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Griscelli Syndrome with Neurological Deterioration: A Case Report

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ABSTRACT

Griscelli syndrome (GS) is an autosomal recessive disorder with partial albinism, silver gray hair, hemophagocytic lymphohistiocytosis (HL). There are three types. Central nervous system involvement may be seen in GS2 without hemophagocytosis.

Keywords: *central nervous system involvement, griscelli syndrome, hydrocephaly*

ÖZ

Nörolojik Kötüleşme ile Giden Griscelli Sendromu: Olgu Sunumu

Griscelli sendromu (GS) parsiyel albinizm, gümüş gri renk saç, hemafagositik lenfohistiyositozun da görüldüğü otozomal resesif bir hasatlıktır. Üç tipi vardır. Santral sinir sistemi tutulumu hemofagositoz olmadan GS tip 2'de görülebilir.

Anahtar kelimeler: *griscelli sendromu, santral sinir sistemi tutulumu, hidrosefali*

INTRODUCTION

Griscelli syndrome (GS) is an autosomal recessive disorder with partial albinism, silver gray hair, hepatosplenomegaly, immune deficiency, hemophagocytic lymphohistiocytosis (HL), and neurological manifestations [1,2]. There are three types: Griscelli syndrome type 1 (GS 1): Early severe psychomotor retardation and a normal immune state; Griscelli syndrome type 2 (GS 2): Immune deficiency, hemophagocytic lymphohystiocytosis, and neurological findings in the absence of a primary neurologic disease; Griscelli syndrome type 3 (GS 3): Includes partial albinism with hypopigmentation of the hair and skin [1]. Central nervous system involvement has been described previously. Here, we describe a case of GS 2 without HL.

CASE REPORT

A three-year old boy was admitted to the hospital with visual impairment of recent onset. He complained of a headache and was anxious for two to three days. His speech was not fluent for the past 10 days. The prenatal, natal, and postnatal history was unremarkable. His developmental milestones were appropriate for age. The patient was the first child of consanguineous parents.

Two months ago the patient was admitted to the hospital with abdominal pain, fever, a generalized tonic-clonic seizure, and confusion. The patient was diagnosed with meningitis. A bone marrow aspirate did not reveal hemophagocytosis. The EEG was normal. The magnetic resonance imaging revealed hyperintensities of the cerebral hemispheres, cerebellum, and brainstem on T2 weighted and FLAIR images; consistent with de-dysmyelinating lesions (Figure 1A). The patient could sit but he could not walk by himself at discharge from the hospital.

PHYSICAL EXAMINATION

The body weight was 11 kg (<5th centile); height was 96 cm (50-75th centile), head circumference 50 cm. The hair, eyelashes and the eyebrows were light gray and the skin was bronzed (Figure 1B). The patient

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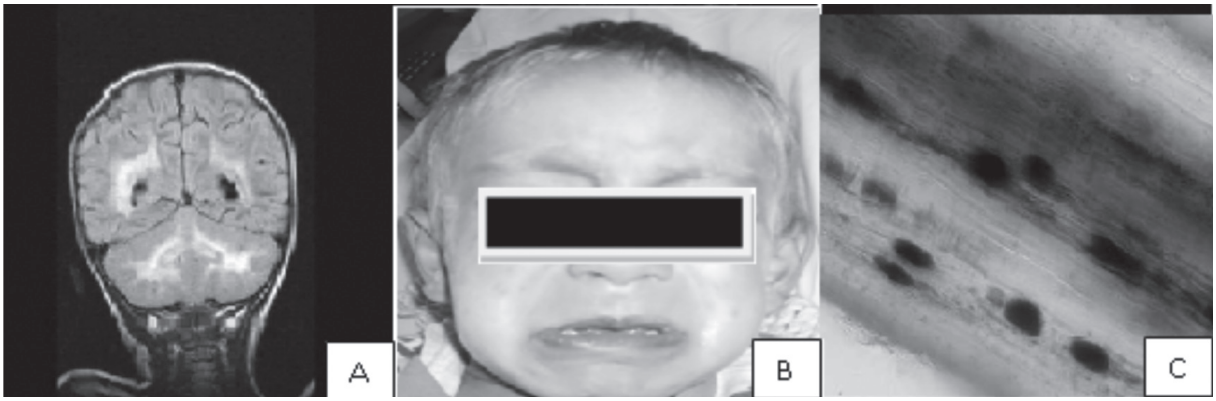

Figure 1. Features of the patient
T2 weighted image and fluid attenuated inversion recovery (FLAIR) images showing (A) Hyperintensities around periventricular region, at cerebellum an brain stem. (B) The patient, showing silver-gray eye brows. (C) Light microscopic views of the patient's hair representing ırregular melanin clusters on hair at light microscope.

was conscious, and was looking around as if he did not know where he was and/or could not see. The left lateral gaze was impaired. There was bilateral papilledema and bilateral nystagmus. The muscle tone was slightly increased, the deep tendon reflexes were hyperactive, the Babinski sign was positive bilaterally, and clonus was present. The patient could not walk or sit. There was no organomegaly or lymphadenopathy.

