

## CASE REPORT

# Griscelli Syndrome and Periodontal Therapy Approach: a Case Report

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## Abstract

Griscelli Syndrome (GS), a rare autosomal recessive genetic disorder characterized with pigmentary dilution of the skin, malfunctions of humoral and cellular immunity, was first described by Claude Griscelli in 1978. In this report, periodontal therapy and follow-up of a 10 year-old girl with GS type 2, who applied to our clinic with complaints of gingival bleeding and redness, was presented. The patient had silvery-grey coloured hair and eyebrow, well-rounded nose radix and tip, and hemiparesthesia at the right part of her body. Intraoral examination revealed pigmentation of the lips, heavy accumulation of microbial dental plaque, hyperemia and edema at gingiva. She was diagnosed with plaque-induced gingivitis, and initial periodontal treatment including oral hygiene instructions, scaling and polishing was performed under recommended antibiotic prophylaxis. She was followed up with 1 month intervals. After 6 months, she attended to the clinic with clinical signs of acute necrotizing ulcerative gingivitis and was treated with diluted hydrogen peroxide and chlorhexidine digluconate (0.2%) rinse. Due to the hyperactivity of T lymphocytes and macrophages, intensive host response to dental plaque in patients with GS can be seen. In conclusion, importance of oral hygiene should be emphasized in establishing high level of oral health and, maintenance of patients with GS should be carried out with short intervals.

**Keywords:** Griscelli syndrome type 2; nonsurgical periodontal debridement; acute necrotizing ulcerative gingivitis

## Introduction

Griscelli Syndrome (GS) was described by Claude Griscelli for the first time in 1978 (1). It is a rare autosomal recessive genetic disorder with about less than 100 cases reported that is characterized with pigmentary dilution of the skin, silvery-grey hair, abnormal accumulation of melanosomes in melanocytes, malfunctions of humoral and cellular immunity, variable immunologic and central nervous system abnormalities (1). Defects in the immune system result in macrophage hyperactivation, which is known as hemophagocytic lymphohistiocytosis (HLH) and is characterized by periods of fever, hepatosplenomegaly and pancytopenia. Three subtypes have been described. Based on affecting gene sequences GS type 1, which has neurological defects, is caused by *MYO5A* gene mutations (2). GS type 2 is characterized by episodes of HLH, which is usually triggered by viruses. Immunodeficiency occurs due to impaired lytic granule exocytosis leading to uncontrolled T-lymphocyte and macrophage activation. Activated T-lymphocyte infiltration in various organs especially the brain is the cause of secondary neurological symptoms. GS type 2 is caused by mutations in *RAB27A*, which is an important protein in organelle-specific protein trafficking in melanocytes and platelets, and plays a key role in vesicular transport and organelle dynamics (3,4). Defects in *RAB27A* result in silvery-grey hair with clumps of pigment in hair shafts. GS type 3, which is restricted to hypopigmentation, is caused by mutations in the melanophilin gene (5).

GS type 2 is very rare among populations, but most of the cases reported are from Turkey (6), most probably due to the high rate of consanguineous marriages. There are only a few case reports presenting dental manifestations and treatment needs of patients with GS (7). In this report, we present periodontal therapy and follow-up of a patient with GS type 2 due to the mutation of gene *RAB27A*.

## Case Report

### History

Ten year-old girl with GS type 2 applied to our clinic with complaints of gingival bleeding and redness. She had silver-grey coloured hair, eyebrow and eyelash, well-rounded nose radix and

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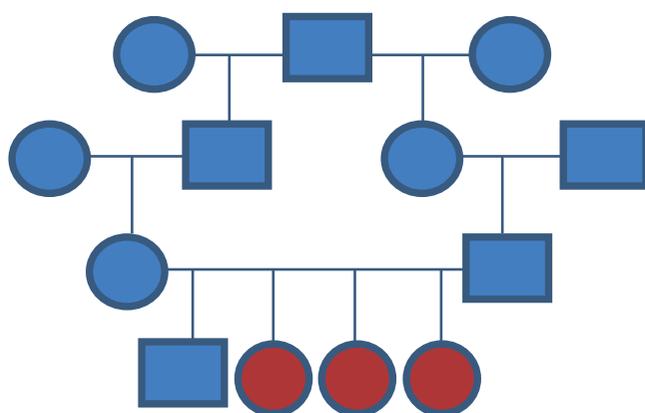
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**Figure 1.** Frontal and lateral appearance of the patient.



