GRISCELLI SYNDROME: A RARE CAUSE OF HAIR AND SKIN HYPOPIGMENTATION

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Abbreviation **GS** = Griscelli syndrome.

Case report. A 7-year-old child, born to non-consanguineous parents, after an uneventful pregnancy and delivery, with normal psychomotor development and updated vaccinations, presented for evaluation of asymptomatic hypopigmented macules and patches present since birth on the trunk and later on the face, neck, hands, upper limbs, and left lower limb.

No significant changes in the number or size of lesions had occurred over the past 5-6 years. Since birth, the parents had noted light-colored hair in the frontal area, with black hair elsewhere. No family members, including siblings or parents, had light-colored hair or other dermatological/systemic disorders.

Physical examination revealed numerous hypopigmented macules, well or poorly defined, some confluent into patches ranging from 4×3 cm to 2×2 cm, located on the face, trunk, both arms, cubital and popliteal fossae, palms, and the dorsum of the right hand. The hypopigmented macules followed a linear or whorled pattern on the right side of the trunk; diffuse hypopigmentation was present in the right umbilical area and right hemiface (Fig. 1-3). Silver-white hair tufts were observed on the vertex, while the remaining scalp hair was black. Nails, teeth, and mucosae were normal. Vital signs, general and systemic examination were within normal limits.

Dermoscopy of the hypopigmented patches showed small white structureless areas.

Examination of the light-colored hair revealed large melanin pigment clumps along the hair shaft (Fig. 4), while black hair shafts appeared normal without pigment clumping.

The final diagnosis of Griscelli Syndrome Type 3 was based on the clinical history, trichological findings, and absence of systemic involvement.

The patient was referred for pediatric and ophthalmologic evaluation, both of which were normal.

The parents were informed of the need for genetic testing targeting the *Melanophilin* and *MYO5A* genes. However, the patient did not return for follow-up.

Discussion. Griscelli syndrome (GS) is an autosomal recessive disorder causing hypopigmentation of the skin and hair, with the characteristic silvery sheen of hair and large melanin clumps within the hair shaft. It may be associated with neurological deficits or severe immunodeficiency (4).

Most reported cases come from the Mediterranean region or the Middle East, often involving patients with consanguineous parents (5). The syndrome usually manifests between 4 months and 4 years of age, with diagnosis occurring between 4 months and 7 years (6).

To understand the etiopathogenesis of Griscelli syndrome it is necessary to remember that melanosome transport from the center to the cell periphery occurs along microtubules and is mediated by motor proteins such as dyneins and kinesins. Myosin Va (Myo5a), a motor protein, binds to melanosomes through interaction with Mlph and Rab27a.

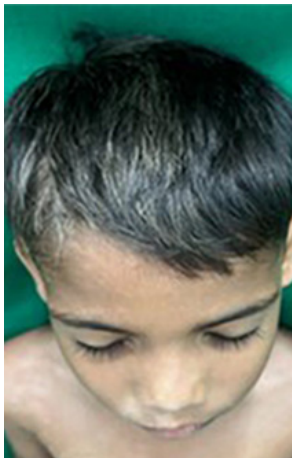
Fig. 1

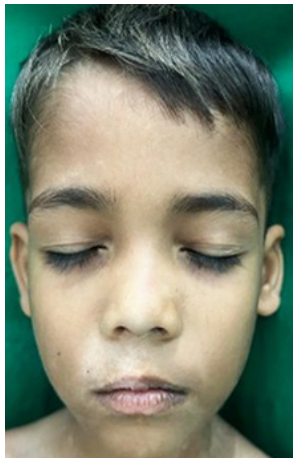
Fig. 2

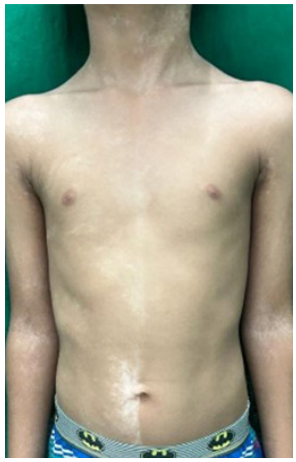
Fig. 3


Fig. 4

Fig. 1, 2, 3, 4: Griscelli Syndrome Type 3 in a 7-year-old child: gray-silvery hair (Fig. 1, 2), hypopigmentation of the right half of the upper lip (Fig. 2) and the right periumbilical area (Fig. 3). In Fig. 4, clumps of melanin regularly distributed along the hair shaft.

This tripartite complex (*Rab27a*, *Mlph*, *Myo5a*) is essential for vesicle transport and trafficking within cells, including melanocytes and neurons. A mutation in one of the complex components impairs melanosome transport, leading to perinuclear accumulation and failure to transfer pigment to keratinocytes, resulting in cutaneous hypopigmentation and silvery hair. Genetic characterization has shown that mutations in each component lead to distinct GS subtypes (1).

Type 1 GS, caused by *MYO5A* mutations, presents with severe early-onset neurological deficits (psychomotor delay, muscular hypotonia, intellectual disability). Management is supportive.

Type 2 GS, due to *Rab27a* mutations, results in immunodeficiency with impaired cytotoxic granule exocytosis in T cells and NK cells, hypogammaglobulinemia and recurrent infections. It is associated with hemophagocytic lymphohistiocytosis, a potentially fatal condition. Allogeneic hematopoietic stem cell transplantation is the curative treatment.

Type 3 GS is caused by *Mlph* mutations or deletion of exon F in the *MYO5A* gene. The *Melanophilin* gene encodes a linker protein between *Rab27a* and *Myo5a*. The mutation results in skin and hair hypopigmentation only, with no systemic involvement. The prognosis is good and no treatment is necessary (1).

Microscopically, all GS types show irregular clumps of melanin in the hair shaft. Histology of hypopigmented patches reveals melanin excess in basal layer melanocytes and poor pigmentation of surrounding epidermis.

Ultrastructural (electron microscopy) examination shows mature melanosomes in melanocytes and to a lesser extent in keratinocytes (7).

Griscelli syndrome must be primarily differentiated from Chediak-Higashi syndrome, which is clinically similar to GS but caused by mutations in the *CHS1* gene and characterized by the presence of giant cytoplasmic granules in neutrophils.

Since prognosis, treatment options, and genetic counseling vary significantly among the different GS types, molecular characterization is essential for accurate diagnosis (8).

Conclusion. This case was presented to remind clinicians that Griscelli syndrome, despite its rarity, should be considered among the numerous causes of cutaneous hypopigmentation, given its potential systemic implications.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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