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CASE REPORT

A RARE CASE OF GRISCELLI'S SYNDROME WITH REVIEW OF LITERATURE

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ABSTRACT: INTRODUCTION: Griscelli syndrome is a rare autosomal recessive disorder characterized by partial albinism and immunodeficiency. The characteristic features include silver hair due to clumped melanosomes in hair shaft. Other features include hepatospleenomegaly, hepatitis, pancytopenia and immune abnormalities. CASE REPORT: A seven years old male child presented with partial albinic features and history of recurrent respiratory tract infection. The child had fever since 2months along with hepatospleenomegaly, pancytopenia and thrombocytopenic purpura. These rare clinical manifestations were diagnosed as GS which was confirmed by bone marrow biopsy and light microscopy of hair shaft. The mean patient age of survival is 5years. As early diagnosis can improve the outcome in such cases, a finding of partial albinism should alert the diagnosis of Griscelli's syndrome. CONCLUSION: We report a rare case of GS with characteristic manifestation surviving beyond the mean age of reported survival.

KEYWORDS: Griscelli's Syndrome, immunodeficiency, hemophagocytosis, partial albinism, lymphohistiocytic proliferation.

ABBREVIATION: GS, HLH, CBP, CUE

INTRODUCTION: Griscelli syndrome (GS) is a rare disorder associated with partial albinism and immunodeficiency.(1) The maximum incidence is seen in Mediterranean region and this syndrome has no gender predilection. The classical manifestation of GS includes silver hair due to clumped melanosomes in hair shaft. Other features include hepatospleenomegaly, hepatitis; pancytopenia and immune abnormalities. The diagnosis is confirmed by light microscopy of hair and Bone marrow biopsy. Major of children succumb to death by 5years of age. The most common complication that leads to death is lymphohistiocytosis involving different organs.

CASE REPORT: A seven years old male child was brought to the hospital with the history of fever since two months. It was insidious in onset, low grade and intermittent type. Inter-febrile period the child was dull and sick. There was no history of evening rise of temperature, chills, rigors, burning micturition, joint pains, swelling, headache, seizure, vomiting's, abdominal pain, loose motions, cough, cold, contact with TB patient. History of loss of weight and appetite was associated with the fever. On examination the child was dull sick looking. There was pallor along with features of partial albinism (greying of scalp, eyebrows, eyelashes and body hair – as shown in figure 1.) Child was febrile, with tachycardia and petechiae over the lower limbs.

There were no ecchymotic patches, cyanosis, clubbing, lymphadenopathy and icterus. There was hepatomegaly (liver palpable 4cms below right subcostal margin rounded border, firm, non-tender, smooth surface) along with splenomegaly (palpable 3cms below left subcostal margin and was firm, non-tender).Other system examination was not significant. The Baseline investigations revealed pancytopenia. However Widal, smear for Malaria Parasite, montoux test and smear for

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abnormal cells, were negative and CUE was normal. The Clinical differential diagnosis of Griscelli syndrome, haematological malignancy and immune deficiency disorder (Chediak Higashi syndrome) were considered. Elejalde syndrome was not considered as neurological involvement was absent. Hence the child was further investigated with Bone marrow biopsy which showed mild erythroid hyperplasia along with hemophagocytosis.

Light microscopy of the hair revealed uneven aggregates of melanin pigment with areas of hypopigmentation. Skin biopsy showed large clumps of melanin granules in melanocytes. These characteristic findings confirmed the diagnosis of Griscelli syndrome (in accelerated phase) with sepsis. The genetic study could not be done due to financial restraints. The child was given supportive and symptomatic treatment. However the parents were counseled regarding the need for bone marrow transplantation.

DISCUSSION: Griscelli syndrome was first described by Griscelli, in the year 1978. Itis a rare autosomal recessive disorder characterized by partial albinism and immunodeficiency which leads to death in early childhood.[1] The prevalence of this condition is <1/100000, with about more than 60 cases reported world wide.[2] GS is a rare disorder of melanosome transport and uncontrolled T-lymphocyte and macrophage activation sydrome[3] and is divided into several types[4, 5] Type 1 Elejalde syndrome, Type2 Partial albinism with immunodeficiency, Type 3 Partial albinism. The genetic defects commonly involving MYO5A, RAB27A genes[6].

