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Case Report

Griscelli Syndrome: A series of three cases

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Abstract Silvery white hair is an infrequent clinical manifestation seen in Chediak Higashi syndrome, Elejalde disease and Griscelli syndrome. Pigmentary dilution is common to all the three conditions. Clinical examination, hair and skin microscopic examination are instrumental in differentiating these syndromes. Presence of silvery hair in a patient should prompt the physician to look for any associated features. Presence of neurologic and immunologic impairment carries a poor prognosis. Here we describe a series of three cases of Griscelli syndrome.

Key words
Silvery hair, Griscelli syndrome, hair microscopy.

Introduction

Silvery white hair syndrome is a group of rare autosomal recessive conditions which are of childhood onset and include Chediak Higashi syndrome (CHS), Griscelli syndrome (GS) and Elejalde disease (ED).[1] Chediak Higashi syndrome is associated with partial oculocutaneous albinism, recurrent pyogenic infections and presence of large abnormal granules in leukocytes and other granule containing cells.[2] Griscelli syndrome is characterized by silvery grey sheen to hair, partial albinism, large clumps of melanosomes in hair shaft and variable cellular immunodeficiency.[3] Three genetic types of Griscelli syndrome are known with pigmentary dilution common to all three and the only manifestation in type 3. Type 1 is associated with neurological abnormalities and type 2 with immunodeficiency.[4] Elejalde disease is characterized by pigmentary changes, skin tanning, and central nervous system abnormalities.[5] Detailed history clinical examination, light microscopy of hair shaft, skin biopsy, immunological and peripheral blood smear examination are necessary to make the correct diagnosis and to differentiate between these conditions.

We hereby report three cases of Griscelli syndrome (two cases from one family and another case from a different family) with characteristic confirmatory microscopic hair and skin features. This series is reported because of its rarity and characteristic pigmentary abnormality seen. Awareness about this condition will assist in early diagnosis and can prompt to look for associated features which may help to avoid long term complications.

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Case 1

A 9-months old baby, who was born out of 2nd degree consanguineous marriage, presented to our outpatient department with history of light

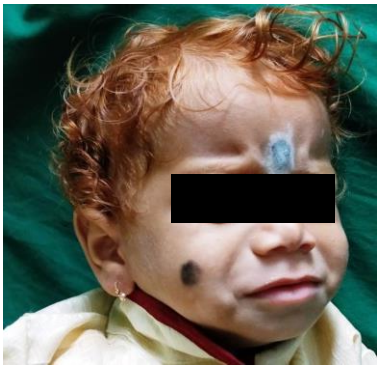

Figure 1a Clinical photograph of Case 1 with diffuse, golden brown hair over the scalp, eyebrows and eyelashes.

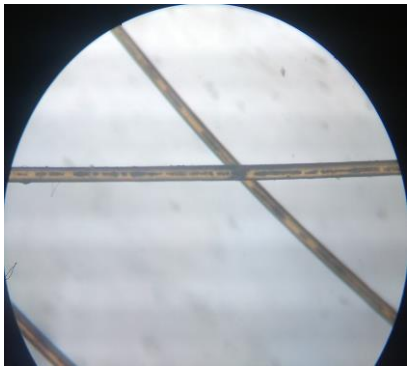

Figure 1b Hair microscopy of Case 1 showing clumping of irregular and large melanosomes in medulla of the hair shaft.

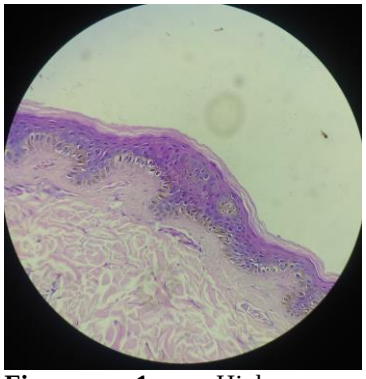

Figure 1c High power (magnification 400x) skin microscopy (H&E stain) of Case 1 with uniform distribution of melanin in the basal layer.

colored hair over scalp, eyebrows and eyelashes since birth. There was no history of seizures or recurrent skin or respiratory infection. Antenatal, natal and post-natal history was normal. The child was of appropriate development for age and the vaccination status was up to date.

Clinical examination revealed diffuse, golden brown hair over the scalp, eyebrows and eyelashes **(Figure 1a)**. Nervous system examination was within normal limits. There was no abdominal distension or jaundice or hepatosplenomegaly or peripheral lymphadenopathy.

Investigations including complete hemogram, peripheral smear, routine serum biochemistry and USG abdomen were within normal limits.

