CASE REPORT
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Griscelli Syndrome Type 2; A Pediatric Case with Immunodeficiency

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ABSTRACT

A 3.5 month-old girl was admitted with silvery gray hair, light colored skin, recurrent diarrhea, chest infections, hepatosplenomegaly, episodes of pancytopenia, and hemophagocytosis in the bone marrow. Light microscopy of hair showed characteristic large and irregular clumps of melanin in the middle of hair shaft. Peripheral blood smear examination did not show giant granules in granulocytes. On the basis of these clinical and laboratory findings, Griscelli syndrome was diagnosed. The child succumbed to infection during an accelerated phase of the disease.

Key words: Griscelli Syndrome; Immunodeficiency; Phagocyte Disorders

INTRODUCTION

Griscelli syndrome (GS) is a rare autosomal recessive disorder with partial albinism[1-3] which may be accompanied by neurologic impairment (type 1),[1] or immunodeficiency (type 2),[2] with absence of delayed-type hypersensivity and impaired natural killer cell activity,[2] or no other abnormalities (type 3).[2] Unlike Chediak- Higashi syndrome (CHS), granulocytes in GS do not demonstrate giant granules.[3] Hair microscopy characteristically revealed large and irregular clumps of pigment in the middle of hair shaft.[3] we report a case with type 2 GS.

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CASE REPORT

A 3.5 month-old female infant which presented with pallor, fever, and abdominal distension since one month of age. At birth she was noticed to have silvery gray hair with a metallic shine. She developed fever with diarrhoea and cough. Evaluation at another hospital revealed hepatosplenomegaly, severe anemia, salmonella in stool culture and infiltrate in the right upper lobe of lung. She was treated with antibiotics and received two blood transfusions. After two weeks she was discharged. Three weeks later she was brought again to our center for further evaluation. She was the second child of a consanguineous marriage. There was no history of silvery gray hair in any of the family members. The other sibling in the family was healthy. There was no delay in the achievement of developmental milestones.

On admission her body weight was 4.100 kg. The child was pale. Hairs on the scalp were silvery gray with a metallic shine. She had crepitations in the lungs. Abdominal examination revealed hepatosplenomegaly. Neurologic, cardiovascular and ophthalmologic examinations were normal. Light microscopy of scalp hair showed large aggregates of pigment granules in the middle of hair shaft. A hemogram revealed anemia, neutropenia and thrombocytopenia. Peripheral blood smear showed normocytic normochromic red blood cells and was notable for the absence of giant granules in the granulocytes. Liver and renal function tests were within normal limits. Serum immunoglobulin levels were normal for her age. The Mantoux test produced negative result. Serology tests for Kala Azar and EBV (Epstein-Barr Virus) infections were also negative. Chest radiography showed infiltration in the left lung. Her pneumonia responded well to treatment with antibiotics in hospital for one week, and she was discharged. Stool examination and culture were negative. After a few days she was brought to emergency department with high fever. Physical examination showed severe abdominal distension and tachycardia. The abdomen was distended; the liver and spleen were enlarged. Investigations revealed pancytopenia. Blood and bone marrow cultures were positive for Candida. Bone marrow aspiration slides revealed large histiocytes ingesting blood elements. She was treated with intravenous Ceftazidime, Vancomycin and antifungal drugs. However her condition deteriorated and she died due to septic shock.

DISCUSSION

In 1978, Griscelli et al first reported a syndrome associated with partial albinism and immunodeficiency in two patients with silvery hair and frequent pyogenic infections that clinically resembled CHS.[1-3] However, giant granules were not seen in granulocytes. Light and electron microscopic examination of the hair and skin revealed differences, and there were defects in cellular and humoral immunities.[3] Since then, a little more than 60 cases of GS have been reported in the literature in association with primary neurologic manifestations, with immunologic abnormalities or with silvery gray hair and hypopigmented skin as the sole abnormality. GS is now classified into 3 types on the basis of genetic and molecular features: GS type 1 (GS1) represents hypomelanosis with a primary neurologic deficit and without immunologic impairment or manifestations of hemophagocytic syndrome.[2] GS type 2 (GS2) which is characterized by hypomelanosis and immunologic abnormalities with or without neurologic impairment, is caused by mutation in the RAB 27 A gene located on chromosome 15q21.[4] GS type 3 (GS3) is characterized with partial albinism as the only presentation and results from mutation in the gene that encodes melanophilin (Mlph).[1]

The pigmentary disorder is characterized by large irregular clumps of pigment in the middle of hair shafts and an accumulation of melanosomes in melanocytes.[4] Despite an adequate number of T and B lymphocytes, the patients are hypogammaglobulinemic, deficient in antibody production, and incapable of delayed skin hypersensitivity and skin graft rejection. Our patient had silvery gray hair with coarse and irregular clumps of melanin in the middle of hair shaft (Figure 1), light-colored skin, recurrent diarrhea and chest infections, hepatosplenomegaly and pancytopenia.Bone marrow was suggestive of hemophagocytic lymphohistiocytosis (Figure 2) without giant cytoplasmic granules in neutrophils.

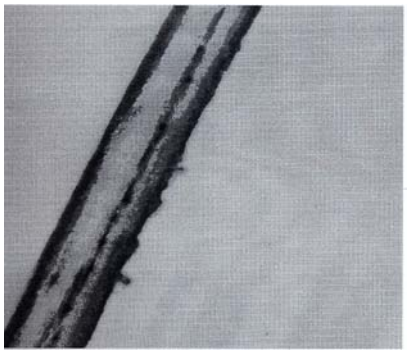

Figure 1. Coarse and irregular clumps of melanin seen in middle of hair shaft.

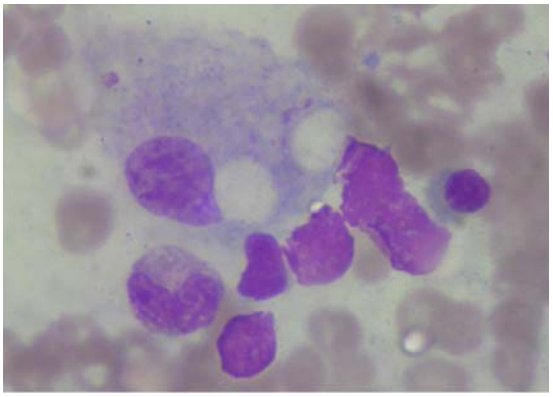

Figure 2. Large macrophage ingesting blood elements in bone marrow.

The prognosis and treatment of this disease depends on its particular type of the disease. In patients with GS type 1, there is no definitive care, and the outcome depends on the severity of neurologic manifestations. GS type 2 has a grave prognosis and proves fatal unless bone marrow transplantation is instituted which is the only reliable way to prevent recurrences of the accelerated phase and early death in GS syndrome, as our patient who died early. High doses systemic steroids and other immunosuppressives can be used[5] until bone marrow transplantation is carried out. GS type 3 does not pose a threat to those affected and needs no active intervention.

Diagnosis of our patient was based on clinical symptoms and morphologic examination of bone marrow and hair shaft, although diagnosis of GS type 2 was rather clear cut in our patient, but genetic study is required for definitive diagnosis.

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