



Griscelle syndrome type 2 in a girl child in India with review of literature

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Abstract

Griscelle syndrome type 2 is a rare autosomal recessive disorder due to mutation in RAB 27 gene. Silvery grey hair and light coloured skin with variable immunodeficiency is the characteristic clinical features. We report a girl child with Griscelle syndrome type 2 with typical clinical features and review of literature.

Introduction

Griscelle syndrome (GS) is rare autosomal recessive disorder leading to pigmentary dilution of the skin and hair with the presentation of huge clumps of pigment granules in hair shafts that results in silvery grey hair along with variable cellular immunodeficiency with or without severe neurological deficits^[1].

Griscelle Syndrome Type 2 is caused by mutation in RAB 27 Gene. RAB 27 Gene encodes the small GTPase protein Rab27a, Rab27a is associated with melanosomes in pigment cells and regulates melanosome transport via its interaction with actin based cellular such as myosin Va and myosin VIIa. Myosin Va and myosin VIIa do not interact directly with Rab27a but require linker proteins, melanophilin and mrip respectively. RAB 27A gene mutation results in pigmentary dilution of skin and hair, the presence of large clumps of pigment in hair shafts and an accumulation of melanosomes in melanocytes. Rab27a is also required for secretion of lytic granules in cytotoxic T lymphocytes. In RAB 27A gene

mutation, capacity of the lymphocytes and NK cells to lyse target cells is impaired or absent which results in primary immunodeficiency^[2].

GS-II is very rare disease, worldwide 101 cases are reported in literature^[3], with 10 cases reported from India^[4]. Most cases are described in Turkish and Mediterranean populations^[5].

Case Report

A two year old female child, born out of 2^o consanguineous marriage, came to our hospital for blood transfusion. She was the only child born to parents with a married life of 4 years. There were no complaints of fever, cough, cold, vomiting, loose stools, burning micturition, jaundice, anasarca, itching, repeated boils, convulsion or history of frequent chest infection in the past and hospitalization. Child was evaluated in a tertiary care hospital at the age of 1 year and diagnosed as Griscelli Syndrome Type II with hair shaft microscopy, skin biopsy and mutation study. On examination the child was afebrile, her vital parameters were normal. Hairs on scalp, eyebrow,

eye lashes were silvery grey in colour. She was pale. She had delayed gross motor, fine motor, social and linguistic milestones. Her abdomen was distended with liver 6cm below right costal margin with smooth surface, firm in consistency with sharp margin. Liver span was 12cm. the spleen was palpable 13cm below left costal margin and was firm in consistency. Other systemic examination was normal. Her investigation revealed hemoglobin-9.6gm/dl, TLC-2600cells/mm³, platelet count-1.27lakhs/mm³. Peripheral smear showed pancytopenia with normocytic normochromic anemia. There were no giant cytoplasmic granules in leucocytes. LFT was normal. Ultrasound abdomen showed hepatosplenomegaly. Blood group was B positive. As the anemia was mild she was started on oral iron supplements and asked them to follow up after 3 months. Child was discharged in stable condition.

Discussion

Griscelli syndrome was first described by Griscelli and Pruniera in 1978^[6]. The common age of diagnosis is 4 months to 7 years of age^[7]. Patients with Griscelli syndrome type-II have immune system abnormalities in addition to having hypopigmented skin and hair. Affected individuals are prone to recurrent infections. They also develop an immune condition called hemophagocytic lymphohistiocytosis (HLH), in which the immune system produce too many activated immune cells called T-lymphocytes and macrophages (histocytes). Over activity of these cells can damage organs and tissues throughout the body, cause life threatening complication if the condition goes untreated. GS type II is related to RAB 27A^[8]. Due to different mutations in the RAB 27A gene, GS- II clinical symptoms can differ from case to case^[9]. The treatment of choice for GS type II is Bone marrow transplantation^[10]. Amniotic fluid cells and chorionic villi cells can help in prenatal diagnosis of Griscelli syndrome. Prenatal diagnosis of GS has been accomplished by examination of hair from a biopsy sample of

fetal scalp obtained at 21weeks of gestation. A fetus that had such a biopsy was aborted. These results were confirmed by postabortion examination of the fetus revealing silvery hair and characteristic microscopic findings^[11].

The differential diagnosis for Griscelli syndrome are Chediak Higashi syndrome, Elejalde syndrome, Hermansku Pudlak syndrome and neutrophil function abnormalities condition such as Wisckott Aldrich, Chronic childhood granulomatosis and hyper IgA syndrome^[12].

GS long term prognosis is poor and in most cases, death happens in the first decade of life. There are a few reports of survival longer than a decade^[12]. In hematological life threatening complications, bone marrow or stem cell transplant is recommended although the success rate is poor^[13]. Here is an example of how important is to prepare the health care services to early recognize of this disease and propose effective treatment in time. Cases of successful bone marrow transplant are reported and immunosuppressive therapy (high dose systemic methyl prednisolone, cyclosporine and etoposide) is also used to maintain the patient stable as a palliative therapy or to induce remission until bone marrow transplantation^[13,14]. Bizario et al^[15] showed rescuing of cytotoxic T lymphocyte activity using a retroviral vector to mediate the transfer of RAB 27A gene, opening an alternative possibility for Griscelli syndrome treatment.

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