Hair microscopy revealed clumping of melanosomes in medulla of the hair shaft which were irregular and large **(Figure 1b)**. Biopsy from the skin over leg showed uniform distribution of melanin in the basal layer **(Figure 1c)**.

With the above findings, a diagnosis of Griscelli syndrome type 3 was made.

Case 2

A 9-month old girl was admitted in the Pediatric ward with history of 2 episodes of convulsions of one-day duration and was referred to our department for the abnormal color of hair over the scalp. There was no history of consanguinity and the antenatal, natal and postnatal history was normal. Birth weight was 2.25 kg. The developmental milestones were adequate for her age. There was no history of bleeding or recurrent infections since birth. There was similar appearance of hair in the sibling (which is our 3rd case in this case series). On examination, the child had silvery white hair over the scalp, eyebrows and eyelashes **(Figure 2a)**. There was no focal neurologic deficit at the time of examination. There was no hepatosplenomegaly or peripheral lymphadenopathy. Fundoscopic examination revealed papilloedema.

Investigations including complete hemogram, peripheral smear and serum biochemistry were normal. Hair microscopy showed clumping of melanosomes in medulla which were large and irregular **(Figure 2b)**. Parents were not willing for skin biopsy and neuroimaging, and hence were not done.

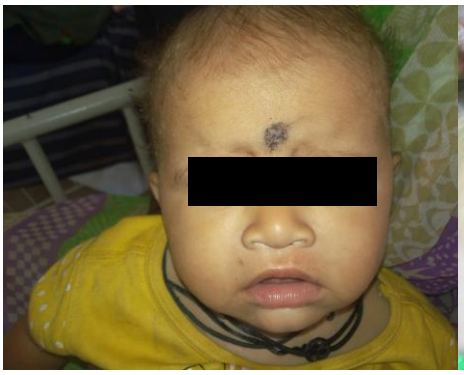

Figure 2a Clinical photograph of Case 2 with silvery white hair over the scalp, eyebrows and eyelashes.

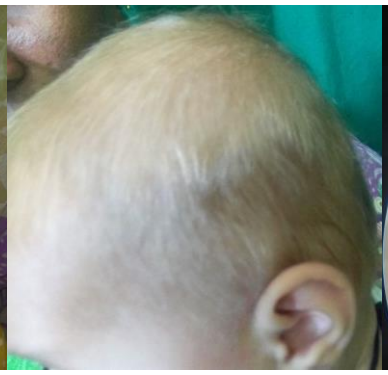

Figure 2b Clinical photograph of Case 2 with silvery white hair over the scalp, eyebrows and eyelashes.

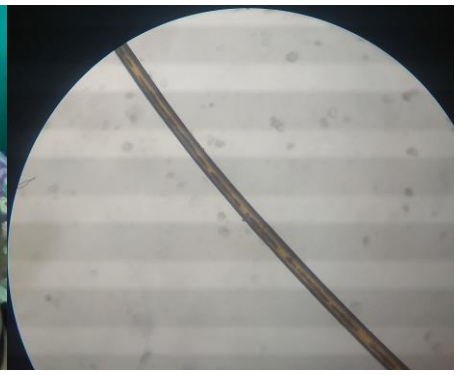

Figure 2c Hair microscopy of Case 2 showing clumping of melanosomes in medulla which are large and irregular.

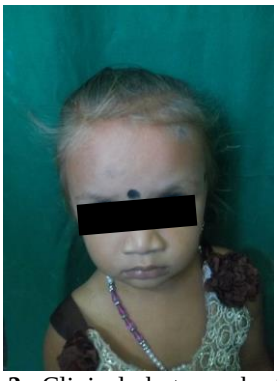

Figure 3a Clinical photograph of Case 3 showing hypopigmented hairs over scalp and eyebrows.

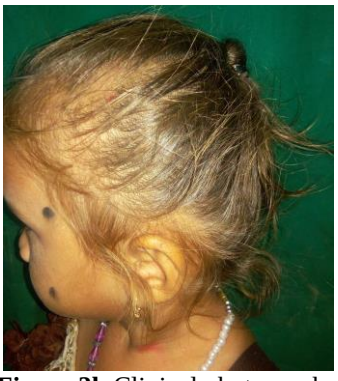

Figure 3b Clinical photograph of Case 3 (lateral) showing hypopigmented hairs over scalp and eyebrows.

