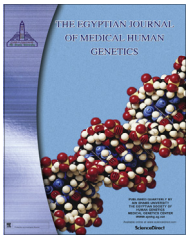
The Egyptian Journal of Medical Human Genetics (2016) 17, 229–232

HOSTED BY

Ain Shams University

The Egyptian Journal of Medical Human Genetics

www.ejmhg.eg.net
www.sciencedirect.com



CASE REPORT

Griscelli syndrome type 2 – A case report and clinical approach to silver blonde hair

Sana Durrani [a], **Michael Chicka** [b], **Bushra Afroze** [c,*]

[a] *Aga Khan Medical University, Karachi, Pakistan*
[b] *PreventionGenetics, Marshfield, WI, USA*
[c] *Department of Pediatrics and Child Health, Aga Khan University Hospital, Karachi, Pakistan*

Received 23 July 2015; accepted 26 August 2015
Available online 29 September 2015

KEYWORDS

Griscelli syndrome;
Silver blonde hair;
Bone marrow transplant;
Pakistan

Abstract Griscelli syndrome type 2 is a rare autosomal recessive disease caused by mutations in the RAB27A gene. It is characterized by pigmentary dilution of the skin and hair causing silvery gray hair, hemophagocytic lymphohistiocytosis and characteristic light microscopy findings in scalp hair shaft seen as large irregular clumps of pigment as opposed to the evenly distributed pigment along the hair shaft without any clumps. We describe a boy with classic features of Griscelli syndrome type 2 from Pakistan in whom a homozygous mutation in the RAB27A gene was identified that showed a single base substitution (c.598C > T) predicted to cause premature protein termination (p.Arg200*). We also present a clinical approach to silver blonde hair differentiating between the Griscelli syndrome types 1, 2 and 3, Chediak Hegashi Syndrome and Elejalde Syndrome.

1. Introduction

Griscelli syndrome (GS) is a rare autosomal recessive disorder that was first described by Griscelli et al. in 1978 [1]. Silvery hair and hypopigmentation along with varying degrees of immunologic and neurologic dysfunction are the prominent clinical features of GS. Three subtypes, GS-1-3, share similar pigmentary dilution of the skin and hair causing silvery gray hair [2]. Mutations in the *MYO5A* gene causing GS-1 (OMIM # 214450) are clinically similar to Neuroectodermal melanolysosomal disease (Elejalde Syndrome OMIM # 256710) [3]. Both are characterized by neurological impairment without immunological impairment. GS-2 (OMIM # 607624) is caused by mutations in the *RAB27A* gene and is characterized by severe immunological impairment without primary neurological impairment [4]. The neurological deficit that occurs in GS-2 seems to be secondary to the infiltration and proliferation of leukocytes in the brain [5]. GS-3 (OMIM # 609227) is caused by a defect in the *MLPH* gene and presents with only partial albinism and silvery hair without the neurologic and immunologic involvement [2]. Prognosis of GS depends on the subtypes. There is no treatment for GS-1 and quality of life depends on the severity of neurological impairment. GS-3 does not require treatment. Patients with GS-2 succumb to illness due to the accelerated hemophagocytic syndrome phase secondary to immunological impairment unless an early bone marrow transplant (BMT) is performed [6]. Therefore, early recognition of GS-2 is critical.

* Corresponding author at: Department of Pediatrics and Child Health, Aga Khan University Hospital, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan. Tel.: +92 21 34864387.
E-mail address: bushra.afroze@aku.edu (B. Afroze).
Peer review under responsibility of Ain Shams University.

http://dx.doi.org/10.1016/j.ejmhg.2015.08.008

More than one hundred cases of GS have been reported worldwide [7] including one GS case from Pakistan, which was diagnosed clinically without molecular characterization of the subtype [8]. We present the first case of GS-2 from Pakistan in whom a homozygous non-sense mutation in the *RAB27A* gene was confirmed.

