

Paediatric Dermatology Column: Case Report

Silvery hair syndromes: report of familial cases of Griscelli syndrome in three siblings

銀髮綜合徵：一個三姐妹患有格里塞利綜合徵的家族案例報告

A Molina-Leyva and MA Fernandez-Pugnaire

Silvery hair is a rare clinical feature, common in a group of rare syndromes, which usually present in the paediatric age group termed together as "silvery hair syndromes". We report a consanguineous family in which three out of four siblings had silvery hair and neurological deficits and were diagnosed to have Griscelli syndrome. The diagnosis of Griscelli syndrome in our cases was based on clinical findings with severe neurological impairment in the absence of immunodeficiency and the characteristic findings of hair light microscopy.

銀色頭髮是一種罕見的臨床特徵，常見於一羣罕見的綜合徵，通常出現在兒童年齡組，統稱為「銀髮綜合徵」。我們報告一對近親婚姻父母的四個子女，當中三姐妹有著銀色頭髮和神經系統殘疾，她們被確診患有格里塞利綜合徵。這些病患的格里塞利綜合徵診斷是建基於沒有免疫力缺乏下的嚴重神經損傷的臨床表現和頭髮在顯微鏡下的特徵表現。

Keywords: Griscelli syndrome, silvery hair syndromes

關鍵詞： 格里塞利綜合徵、銀髮綜合徵

Introduction

Silvery hair is a rare clinical feature, common in a group of rare syndromes, which usually present in the paediatric age group and are termed

together as "silvery hair syndromes." These consist of Chediak-Higashi syndrome (CHS), Griscelli syndrome (GS) and Elejalde disease (ED).¹ The hypopigmentation of these rare autosomal recessive disorders is the result of a defective transfer of melanin to keratinocytes due to impaired melanosome transport. The main difference from oculocutaneous albinism is that in these syndromes, the melanin synthesis is unaffected.

Department of Dermatology, University Hospital, Granada, Spain

A Molina-Leyva, MD
MA Fernandez-Pugnaire, PhD

Correspondence to: Dr. A Molina-Leyva

Department of Dermatology, San Cecilio University Hospital,
Hospital Universitario San Cecilio, 18012, Granada, Spain

Case report

We report a consanguineous family in which three

out of four siblings had silvery hair and neurological deficits. The affected siblings are all girls while the unaffected one is a boy who had normal hair and enjoyed good health (Figure 1).

On physical examination, the hair of the three sisters over the entire body and scalp was silvery in colour including the eyelashes and eyebrows. These patients had photo-tanning with freckles over the face and other exposed parts. Neurological examination revealed generalised hypotonia and psychomotor retardation. Hair microscopy of the shaft showed evenly distributed



Figure 1. Older sister with silvery white hair, including eyelashes and eyebrows.



Figure 2. Light microscopy examination of hair shaft. Compound microscopy showing evenly distributed melanin granules of regular diameter which were bigger than those seen in normal hair (x40).

melanin granules of regular diameter that were bigger than those seen in normal hair (Figure 2).

Peripheral blood smear was normal and no prominent granules were found in the leucocytes in the smears performed in each visit for six times in the past one year. The immunological status was normal and there was no increase of opportunistic infections. The immunoglobulin levels were normal as well as lymphocytic populations. Therefore, the diagnosis of GS type 1 was made.

Discussion

Griscelli syndrome, first described by Griscelli and Prunieras in 1978, is characterised by reduced skin pigmentation, and is often referred to as partial albinism. There is silvery grey hair in combination with variable neurological impairment and immunodeficiency.² Three different types of GS have been identified: all share the same cutaneous phenotype but differ in the genetic substrate and in the extracutaneous manifestations. Approximately 60 cases have been reported but only two cases have been described in siblings.^{3,4}

In GS, hair microscopy reveals large clumps of pigment distributed irregularly along the hair shaft. Granulocytes have no giant granules. Hair shaft light microscopy shows large, irregularly shaped melanin granules, mostly located in the vicinity of the medullar zone. GS is classified into three types.⁵ In GS type 1, patients have silvery-grey hair, light-coloured skin, severe neurological defects and normal immune status.⁶ It is caused by a mutation in the myosin Va (*MYO5A*) gene located on chromosome 15q21. In GS type 2 patients have silvery-grey hair, pyogenic infections, haemophagocytic lymphohistiocytosis with an "accelerated phase" and variable neurological defects in the absence of primary neurologic disease.⁷ It is caused by a mutation in the *Rab27a* (*RAB27A*) gene located on chromosome 15q21.

In GS type 3, patients present with skin and hair hypopigmentation without nervous or immune system abnormalities. There are two different mutations associated with this type: the first is located in chromosome 2q37.3 (causing a mutation in *MLPH* gene) and the second is caused by an F-exon deletion in the *MYO5A* gene.⁷ Patients with GS type 3 do not need treatment and have a good prognosis. Long-term survival for GS type 1 and 2 is poor. The only curative therapy for the haemophagocytic lymphohistiocytosis in GS type 2 is allogeneic bone-marrow transplantation. Immunosuppressive regimens have also been used to attenuate the haemophagocytic syndrome.⁶ No specific treatment exists for the neurological impairment and the retarded psychomotor development of GS type 1 and 2. Recurrent infections can be easily managed with antibiotic treatment. Individuals who have GS or with a family history of GS should undergo genetic counselling before conceiving a child.⁵ Genetic counsellors can explain the different options like preimplantation genetic diagnosis or amniocentesis.

Our patient had silvery hair, skin pigmentation abnormalities, hypotonia and psychomotor retardation but no evidence of recurrent infections. Light microscopy showed small and large clumps of melanin in irregular pattern in the hair shaft.

The diagnosis of GS type 1 in our cases was based on the clinical findings of severe neurological impairment in the absence of immunodeficiency and the characteristic findings of hair light microscopy: small and large clumps of melanin in irregular pattern.

In conclusion, we report the first case series of Griscelli syndrome involving three siblings. We would like to emphasise that silvery grey hair provides a clue to the underlying disease and hence should alert the clinician to consider CHS, GS and ED. The workup of a patient with silvery hair should include a complete immune status assessment, neurological examination and light microscopy analysis of the hair shafts.

References

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