The initial laboratory evaluations showed: WBC: 5,280 µL, Hb: 12.1 g/dl, Plts: 327,000 µL; the blood smear showed 48% neutrophils, 52% lymphocytes; the erythrocytes were normochromic and the thrombocytes were clustered. The biochemical parameters were normal. The serum immunoglobulins were also normal.

The Ophthalmologic examination did not reveal ocular albinism. The bone marrow aspirate did not reveal hemophagocytosis. Microscopic examination of the patient's hair showed melanin clumps in the center of the hair shaft (Figure 1C). The cranial CT revealed hydrocephaly in both lateral ventricles and the third ventricle, and hypodensities in the periventricular region.

Upon follow up, the neurosurgery department was consulted, before surgery dexamethasone had started for cerebral edema, diazomide was added for papilledema. There was stiffness around the entire body; he had an opisthotonic posture in the bed. His deep tendon reflexes were increased, and he became confused. His respirations were shallow. The tonic convulsions did not respond to phenytoin treatment. After ventriculo-peritoneal shunt surgery, the convulsions continued for two days. The convulsions were treated using a midazolam infusion. The patient was unconscious with an intermittent tonic posture. Clonazepam was started. The papilledema resolved after seven days. He could not sit or walk 10 days after the operation. He was discharged on the 20th day after admission. There was nystagmus of both eyes. The deep tendon reflexes were hyperactive, the Babinski sign was positive, and he could not see anything around himself. He could not walk or speak fluently. He was using signs only to communicate. The patient could sit by himself and look around. He had ataxia while sitting. The nystagmus resolved on follow-up, 15 days after discharge.

DISCUSSION

Griscelli syndrome resembles Chediak-Higashi syndrome (CHS) with partial albinism, frequent infections, episodes of fever, neutropenia and thrombocytopenia. Pigmentary dilution of the skin, and the hair (partial albinism), eye lashes and eyebrows, large melanin clumps in hair shafts, cellular type immune deficiency, lymphocyte and macrophage activation, as well as recurrent infections, hepatosplenomegaly, and consequent neurological deficits are seen with GS [1-3].

The RAB27A and MYO5A genes on chromosome 15q21, are responsible for the GS type 1 and 2 [4]. GS

type 3 results from a defect in MLPH (melanophilin) on chromosome 2 or MYO5A on chromosome 15 [2]. GS type 3 presents as hypopigmentation of the hair and skin without other findings [1-4].

GS type 1 (GS1) is characterized by hypomelanosis and primary neurological deficits but no immunologic impairment. Patients have developmental delay, mental retardation early in life. The neurological deficits are stable and do not progress with time [1,8]. There is not an accelerated phase. Congenital cerebellar atrophy may be seen with neuroimaging of GS1 [1,8].

Patients with GS2 have normal psychomotor development at the beginning of their life and then later develop neurological problems including regression as well as hemophagocytosis and histiocytic infiltration of the CNS. The neurological symptoms include: hyperreflexia, hypertonia, seizures, increased intracranial pressure, nystagmus, ataxia, and fatal degeneration. Cerebellar hypodense areas, ventricular dilatation, white matter changes, periventricular and basal ganglia calcifications and hyperdense areas, compatible with inflammatory changes, are neuroimaging findings associated with GS2 [1,4,7].

Chediak-Higashi and Elejalde syndromes must be ruled out in the differential diagnosis of GS [5]. The ophthalmogical examination is normal in Griscelli syndrome [4].

In the case reported here, the silver-gray hair, microscopic changes of the hair helped the diagnosis. The patient did not have prolonged fever, jaundice, splenomegaly, lymphadenopathy, pancytopenia, hypertriglyceridemia, or hemophagocytes in the bone marrow. The patient had developmental milestones appropriate for age. The patient had meningitis at 2 years and 10 months. The development was normal up to that time. The neurological examination revealed slightly increased muscle tone, increased deep tendon reflexes, bilaterally positive Babinski sign, and positive clonus. There were normal ocular findings at first but papilledema developed at the time hydrocephaly was found. The patient had hyper-intensities of the cerebral hemispheres, cerebellum, and brainstem on T2 weighted and FLAIR images, which were consistent with de-dysmyelinating lesions. Also noted were delay in myelination, focal gray and white matter changes, diffuse non-specific atrophy, and calcifications [6]. The neurological manifestations of this patient were compatible with the diagnosis of GS2.

Neurological involvement is seen after an accelerated phase with pancytopenia, hemophagocytosis, hypoproteinemia, and organomegaly; all have been described previously. Rajadhyax et al. [6] reported a case that presented with neurological involvement, obstructive hydrocephalus, without hematological disturbances or organomegaly. The patient reported here had central nervous system involvement without an accelerated phase. Therefore, central nervous system involvement may be seen in GS2 without hemophagocytosis.

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