2. Case report

A 4 month old boy born to healthy first-cousin, once removed parents after an uneventful full term pregnancy was referred to a genetic clinic for the evaluation of hepatosplenomegaly noted from 3 months of age. At birth his weight was 3.3 kg, length was 52 cm and head circumference was 35.4 cm. As compared to the healthy family members, he was noted to have very fair skin, silvery blonde scalp hair, eyebrows and eye lashes. His early developmental miles stones were achieved at appropriate ages. Parents were concerned for his partial albinism in view of the two other children who died at 40 days of life with pneumonia and 6 years of age with sepsis and who also had hepatosplenomegaly. Both the deceased sibs had similar fair skin and silver blonde scalp hair as the proband. None of the other healthy sibs had similar skin hypopigmentation or silvery blonde hair. Parents reported a history of recurrent fever in the patient described in this paper, which were often treated with oral antibiotics. However, he was never admitted with a serious infection nor his blood cultures grew any pathogenic micro-organism. On further interviewing, parents described their deceased six-year old as an intelligent boy who had no neurological impairment. They further informed that with

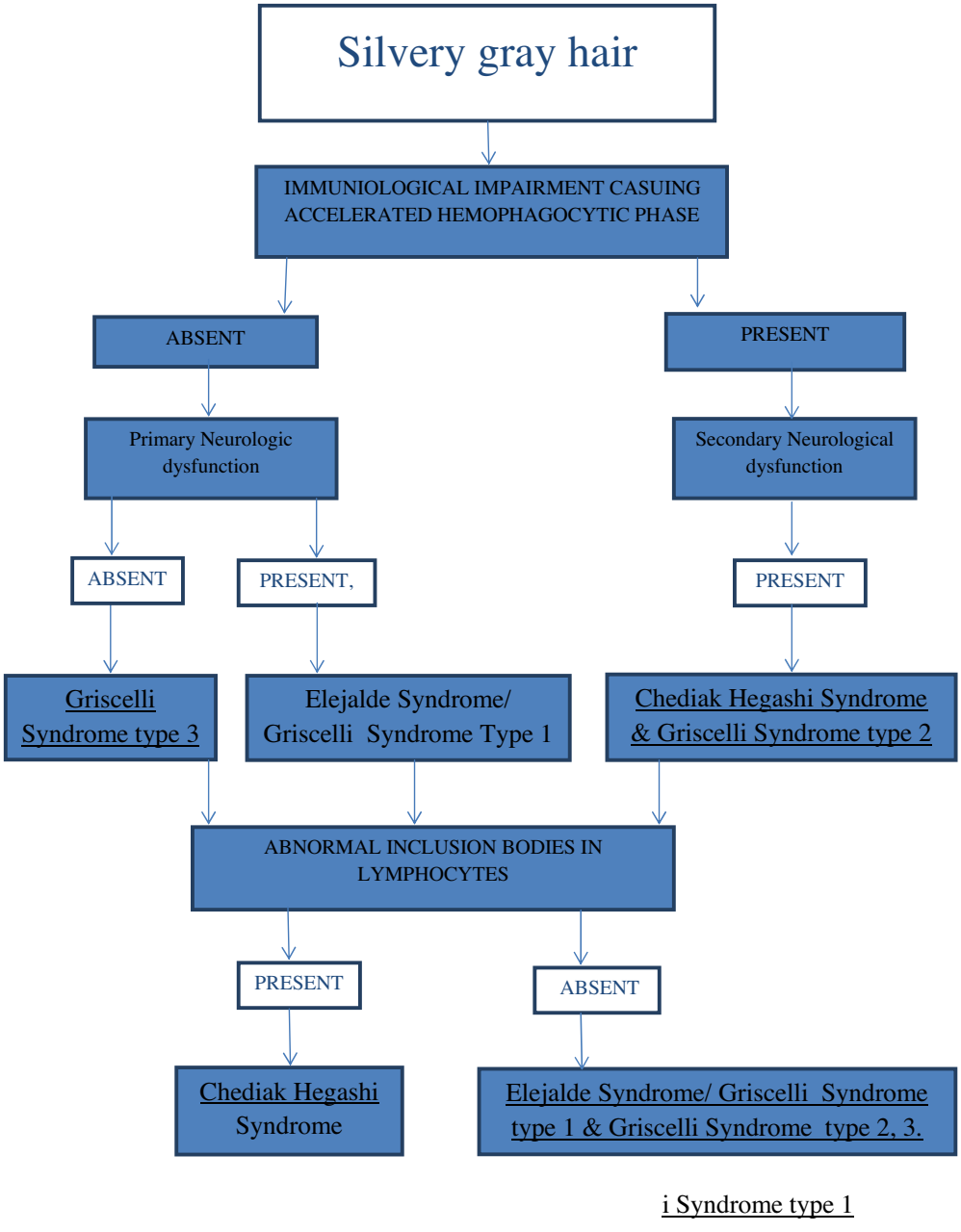


Figure 1 Approach to patients with silver blonde hair.