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Case Report

Griscelli's syndrome in a young adult – a case report with the review of literature

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Abstract Griscelli syndrome is a rare autosomal recessive disorder characterized by partial albinism with variable immunodeficiency. Silvery grey hair with large, clumped melanosomes on microscopy of hair shafts is diagnostic. The commonest complication leading to mortality includes lymphohistiocytic proliferation in various organs, including the brain. There are three types of this syndrome described. We present a young adult with classic clinical features and confirmatory findings of clumped melanosomes on microscopy of hair shaft.

Key words
Griscelli's syndrome, albinism, immunodeficiency.

Introduction

Griscelli's syndrome (GS) is a rare autosomal recessive disorder characterized by pigmentary dilution and variable cellular immunodeficiency. Pathognomonic light and electron microscopic features in skin and hair biopsies in GS differentiate it from Chediak-Higashi syndrome (CHS), which has similar clinical manifestations.[1,2,3] Granulocyte abnormalities seen in Chediak-Higashi syndrome are usually absent in Griscelli's syndrome. The prognosis in both disease entities is grave but out of 3 types of Griscelli syndrome, type 3 has good prognosis.

Case report

A 27-year-old male who had a history of repeated skin infections since childhood, presented this time with the bullous impetigo-like lesions which responded to the given treatment. He also had photosensitivity, partial albinism (**Figure 1**) and nail dystrophy. He did not have any complaint relevant to other systems. There was no hepatosplenomegaly or lymphadenopathy. His parents were cousins and one of his sibling with albinism died at age of 2 years. His investigations revealed a normal blood complete picture and normal immunoglobulin levels: IgE 110 IU/ml (normal upto 720 IU/ml), IgG 1273 IU/ml (normal 800-1800 IU/ml). In view of the clinical features, laboratory investigations and characteristic skin biopsy findings, the final diagnosis of partial albinism with immunodeficiency (Griscelli's syndrome) was made. Skin biopsy showed changes secondary to local infection. Microscopic examination of the hair shaft showed large unevenly distributed melanin aggregates diagnostic of Griscelli's syndrome. The parents were counseled about the nature of the disease, its prognosis, recurrence risk and the therapeutic options.

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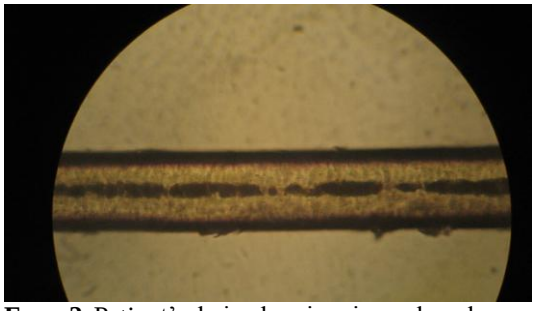
Figure 1 Face of the patient showing photosensitive rash.



Face 2 Patient's hair showing irregular clumps of pigment.

Discussion

Griscelli's syndrome is a fatal and rare disorder. Since the original description of 2 cases by Griscelli *et al*. in 1978, more than 40 cases have been described in the literature thus far.[1-7] It can manifest with silver grey hair, which may be accompanied by neurological abnormalities (type1), immunodeficiency (type 2), or no other abnormality (type3).[4] The present case is one of the unique case from Pakistan.

This disorder has to be differentiated from Chediak-Higashi syndrome which presents as albinism, recurrent infections and abnormal vacuolation in the granulocytes in peripheral blood film, associated with decreased nitro blue tetrazolium test with biopsies of skin, hair and Schwann cells showing abnormal membrane bound lysosomes-like organelles.

A literature search revealed that clinical manifestations such as silvery scalp hair and eyelashes, hypopigmented areas in the fundus, recurrent chest infections and psychomotor retardation are also found in Griscelli's syndrome.[1,6,7] The usual age of onset is between 4 months to 4 years and is characterized by accelerated phases (lymphohistiocytic infiltration of multiple organs) triggered by viral or bacterial infections. These accelerated phases were not clinically evident in the index case. Fibrinogen levels are generally elevated in Griscelli's syndrome but normal values, as was observed in the index case, has been reported earlier.[4] The immunodeficiency in Griscelli's syndrome is best characterized as a defect in natural killer cell function associated with absent delayed type hypersensitivity as seen in this patient. Immunoglobulin levels are variable, low values are seen in the accelerated phase of the disease. Pathognomonic histologic features in skin and hair biopsies can distinguish Griscelli's syndrome. Skin biopsy shows increased deposition of melanosomes in the melanocytes in the dermal layer contrasting with poorly pigmented adjacent keratinocytes.[5] Though functional granulocytic abnormalities do occur in Griscelli's syndrome, these abnormalities are heterogeneous and are not found in all patients.[1,5] Nitro blue tetrazolium test is usually normal, which again helps in differentiating it from Chediak-Higashi syndrome.[1] The neurological impairment and retarded psychomotor development do not improve with time and is a permanent sequele.[6]

Recent identification of mutations in two genes (MY05A and RAB27A) and localised to chromosome15q21.[1,2] It has made prenatal diagnosis feasible in families with defined gene mutations, it is categorized in type 1.[7] Mutation in MY05A gene is associated primarily with neurologic impairment. Immune dysfunction, with susceptibility to infections, and hemophagocytosis is absent. The form due to RAB27A mutation (type 2) has no neurologic features but is associated with an uncontrolled T lymphocyte and macrophage activation syndrome leading to death in absence of bone marrow transplantation. Griscelli's syndrome type 3 represents the restricted expression of the disease characterized only by hypopigmentation in hair and skin,[8] only two cases are reported, one of that caused by an F-exon deletion in the MYO5a gene. Various chemotherapeutic agents such as etoposide, methotrexate, steroids and cyclosporine have been tried in the accelerated phase with variable success.[1] Allogenic bone marrow transplantation remains the only curative treatment in this disease.[3]

The prognosis for long-term survival of Griscelli's syndrome patients is relatively poor; it is usually rapidly fatal within 1 to 4 years without treatment at onset of an accelerated phase. But this may be the type 3 Griscelli's syndrome as this patient has no other accompanying feature except superficial skin infections. In patients with GS type1, there is no definitive cure, GS type 2 have a grave prognosis while GS type3 does not pose a threat to those affected and needs no active intervention.

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