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Case report

Cutaneous granulomas in Griscelli type 2 syndrome

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Introduction

Griscelli syndrome (GS) is a rare autosomal recessive disease that may compromise the skin, nervous, immune, and lymphoreticular systems as well as solid internal organs. Mutations in genes responsible for cellular membrane trafficking control have been identified. This may explain the dysfunction of melanocytes, neurons, and immune cells.[1] Correlation between genetic defects and clinical manifestations have been reported: neurologic defects are frequent and severe in type 1 GS, milder in type 2, and absent in type 3. Immunological abnormalities such as hypogammaglobulinemia, natural killer cell dysfunction, and infiltration of lymphoid organs are observed only in types 2 and 3.[2] Type 2 GS has a poor prognosis, with rapid development of hemophagocytic syndrome and death in the absence of bone marrow transplantation. Dermatological signs are usually limited to characteristic silvery scalp hair and eyebrows and skin hypopigmentation.[3] Few reports of other cutaneous manifestations in GS have been published. In this case, we describe a child with type 2 GS associated with granulomatous lesions.

Case presentation

A 1-year-old boy was admitted with a 2-month history of fever, worsening of his general condition, and persistent skin lesions on the face. His parents were first-degree cousins; pregnancy and birth records were normal. His medical file reported several upper respiratory tract infections and delay of neurologic milestones. Clinical examination revealed intense skin and mucosal pallor with shiny silver-colored hair in the scalp and eyebrows. Multiple 1–2 mm red, crusted papules were observed on the cheeks and thighs (Fig. 1). Splenomegaly was also noted. Laboratory work-up revealed anemia and thrombocytopenia. Bone marrow biopsy revealed mild dysplasia of the erythroid lineage. Immune tests were normal for

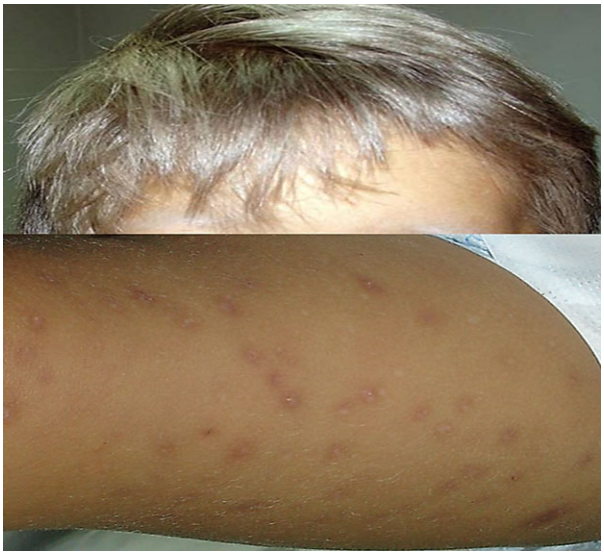

Figure 1 Shiny silver-colored scalp hair and eyebrows and crusted red papules on the left thigh

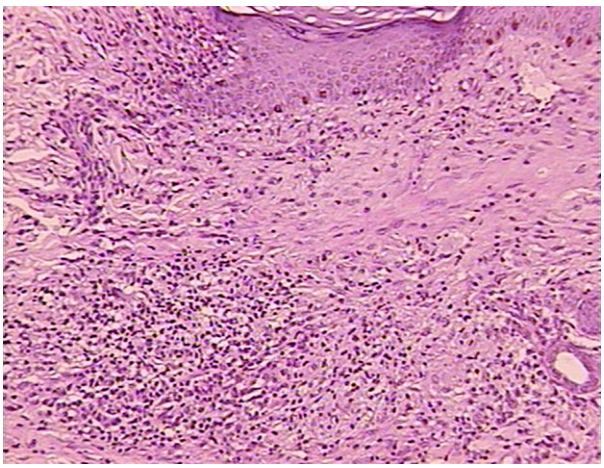

Figure 2 Biopsy from facial lesion showing granulomas, large epidermal melanocytes, and scant pigmentation of surrounding keratinocytes (hematoxylin and eosin stain, original magnification ×40)

chemotaxis, phagocytosis, and immunoglobulin count. Histopathology of the cutaneous lesions showed necrobiotic granulomas along with large, hyperpigmented epidermal melanocytes with scarce pigmentation of surrounding keratinocytes (Fig. 2). Ziehl–Neelsen stain and Koch culture were negative. Light microscopy of scalp hair shafts showed few and large centrally located melanin granules. Genetic analysis confirmed an intragenic deletion in Rab27a in chromosome 15q21. These findings were consistent with GS type 2. A computed tomography scan revealed focal demyelinization in the brain and splenomegaly. While waiting for bone marrow transplant, the patient presented with seizures, urinary sepsis (due to *Proteus mirabillis*) associated with lymphocytosis, hepatosplenomegaly, and Epstein–Barr infection. This was interpreted as hemophagocytic lymphocytosis and treated with the HLH-94 protocol (etoposide, dexamethasone, and cyclosporine A) with recovery of neurologic status and resolution of cutaneous lesions. However, a few months later, pulmonary infection led again to hemophagocytic lymphocytosis and death before he could be transplanted. The formation of granulomas in this case, like other phagocytic immunodeficiency diseases, may result from hyperactivation and hyperproliferation of cytotoxic T cells and macrophages as well as hypercytokinemia. This leads to accumulation of lymphohistiocytic infiltrates in the skin as well as other organs.[4] Triggers of this overactive immune response are most likely infectious, such as virus, bacteria, fungi, and parasites. In the setting of a child with recurrent and severe infections, the presence of cutaneous granulomas may not only help early detection of a primary immunodeficiency but also be associated with systemic involvement and poor prognosis.

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