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Case Report Open Access

Haemophagocytic Lymphohistiocytosis with Partial Albinism-Griscelli Syndrome Type II

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Abstract

Hypopigmentation syndromes represent a readily distinguished group of diseases. Pigment dilution may involve skin, hair and iris, and is generally manifested at birth. Genetic defects of melanin biosynthesis are inherited as autosomal recessive. Griscelli syndrome is a rare autosomal recessive disorder characterised by partial albinism with or without neurological/immunological abnormalities. We report a nine year old child with Griscelli Syndrome type II with Hemophagocytic Lymphohistiocytosis.

Keywords: Partial albinism; HLH

Introduction

Griscelli syndrome (GS) is a rare autosomal recessive disorder first described in 1978 by Claude Griscelli and Michel Prunieras, characterised by pigmentary dilution of the skin and hairs with variable neurological involvement and immunodeficiency [1]. It usually manifests in infancy commonly between four months to four years of age. Majority of case reports are from Iran and Turkey, there are only few reports from India. We report a case of Griscelli Syndrome type II (GS2), presenting for the first time at the age of 9 years.

Case report

A 9yr old developmentally normal female child, born to a nonconsanguinous couple, with h/o hypopigmentary changes of skin and hair from neonatal period, presented with high grade fever since 10days. She was febrile and hemodynamically stable. The anthropometric parameters were within the 25th to 50th centile [Weight =24Kg, Height=129cm and Head Circumference =51cms]. Child was pale with generalized hypopigmentation of the skin. Hairs were silvery grey as shown in (Figure 1). There was significant hepatosplenomegaly with liver span of 15cm and splenomegaly of 9.5cm. On CNS examination, higher mental functions, cranial nerves, motor and sensory examinations were normal.

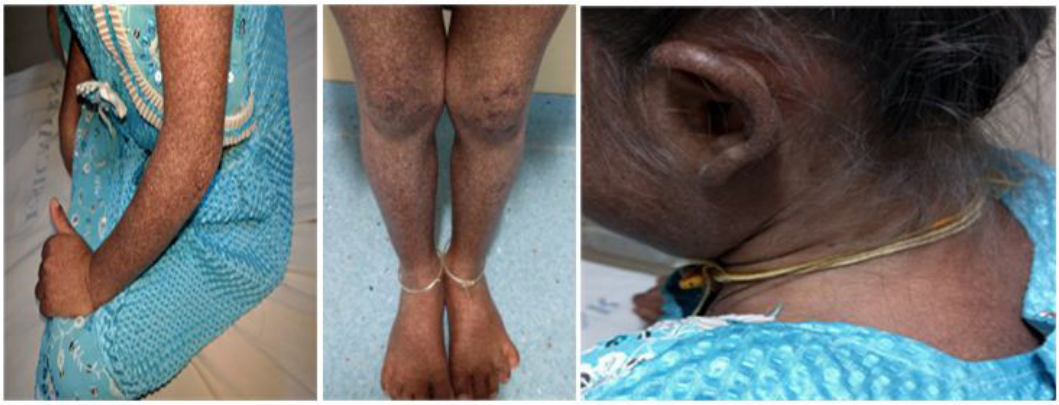

Figure 1: Shows hypopigmented skin and silvery grey hair

Complete hemogram showed hemoglobin of 6.3gm/dl, platelet count of 75000/mm^3 and white cell count of 3300/mm^3. Peripheral smear showed pancytopenia with microcytic hypochromic anemia, thrombocytopenia and neutropenia without any lysosomal inclusions. Bleeding time was normal (1min).

In the background of silvery hair, skin changes of partial albinism, fever, pancytopenia, hepatosplenomegaly and normal CNS examination the diagnosis of GS2 was made and child was investigated for hemophagocytic lymphohisticytosis (HLH). Liver function tests were normal. Serum triglycerides were 500mg/dl, Serum ferritin-156ng/ml, Serum fibrinogen-220mg/dl, CD56/16 and Interleukin2 levels-normal. Serum Immunoglobulin levels could not be done. Bone marrow showed hemophagocytosis as shown in (Figure 2). There was no indication for neuroimaging in our case. The child was treated with ceftriaxone for ten days. Child became afebrile, however parents refused further investigations and treatment and discharged against medical advice.

Light microscopy of hair showed irregular arrangement of small and large clumps of melanin as shown in (Figure 3).

