



Case Report

A Child with Silvery Hair and Fatal Immune Dysfunction: Griscelli Syndrome Type 2: A Case Report

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ABSTRACT

Griscelli syndrome type 2 (GS2) is a rare autosomal recessive disorder characterised by hypopigmented silvery-grey hair, immunodeficiency and pre-disposition to haemophagocytic lymphohistiocytosis (HLH), a life-threatening hyperinflammatory condition. We report a genetically confirmed case of GS2 in a 3-month-old male born to consanguineous parents, presenting with silvery hair, recurrent fever and hepatosplenomegaly. Hair shaft microscopy revealed large, uneven melanin clumps - a hallmark feature of GS. Laboratory evaluation showed neutropenia, elevated ferritin and hypertriglyceridaemia, meeting HLH criteria. Genetic testing confirmed a homozygous RAB27A mutation. A significant family history of a sibling with similar features and early death emphasised the importance of pedigree analysis. Early clinical suspicion, supported by microscopy and timely genetic confirmation, enabled pre-HLH diagnosis and referral for haematopoietic stem cell transplantation. This report contributes to the limited global literature and highlights the diagnostic significance of clinical, microscopic and familial clues in identifying GS2 early.

Keywords: Diagnosis, Griscelli syndrome, Haemophagocytic lymphohistiocytosis, Immunodeficiency, Pigmentary disorder

INTRODUCTION

Griscelli Syndrome (GS), first described by Griscelli *et al.* in 1978, is a rare autosomal recessive disorder classified under the group of 'silvery hair syndromes.' It shares phenotypic similarities with Chediak-Higashi syndrome (CHS) and Elejalde syndrome^[1] but has distinct genetic mutations and clinical features. GS presents in early childhood with silvery-grey hair, skin hypopigmentation and variable degrees of immune or neurological involvement depending on the subtype. The syndrome typically presents around 17.5 months of age, with no clear sex predilection.^[2]

GS is categorised into three subtypes: GS type 1 (MYO5A [Myosin VA] mutation and neurological involvement), GS type 2 (RAB27A [Ras-related protein Rab-27A] mutation, immune dysfunction with haemophagocytic lymphohistiocytosis [HLH]) and GS type 3 (Melanophilin MLPH mutation, limited to pigmentation defects). Amongst these, GS2 is the most severe due to its association with HLH, a fatal hyperinflammatory condition characterised by uncontrolled immune activation, cytopenias, hepatosplenomegaly, hyperferritinaemia and hypertriglyceridaemia.^[3]

Diagnosis relies on clinical presentation, microscopic hair shaft examination and genetic testing. Early recognition is crucial, as haematopoietic stem cell transplantation (HSCT) is the only

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curative treatment. We report a case of GS2 diagnosed in a 3-month-old infant before the onset of overt HLH, adding to the limited number of approximately 160 cases reported worldwide.

CASE REPORT

A 3-month-old male infant presented with fever (37.8°C), wheezing and chest congestion. The scalp hair, eyebrows and eyelashes were diffusely silvery-grey since birth. He was the fifth child of consanguineous parents (third-degree relatives). A family history revealed that his mother's second child, a girl with similar hair colour, had recurrent fevers and died at 3 years of age. Another 3-year-old sibling exhibited mild hair hypopigmentation without systemic symptoms. These findings suggest a strong familial pattern and underscore the potential fatal nature of the disease if left undiagnosed. The recurrence in multiple siblings supports the autosomal recessive inheritance pattern and highlights the need for cascade family screening.

The infant was born full term through normal vaginal delivery, with a birth weight of 2.8 kg, and had an uneventful perinatal period. Developmental milestones were appropriate for age and immunised for age.

On clinical examination, the infant was alert and well-nourished, with fair skin and silvery-grey hair. Ocular examination revealed light grey irides [Figure 1]. Neurological examination revealed normal tone, preserved deep tendon reflexes and an extensor plantar response. Systemic examination revealed hepatosplenomegaly, with the liver palpable 3 cm below the right costal margin and the spleen 2 cm below the left costal margin.



Figure 1: Clinical image of a 3-month-old infant diagnosed with Griscelli syndrome, showing silvery grey scalp hair, eyebrows and eyelashes. Facial features include a broad forehead and prominent cheeks. Eyes are digitally covered to ensure anonymity. Appropriate patient consent has been obtained for the use of clinical images.

Laboratory investigations showed normocytic, normochromic anaemia (haemoglobin 11.5 g/dL), neutropenia (18%) and lymphocytosis (55%). Peripheral blood smear revealed no giant azurophilic granules in neutrophils, helping to exclude CHS. Liver function tests showed elevated serum glutamic pyruvic transaminase (126 U/L) and alkaline phosphatase (226 U/L). Hypertriglyceridaemia (220 mg/dL) and elevated ferritin (1280 ng/mL) were noted, suggestive of HLH. Abdominal ultrasonography confirmed hepatosplenomegaly.

Hair shaft microscopy demonstrated large, irregular clumps of melanin pigment within the medulla of the hair shaft, a classical feature of GS [Figure 2]. Based on clinical features, family history and hair microscopy, a diagnosis of GS2 was strongly suspected. Genetic testing confirmed a homozygous mutation in the *RAB27A* gene, thereby establishing the diagnosis.