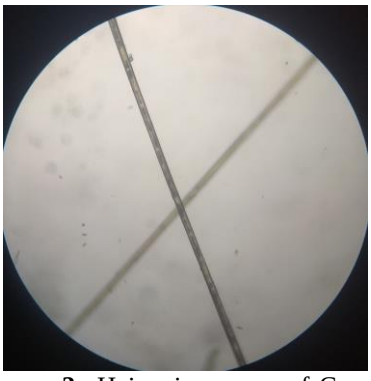

Figure 3c Hair microscopy of Case 3 showing regular clumping of melanosomes in medulla.

With the characteristic clinical and hair microscopic features, a diagnosis of Griscelli syndrome type 1 was made.

Case 3

A two-year-old girl presented with light colored hair over the scalp and eyebrows. Her developmental milestones were normal and adequate for her age. There is no history of seizures, recurrent skin or respiratory infections. Her younger sibling had similar light colored hair (our Case 2). On cutaneous examination, there were hypopigmented hairs over scalp and eyebrows **(Figure 3a)**. Systemic examination was unremarkable. Complete hemogram with peripheral smear and serum biochemistry were normal. Hair microscopy showed regular clumping of melanosomes in medulla which were large and irregular **(Figure 3b)**. Parents were not willing for skin biopsy.

Though the patient did not have any neurological abnormalities at the time of presentation, the possibility cannot be ruled out since the younger sibling had presented with seizures. The patient is on follow up and the parents counseled regarding the possibility of later onset neurological involvement. Thus a diagnosis of Griscelli syndrome type 1 was made.

Discussion

Griscelli syndrome is a rare autosomal recessive disorder associated with pigmentary dilution and

Table 1 Investigations to differentiate between Griscelli syndrome, Chediak Higashi syndrome and Elejalde disease.

Investigation	*Griscelli syndrome*	*Chediak Higashi syndrome*	*Elejalde disease*
Peripheral blood smear	No detectable alteration	Prominent granules in leucocytes and giant organelles	No detectable alteration
Light microscopy of hair	Large clumps of melanin irregularly distributed	Small clumps of melanin regularly distributed	Small and large clumps of melanin in irregular pattern
Histopathology of skin	Excess pigmentation of melanocytes at basal layer and scanty pigmentation of skin surrounding the pigmented areas.	Large melanosomes in both melanocytes and keratinocytes	Irregular sized melanin granules dispersed in basal layer
Electron microscopy of skin	Mature melanosomes in melanocytes and to some extent keratinocytes	Large melanosomes in both melanocytes and keratinocytes	Melanosomes at different stages of formation in the melanocytes

variable cellular immunodeficiency. The pigmentary dilution is characterized by generalized skin pigmentation, silvery grey hair, large clusters of pigments in the hair shafts and an aggregation of melanosomes in melanocytes, with abnormal transfer of the melanin granules to the keratinocytes.[7]

GS classified into 3 types. GS1 is characterized by neurological abnormalities without any features of immune dysfunction. GS2 presents with Hepatosplenomegaly, recurrent infection, and pigment dilution. GS3 is characterized by hypomelanosis without showing any features suggestive of immunological or neurological abnormalities. Presence of grayish hair is the most important feature of all the three types of GS patients. Genetic loci for the three different phenotypes (GS1, GS2, and GS3) are MYO5A, RAB27A, and MLPH respectively.[8,9] Specific treatment for GS1 is not available, GS2 responds well with bone marrow transplantation and GS3 does not require any specific treatment since it involves altered pigmentation only.[6,10]

Hairs from Chédiak-Higashi patients exhibit evenly distributed, regular and larger melanin granules, when compared to normal hairs. Under polarized light microscopy, shafts exhibit a bright and polychromatic refringence appearance. In contrast, hair from patients with Griscelli syndrome, under light microscopy, exhibit bigger and irregular melanin granules, distributed mainly near the medulla. Under polarized light microscopy, shafts appear monotonously white.[6] Though these syndromes have overlapping features, it can be differentiated based on some additional investigations **(Table 1)**.[1] Polarized microscopy was not done, as it is not available in our centre. Conclusive diagnoses were made in our cases due to the presence of characteristic clinical features and light microscopic features. Since there are not many case series of syndromes with silvery hair, we are hereby reporting this series. Though the onset of seizures in many reports is early, rarely, as in our case, the onset maybe delayed. Hence the diagnosis of GS type 3 should be made solely based on genetic analysis. If such facilities are not available, patient might need long term follow up to look for neurological involvement. In our series, we had two siblings with GS, where one sibling had seizures pointing the diagnosis towards GS type1, whereas the other sibling had only features of pigment dilution suggesting a diagnosis of GS type 3. Hence follow up of patients even in the absence of seizures is essential to look for development of late onset neurologic involvement.

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