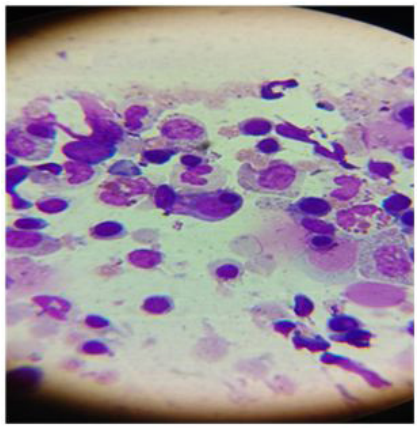

Figure 2: Shows hemophagocytosis in the bone marrow

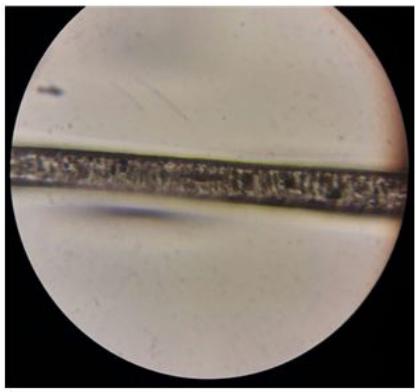

Figure 3: Shows light microscopy of the hair follicle in Griscelli type II

Discussion

Griscelli Syndrome belong to the genetically inherited group of hypopigmentation syndromes. It is due to genetic defect in transport of melanosomes in melanocytes. Normally, melanosomes are transported on microtubules in the melanocytes. In melanocytes, RAB27A associates with melanosomal membrane, recruits MLPH and together interact with MYO5A to form a tripartite complex facilitating vesicular trafficking, intrracellular melanosome transport and secretion. Loss of any one of these proteins interrupts the melansome transport and results in hypopigmentation and clustering of melanin pigment in hair shafts [2].

There are three types based on gene mutations. GS1 is characterised by partial albinism with neurological involvement due to defect in MYO5A. It uusally presents early in infancy with delayed development, neuroregresssion, seizures and facial palsy. In GS2 there is partial albinism with immunological abnormalities with or without neurological impairment due to mutation in the RAB27A gene, that maps to chromosome 15q2 [3]. Immunological abnormalities include natural killer cell function defect with absent delayed hypersensitivity. Secondary hypogammaglobulinemia occurs in the accelerated phase. GS3 has partial albinism due to mutation in the gene encoding melanophilin MLPH without any system involvement.

GS2 usually presents between 4 months to 4 years of age. Majority of case reports are from Iran and Turkey. Clinical features include silver-gray hair, relatively light skin color and increased susceptibility to recurrent pyogenic infections. It may present with HLH. In the majority of GS2 patients, the development of HLH, known also as the "accelerated phase", occurs from 6 to 12

months of age [4]. Diagnosis is made by light microscopic examination of hair shafts showing irregular large clumps of melanin pigment. Electron microscopy of skin reveals numerous mature melanosomes in melanocytes with few melanosomes in adjacent keratinocytes. Giant granules are absent in peripheral leukocytes. GS2 is usually fatal because of HLH without hemopoietic stem cell transplantation (HSCT). Immunosuppressive therapy is reported to improve patient symptoms as a palliative treatment or to induce remission until HSCT can be performed.

Our child presented for the first time, at the age of 9years with febrile pancytopenia without any previous history of recurrent infections. The closest differential diagnosis for GS2 is Chediak Higashi Syndrome (CHS) which is characterized by partial albinism with CNS manifestations, lysosomal inclusions in peripheral smear, even distribution of pigment clumps along the hair shaft on light microscopy and prolonged bleeding time. Table 1 shows differentiating features between the CHS and GS2 [5,6].

Investigations	Griscelli syndrome	Chediak-Higashi syndrome
Peripheral blood smear	-	Prominent granules leucocytes and giant organelles
Light microscopy of hair	Small and large clumps of melanin in irregular pattern	Regularly arranged, small clumps of melanin
Histopathology of skin	Excess pigmentation of melanocytes at basal layer and scanty pigmentation in skin surrounding the pigmented areas	Large melanosomes in both melanocytes and keratinocytes
Electron microscopy of skin	Mature melanosomes in melanocytes and to some extent in keratinocytes	Large melanosomes in both melanocytes and keratinocytes

Table 1: Differentiating features between the CHS and GS

In our case, child had partial albinism and HLH [Child met 5/8 criteria for HLH, i.e., fever, splenomegaly, cytopenia (affecting ≥2 cell lineages), hypertriglyceridemia (≥265 mg/dL) and hemophagocytosis in the bone marrow], with no neurological involvement. She had normal bleeding time with classical hair changes suggestive of Griscelli on light microscopy. Genetic analysis for RAB27A mutation and histopathology of skin were not done as the child was lost for follow up.

Conclusion

A high index of suspicion is required when child presents with partial albinism. Proper clinical history, clinical examination and light microscopy of hair shaft helps in early diagnosis.

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