The patient fulfilled five of the eight HLH-2004 diagnostic criteria (fever, splenomegaly, cytopenia, hyperferritinaemia, hypertriglyceridaemia), placing him at imminent risk for developing overt HLH [Table 1].^[4] He was managed symptomatically for acute bronchitis and discharged under close surveillance with immunology consultation and referral for HSCT evaluation. Genetic counselling was initiated for the family.

DISCUSSION

GS2 is a rare disorder caused by *RAB27A* mutations, resulting in impaired lytic granule trafficking in cytotoxic T and natural killer cells.^[5] This defect leads to uncontrolled immune activation and pre-disposition to HLH, a potentially fatal condition if not diagnosed and treated early.^[6]



Figure 2: Light microscopy of hair shaft from a 3-month-old infant with Griscelli syndrome (unstained, ×400 magnification), showing large, irregularly distributed clumps of melanin pigment along the shaft, characteristic of melanin granule clumping (black arrow). Scale bar: 50 micrometers.

Table 1: HLH-2006 diagnostic criteria used in the diagnosis of haemophagocytic lymphohistiocytosis associated with Griscelli syndrome.

Category	Criterion	Threshold
Primary criteria (5/8 or genetic confirmation)	Fever	≥38.5 fever°C for >7 days
	Splenomegaly	Clinically detected
	Cytopenias	Hb<9g/dL, Platelets<100,000/μL, Neutrophils<1,000/μL
	Hypertriglyceridaemia/hypofibrinogenaemia	TG≥265 mg/dL, Fibrinogen≤150 mg/dL
	Haemophagocytosis	In marrow, spleen, nodes or liver
	Low NK cell activity	Functional assay
	Hyperferritinaemia	Ferritin≥500 ng/mL
	Elevated sCD25	≥2400 U/mL
Supportive findings	D-dimer, LDH, AST/ALT	Elevated
	CNS involvement	Seizures, encephalopathy
Genetic confirmation	HLH Mutations	RAB27A (GS-2), PRF1, UNC13D, STX11

LDH: Lactate dehydrogenase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CNS: Central nervous system, HLH: Haemophagocytic lymphohistiocytosis, NK: Natural killer

The novelty of this case lies in the early diagnosis made at 3 months of age, before the progression to severe immune dysregulation. Most GS2 cases are identified late, often after the development of overt HLH symptoms. In our case, early clues, including hair pigmentary changes, hepatosplenomegaly and a positive sibling history, guided suspicion towards GS2. Hair shaft microscopy, an inexpensive and non-invasive bedside tool, played a crucial role in narrowing the differential.^[7]

The differential diagnosis includes CHS, which was ruled out by the absence of giant azurophilic granules in neutrophils. CHS can also progress to HLH in its accelerated phase, making early differentiation essential. Elejalde syndrome, characterised by neurological but not immunological involvement, was also excluded.^[8] Genetic confirmation of a RAB27A mutation clinched the diagnosis.

CONCLUSION

This familial case with three affected siblings, one of whom died likely due to undiagnosed HLH, underscores the strong genetic association of GS2. Early recognition based on pigmentary changes, hepatosplenomegaly, and family history, supported by hair shaft microscopy and genetic confirmation, allows timely referral for hematopoietic stem cell transplantation before the onset of life-threatening HLH. Proactive family screening and prenatal diagnostic options are vital for preventing recurrences and improving outcomes in high-risk families.

Importantly, this is a familial case with three affected siblings, one of whom died likely due to undiagnosed HLH. This underscores the strong genetic association and highlights the

need for proactive family screening and prenatal diagnostic options in future pregnancies.

HSCT, when performed before an HLH crisis, significantly improves survival. This case reinforces the importance of early recognition, prompt immunological referral and genetic counseling, particularly in consanguineous families where recurrence risk is high.

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Ethical approval: Institutional Review Board approval is not required.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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REFERENCES

1. Griscelli C, Durandy A, Guy-Grand D, Daguillard F, Herzog C, Prunieras M. A Syndrome Associating Partial Albinism and Immunodeficiency. *Am J Med* 1978;65:691-702.
2. Moradveisi B, Karimi A, Behzadi S, Zakaryaei F. Griscelli Syndrome in a Seven Years Old Girl. *Clin Case Rep* 2021;9:e04212.
3. Singh J, Adil M, Amin SS, Tuz Zahra F. Griscelli Syndrome with Malnutrition: A Diagnostic Challenge. *Dermatol Rev* 2022;109:142-7.
4. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, *et al.* HLH-2004: Diagnostic and Therapeutic Guidelines for Hemophagocytic Lymphohistiocytosis. *Pediatr Blood Cancer* 2007;48:124-31.
5. Menasche G, Pastural E, Feldmann J, Certain S, Ersoy F, Dupuis S, *et al.* Mutations in RAB27A Cause Griscelli Syndrome Associated with Haemophagocytic Syndrome. *Nat Genet* 2000;25:173-6.
6. Hachohen Y, Gilmour K, Ehl S, Bredius R, Fitzgerald J, Worth A, *et al.* Hemophagocytic Lymphohistiocytosis in Griscelli Syndrome: A Single-Center Report of 10 Cases. *Pediatr Blood Cancer* 2015;62:1020-6.
7. Sarkar R, Ghosh A, Bandyopadhyay SK. Silvery Hair Syndromes: A Brief Review. *Indian J Dermatol Venereol Leprol* 2012;78:72-5.
8. Barak Y, Nir A, Goldman M. Silvery Hair with Immunodeficiency: Diagnostic Challenge between Chediak-Higashi and Griscelli Syndromes. *Pediatr Dermatol* 1999;16:441-4.

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