The three types of the syndrome have different courses. Type 1 manifest primarily with dysfunction of central nervous system. Type 2 develops HLH. Type 3 manifests as merely partial albinism. In most patients, diagnosis occurs between the ages of 4 months to 7 years,[7] with the youngest occurring at first month of life. Males and females are affected equally. The first reported manifestation of GS was silver hair[5, 8] which was seen in our case. Skin manifestations of both GS variants include granulomatous skin lesions, partial albinism, and generalized lymphadenopathy. The appearance of the hair has been described as silvery grey/ silvery / partial albinic as the albinism is not complete. The skin is usually pale which can be attributed to the degree of anemia. Neurologic involvement presents with raised intracranial pressure, cerebellar signs, encephalopathy, hemiparesis and peripheral facial palsy.

Spasticity, hypotonia, seizures, psychomotor retardation and progressive neurologic deterioration may also occur.[9] Immunodeficiency occurs due to defective natural killer cell function which also results in absent delayed hypersensitivity.[10] Other systemic manifestations include hepatospleenomegaly and jaundice with elevated liver enzymes as a result of hepatitis. Patients can also present with pancytopenia leading to bleeding manifestation and petechial rash as seen in index case. Secondary GS can present as hypogammaglobulinemia which is implicated to various infections.[10] Characteristic laboratory features include pancytopenia, hypofibrinogenemia, hypertriglyceridemia and hypoproteinemia which are present in the accelerated phase of the disease. Bone marrow aspiration shows mild erythroid hyperplasia with hemophagocytosis as seen in the index case. Skin biopsy shows melanocytes with massive accumulation of mature melanosomes with adjacent keratinocytes showing only sparse melanosomes.

The differential diagnosis for this case includes Chediak Higashi syndrome and Elejalde syndrome. Unlike GS, Elejalde syndrome does not have immunodeficiency and has spotty hair pigmentation and Chediak Higashi syndrome has abnormal giant cytoplasmic granules in the

leukocytes with predominant involvement of the skin. Supportive management includes treating the associated infections and immunomodulatory therapy (which includes steroids, etoposide, intrathecal methotrexate, cytoarabinoside and cyclosporine).

Amniotic fluid cell, chorionic villi sampling and fetal hair analysis at 21 weeks of gestation aids in prenatal recognition of this condition. The most common complications that lead to mortality are lymphohistiocytosis in different organs and severe life threatening infection. The mean age of survival is 5 years. However bone marrow transplantation and stem cell therapy can extend the life span.[11]

Till date less than100 cases are reported world-wide. Most reported cases are from Turkish and Mediterranean populations.

CONCLUSION: A seven years old male child presenting with a rare autosomal recessive disorder-Griscelli syndrome. Characteristic clinical manifestation include partial albinism, pancytopenia, thrombocytopenic purpura and hepatospleenomegaly. Confirmatory bone marrow report and hair shaft analysis. The child survived beyond the reported mean age of survival makes this case further unique.

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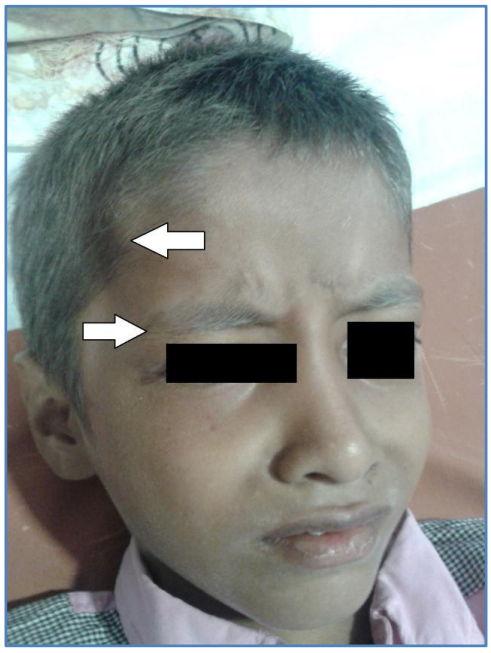

Fig. 1: Shows the typical appearance of partial albinic hair in a case of GS

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