**Figure 2.** Intrafamilial aggregation of GS type 2.



**Figure 3.** Poor oral hygiene, gingival hyperemia and edema and gingiva after periodontal treatment.



**Figure 4.** Acute necrotizing ulcerative gingivitis at the interdental gingiva.



tip, and hemiparesthesia at the right part of her body (Figure 1). She had mental retardation and was able to speak only a few words. She was the second child of a 30-year-old mother and a 38-year-old father who were first degree cousins (Figure 2). The first child was a healthy 11-year-old boy. The third child was a girl who died due to the hypoplastic left heart syndrome after 5 days of

birth. The fourth child was also a girl who had neuromotor retardation and encephalitis and the same hair colour as our patient, and died after hemispherectomy operation at the age of 1.

Medical history revealed that our patient was hospitalized with the diagnosis of tuberous sclerosis at the age of 20 months and was referred to Istanbul University Developmental Neurology Clinic because of the differential diagnosis of GS. She had repetitious pulmonary infections, anemia, thrombocytopenia, hepatosplenomegaly. She had epilepsy and was taking carbamazepine (*Tegretol*<sup>®</sup>, 2x500 mg, Novartis, İstanbul, Turkey). She was under intravenous immunoglobulins (*weekly 150 mg/kg*), cyclosporin A (*Sandimmun-Neoral*<sup>®</sup>, 12 mg per day, Novartis, İstanbul, Turkey) and antibiotic treatment (*Bactrim*<sup>®</sup>, 2x5ml, 3 days every week, Roche<sup>®</sup>, İstanbul, Turkey). In an accelerated phase of the disease, she was given hematopoietic stem cell transplantation (HSCT).

**Oral Findings and Periodontal Treatment**

Intraoral examination revealed pigmentation of the lips, poor oral hygiene, gingival hyperemia and edema (Figure 3). She was diagnosed with plaque-induced gingivitis, and initial periodontal treatment including oral hygiene instructions, atraumatic scaling and polishing was performed under antibiotic prophylaxis (*Rocephin*<sup>®</sup>, 1 gram, im, Saba İlaç, İstanbul, Turkey) as recommended by her physician. She was followed up with 1 month intervals. Gingival hyperemia and edema were not observed at recall visits since good oral hygiene was achieved. After 6 months, she suffered from painful lesion at interdental gingiva of mandibular right central and lateral teeth (Figure 4). She was diagnosed with acute necrotizing ulcerative gingivitis and treated with hydrogen peroxide diluted in water (1:1, v/v) and chlorhexidine-gluconate (*Klorhex*<sup>®</sup> 0.2%, DrogSan, Ankara, Turkey) rinse. The follow-up period was 2 year after which she unfortunately hospitalized due to high fever and HLH and died at the age of 12 due to the respiratory failure.

**Discussion**

We presented oral manifestations and 2 year follow-up of a girl diagnosed with GS type 2. Although different types of GS represent a wide clinical spectrum, the common manifestation is partial pigmentary dilution. Patients with GS type 2 should urgently be treated with HSCT after diagnosis for the risk of HLH (8). Since our patient received HSCT during an accelerated phase of the disease, it seemed to be effective at that time. However, GS patients can enter the accelerated phase at any age. In GS type 1 there is no therapeutic approach for neurologic impairments and GS type 3 do not require any therapy.

The protein *RAB27A* seems to play a key role on cytotoxic granule exocytosis and is involved in the control of immune regulation (9). Patients with GS represent immune impairment and increased susceptibility to infections. GS type 2 is associated with severe primary immunodeficiency causing “accelerated phases” of HLH. Hemophagocytic syndrome is caused by hyperstimulated T cells and macrophages often triggered by infections, and characterized by hepatosplenomegaly, high fever, pancytopenia and hemorrhages (4). The immune defects seen in this syndrome may increase the

risk of periodontal disease, considering periodontopathogen microorganisms as the primary etiological factor of this infectious and inflammatory disease.

The findings of silver-grey hair, hepatosplenomegaly, and immune deficiency should alert clinicians to consider GS, since early diagnosis is of critical importance. Due to the hyperactivity of T lymphocytes and macrophages, excessive host response to microorganisms found in dental plaque in patients with GS may be seen. For this reason, the importance of oral hygiene should be emphasized in achieving healthy oral tissues, and maintenance of GS patients needs to be carried out with short intervals. Moreover, it is advised that the parents of patients with GS should be informed about the need of dental consultation.

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