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GRISCELLI'S SYNDROME: CLINICAL FEATURES OF THREE SIBLINGS*

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Three siblings diagnosed as having Griscelli's syndrome (GS) are presented. The clinical features were partial albinism, silvery hair and absence of giant granules in the white blood cells. The diagnosis of GS was confirmed intra-vitam in the youngest sibling (propositis) at the age of nine months by the demonstration of irregular clumps of pigment in the hair shaft, and in particular melanocytes engorged with melanosomes in the skin biopsy, findings characteristic of this syndrome. A retrospective diagnosis of GS was made in the older two siblings.

The first sibling died at the age of two, having a clinical picture suggestive of bulbar poliomyelitis. However, no tissue was available for histopathologic examination. The second sibling developed fever, jaundice, seizure, hepatosplenomegaly and lymphadenopathy and died at the age of six. Postmortem examination of this sibling revealed lymphohistiocytosis in the liver and spleen. The propositus died at the age of five following development of central nervous system involvement.

Immunologic studies were not available in the first sibling. The IgG level was slightly low and the T-lymphocyte number was normal in the second sibling. The propositus had normal serum immunoglobulin levels and T-cell numbers and skin tests were positive with phytohemagglutinin and candida. *Key words: clinical features, Griscelli's syndrome.*

Griscelli's syndrome, first described in 1978, is characterized by partial albinism and immunodeficiency[1,2]. Patients may develop progressive neurological deterioration and lymphohistiocytosis and usually die of these complications[3-5].

We present a family in which three of five children of consanguineous parents were affected. Two of the children had partial albinism at birth and an absence of giant granules in the blood leukocytes. One sibling died at the age of two, and the other at the age of six. The third sibling, who also had partial albinism, was diagnosed as having Griscelli's syndrome after microscopic examination of the

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hair and electron microscopy of the skin revealed findings consistent with this syndrome. We report three siblings afflicted with Griscelli's syndrome because of the rarity of this disorder and also to stress the importance of differential diagnosis.

Case Reports

The propositus, a nine-month-old girl, who appeared in overall good health, was seen at the Hacettepe University Children's Hospital because of a history of sibling deaths in the family (Fig. 1). Physical examination was unremarkable except for the presence of partial albinism. The pathognomonic granules of Chédiak-Higashi syndrome (CH) were not observed in peripheral blood smears and bone marrow specimens. The peripheral white blood cell (WBC) count with the differential count and the platelets were within normal limits. Serum immunoglobulin (Ig) levels and the T-cell number were also within normal limits. Delayed type skin sensitivity tests were positive with phytohemagglutinin and candida and negative with streptokinase streptodornase.

