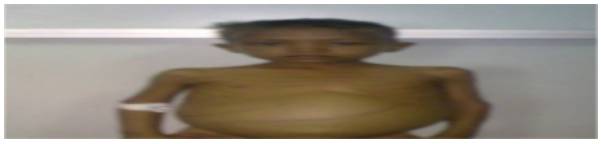
Introduction;

Griscelli syndrome is a rare autosomal recessive disease characterised by pigmentary dilution of skin and hair, variable cellular immunodeficiency and an acute phase of uncontrolled T lymphocyte and macrophage activation leading to fatal hemophagocytic syndrome. It was first described by Griscelli in 1978, and since then only around 65 cases have been reported, mostly from the Turkish and Mediterranean population. The disease is mapped on chromosome 15q21 locus,Mutations of MyoVa (type-1),Rab27a (type-2), & Melanophilin gene (type-3)

Case history

8 Year old male child born 2 nd to 3rd degree consanguinous parents,developmentally normal for his age,admitted with abdominal distension for past 3 years,Recurrent episodes of fever for past 3 years-3 to 4 episodes per month with history of loss of weight &appetite, No h/o hematemesis,malena No h/o yellowish discolouration of eyes,no high coloured urine or pale stools,No h/o altered bowel habits, no h/o seizures with no significant similar illness in the family . General examination of the child shown severe pallor,without icterus and generalized lymphadenopathy. Child had hypopigment =d hair with multiple hyperpigmented macules over the face.





Systemic examination;

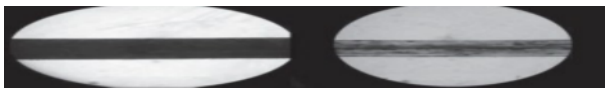
Generalised abdominal distension with dilated veins over the anterior abdominal wall, Umblicus flushed with the surface,Liver palpable 5 cm below the right costal margin,smooth surface ,firm in consistency,Spleen palpable 15 cm from the right costal margin Other systems examination was normal except for the presence of hemic murmur.

Investigations done;

Cbc-hb-6,tc-3000,plt-80,000, peripheral smear was normal, no intra cytoplasmic granules seen in the neutrophils. rft-normal,s.protein-4.2,s.albumin-2.2,s.globulin-2.0,sgot, sgpt-normal, s.triglycerides-normal,s.ferritin-normal mantoux was negative,hiv-negative,prothrombin time,partial thromboplastin time-normal,usg abdomen –hepatosplenomegaly, immunoglobu-lin assay –normal in this child. Hematologist advised hair shaft examination,splenectomy and dermatologist opinion for skin biopsy. bone marrow aspiration; hypercellular, mild erythroid hyperplasia, no lymphohistiocytic infiltrate seen ct brain-mild cortical atrophy Hair shaft examination; Large clumps of pigment granules seen suggestive of GRISCELLI

SYNDROME

Normal Hair Griscelli Hair



Skin biopsy;

Light microscopy of the skin shows hyperpigmented melanocytes with poorly pigmented adjacent keratinocytes, instead of the homogeneous distribution of melanin granules in melanocytes and keratinocytes as seen in normal epidermis.

	GRISCELLI SYNDROME	OUR PATIENT
SILVERY GREY HAIR	+	+
HEPATOSPLENOMEGALY	+	+
PANCYTOPENIA	+	+
TGL		NORMAL
IG ASSAY		NORMAL
SR PROTEINS		
LFT		NORMAL
HAIR SHAFT	LARGE CLUMPS OF PIGMENT GRANULES	LARGE CLUMPS OF PIGMENT GRANULES
USG ABDOMEN	HSM	HSM
CT BRAIN	CORTICAL ATROPHY	MILD CORTICAL ATROPHY
BMA	HYPOCELLULAR,MILD ERYTHROID HYPERPLASIA	HYPERCELLULAR,MILD ERYTHROID HYPERPLASIA
MRI	T2 INTENSITY	-
MUTATION ANALYSIS	CHROM 15q21	NOT DONE

Management;
Red blood cell & platelet transfusion Pneumococcal, meningococcal & H.infleunza vaccination was given Splenectomy was done in view of hypersplenism & falling RBC & Platelet levels despite transfusions Post operative course was uneventful

Post operative counts;
Hemoglobin – 9.8 g / dl,Total count - 9800, Platelets - 2.4 lakh Counts improved after splenectomy.

Discussion
Rare autosomal recessive disease, TYPE 1 – Mutation of MYOVA gene (severe neurological impairment with no immune deficiency) TYPE 2 – Mutation of RAB27A gene (abnormal lymphocyte cyto toxic activity,hemophagocytic syndrome)
TYPE 3 – Homozygous missense mutation of melanophilin

Pathogenesis ;
There is Impairment of intracellular trafficking and secretion of lysosomal proteins including melanin from melanocytes & the lytic enzymes from cytotoxic cells occurs. The secretory defect accounts for the hypopigmentation and the cellular immunodeficiency. The immunologic abnormalities are restricted to the patients with Rab27a mutation because, the capacity of the lymphocytes and NK cells to lyse target cells is impaired or absent, due to a consistent inability to secrete cytotoxic granules. MyoVa defect does not affect cytotoxic granule secretion and hence they never develop accelerated phase

Diagnosis;
Microscopic examination of the hair shaft - strong support for the diagnosis The hair shaft contains a typical pattern of uneven accumulation of large pigment granules, instead of the homogeneous distribution of small pigment granules seen in normal hair. In GS the clusters of melanin pigment on the hair shaft are six times larger than in CHS.

Treatment;
Allogenic bone marrow transplantation is the only curative treatment In MyoVa defect the neurological impairment and psychomotor delay do not improve and hence no role for bone marrow transplantation. Etoposide -effective in some cases during the accelerated phase Antithymocyte globulin & cyclosporin A have also achieved remission in a few cases. The prognosis for long term survival in GS due to Rab27a defect is relatively poor. Rapidly fatal during the accelerated phase of the disease.

Differential diagnosis;
1. Chediak higashi syndrome
(Presence of intracytoplasmic granules and fine granular pigment in the hair of the patients)
2. Elejalde syndrome or Melanolysosomal neuroectodermal syndrome (The major clinical features include silver-leaden hair, bronze skin after Sun exposure, and profound dysfunction of the central nervous system (seizures, severe generalized hypotonia, hyperactive deeptendon reflexes, and mental retardation).

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answers to the suggestions;
1.WHY CHROMOSOMAL STUDY NOT DONE?
Due to the economic constraints of the parents,chromosomal study was not done.(they knew the prognosis of the child,so also they were not interested)
2. why immunoglobulin profile normal?
immunoglobulin profile of our child was normal. It is not that all patients should have abnormal immunoglobulin profile. As per the literature search, Consistent immunologic abnormalities were characterized by absent delayed-type cutaneous hypersensitivity and impaired natural killer cell function. Some patients had secondary hypo gammaglobulinemia, impaired major histocompatibility complex-mediated cytotoxic effects, a decreased capacity of lymphocytes to trigger a mixed lymphocyte reaction, or various functional granulocytic abnormalities.

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