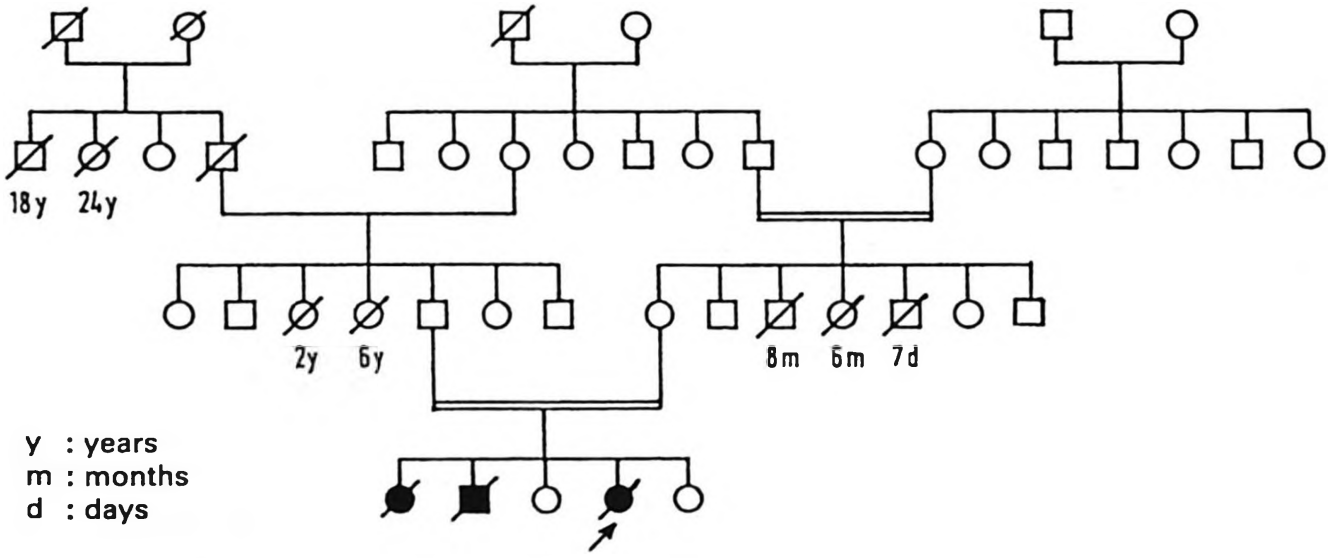

Fig. 1

Light microscopy of the hair revealed irregular clumps of pigment in the hair shaft and a random skin biopsy revealed rather large melanin granules in the deep portion of the epidermis, especially in the basal layer associated with a lesser degree in the dermis (Fig. 2a). Electron microscopy of the skin biopsy showed melanocytes engorged with melanosomes and very few melanosomes in the surrounding keratinocytes (Fig. 2b).

The patient was lost to follow-up. Recent contact with the family disclosed that at the age of five she developed progressive deterioration including ataxia,

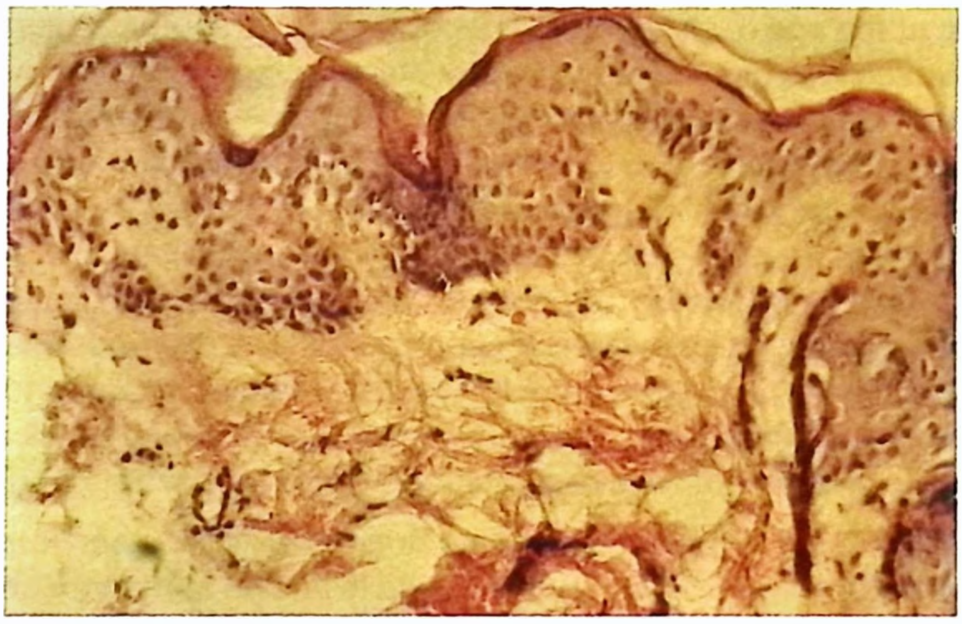

Fig. 2a

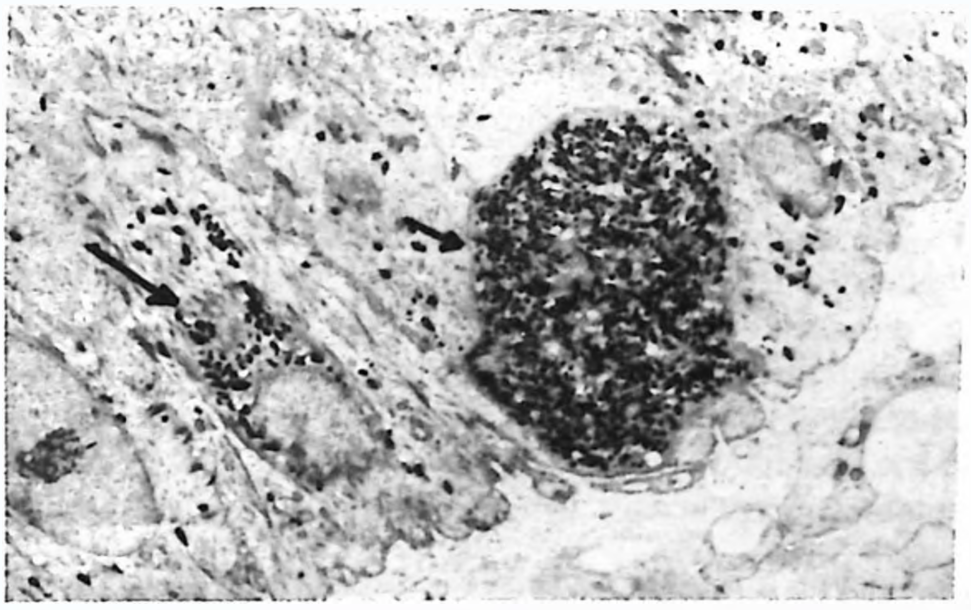

Fig. 2b

dysmetria, involuntary movements, pigmented lesions on the cheeks (which developed at the age of two), and thrombocytopenia. The patient died in another hospital within a period of two months. Her past history was unremarkable except for recurrent upper respiratory tract infections.

The first-born child of the family also had silvery hair and died at the age of two. The clinical picture was suggestive of viral paralytic disease, but no tissue was available for histopathological examination.

The older brother, who also had silvery hair, developed fever, jaundice, seizures, hepatosplenomegaly, lymphadenopathy, atypical lymphocytosis, and throm-

bocytopenia at the age of six. He had a peculiar dark red-purplish pigmentation on his cheeks which was described by his parents as being more prominent than that seen on the other two affected siblings. He died on the 22nd day of hospitalization. His white blood cell count varied between 2,000-14,000/mm^3, with a distribution of 20-66% lymphocytes, 39-75% neutrophils, a hemoglobin of 5.9-9.8 g/dl, and markedly decreased platelets on blood smears. No giant granules were noted in the blood leukocytes. Serum bilirubin and transaminase levels were elevated as were the uroporphyrin and coproporphyrin concentrations in the urine. The serum IgG level was slightly low (IgG subclasses were not determined) and the T-lymphocyte number was normal. Postmortem histopathological examination of the liver and spleen revealed infiltration of lymphocytes and histiocytes.

The parents were first cousins and they, along with two other female children who had dark hair, were healthy. A paternal uncle and an aunt, both of them blond, died of unknown causes at the age of 18 and 24, respectively.

Discussion

The diagnosis of Griscelli's syndrome is arrived at on the basis of the presence of a typical clinical phenotype (light skin color with silvery hair) and microscopic examination of the skin biopsy.

The clinical symptoms of patients with Griscelli's syndrome are similar to that seen in Chédiak-Higashi (CH) syndrome, but the granulocytes show giant cytoplasmic granules. In our patients, pigmentary abnormalities, clinical symptoms and the course of the disease suggested CH or Griscelli's syndrome. The absence of giant granules in the white blood cells, the microscopic findings of the hair and the electron microscopic changes seen in the skin of the propositus were consistent with Griscelli's syndrome.

Immunodeficiency is a feature of Griscelli's syndrome. Defects in T and B cell immunity having no consistent pattern have been described in these patients[3-6]. However, the stage at which immunologic studies performed may determine the results. By way of an example we cite the case described by Schneider et al[4] of a three-month-old girl with Griscelli's syndrome. She had normal T and B cell immunity before successful bone marrow transplantation, while her older brother, afflicted with the same disease, showed a decreased number of T cells, poor T cell mitogen stimulation with concavalin A and pokeweed mitogen. He died at the age of eight months.

Although detailed immunological studies were not performed, one of our patients had normal serum immunoglobulin levels, another had a slightly low IgG level, and both had normal T cell numbers.

Successful treatment of the syndrome with allogeneic bone marrow transplantation has been reported and seems to have a curative effect when performed early in the course of the disease[4].

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