

Griscelli Syndrome - A Case Report

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Griscelli syndrome is a rare autosomal recessive disorder characterized by partial albinism with variable immunodeficiency. Silvery gray hair with large, clumped melanosomes on microscopy of hair shafts are diagnostic. The commonest complication leading to mortality includes lymphohistiocytic proliferation in various organs, including the brain. We present a child with classic clinical features and confirmatory findings of clumped melanosomes on microscopy of hair shaft.

Key words: *Griscelli syndrome, Hemophagocytosis, Lymphohistiocytic proliferation.*

Griscelli syndrome (Partial albinism with variable immunodeficiency) is an uncommon disorder characterized by pigmentary dilution and variable cellular and humoral immunodeficiency(1). It is inherited as an autosomal recessive disorder. Features include hepatosplenomegaly, silvery gray sheen to the hair, large clumped melanosomes in hair shafts, pancytopenia, hepatitis and immunologic abnormalities. As of January 2003, 60 cases have been described in world literature(2,3).

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Case Report

A one year and ten-month-old child was referred to us for severe pallor. Her chief complaints were fever (3 months off and on), abdominal distension (2 months), jaundice (1 month), and anasarca (15 days). There was a past history of jaundice and abdominal distension, 4 months prior to this episode, which resolved spontaneously. There was no history of vomiting, urinary or bowel complaints, or bleeding from any site. There was no history of transfusions received in the past. There was a history of death of the first female sibling at 6 months age with fever. This sibling, on enquiry, also had light coloured hair. On examination, her vital parameters were normal. She had significant pallor, silvery gray hair (*Fig. 1*), low set ears and insignificant lymphadenopathy. Abdomen was distended, with the liver 6.5 cm palpable, firm and non-tender. The spleen was palpable 7 cm below left costal margin and was firm in consistency. The skin, iris and retina had normal pigmentation. Rest of the physical examination was unremarkable.

Investigations revealed a hemoglobin of 5.5 g/dL, a total leucocyte count $8 \times 10^3/\text{mL}$, a platelet count of $83 \times 10^3/\text{mL}$ and a reticulocyte count of 8.8%. There were no giant cytoplasmic granules in leucocytes. Serum bilirubin was 0.5 mg/dL, total proteins were 8.4 g/dL with albumin -3.8 g/dL, globulins -4.6g/dL and ALT -68 IU/L. Prothrombin time was 22/11 seconds (Internationalized Normalized Ratio of 2.1), PTTK (Partial Thromboplastin Time) -47.5/37.5 seconds and TT (Thrombin Time) -26.5/23.1 seconds. Plasma fibrinogen level was 223 mg/dL and D-dimers were negative. HBsAg, and antibodies for HIV and HCV were negative. Bone marrow aspiration and biopsy were done during the accelerated phase of the disease (Griscelli syndrome) for suspected hemo-

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phagocytosis. It showed gametocytes and trophozoites of *P. vivax* with mild megaloblastic and dysplastic changes, but did not reveal hemophagocytosis. The serum triglycerides, plasma fibrinogen and serum albumin were normal. CD4 counts were 788/mL (NR : 1020 to 3600/mL), CD8 - 1425/mL (NR: 570 to 2230/mL) and CD3 - 2522/uL (NR:1460 to 5440/mL), which suggested moderate immunosuppression (as per 1994 Revised CDC criteria for children infected with HIV). Her serum IgG and IgM were elevated—1770 mg/dL (NR - 350 to 1180) and 701 mg/dL (NR - 36 to 104) respectively and IgA was 55.7 mg/dL (NR 36 to 165). MRI brain showed patchy areas of altered signal intensity in both cerebral hemispheres and left cerebellar hemisphere, with focal signal abnormalities in the right lentiform and left dentate nucleus, suggestive of lymphohistiocytic infiltration. These were consistent with findings seen in Griscelli syndrome. Microscopic examination of the hair shaft showed large unevenly distributed melanin aggregates diagnostic of Griscelli syndrome.

The child was treated with antimalarials (quinine and mefloquine) and packed red cell transfusion initially. She responded to mefloquine. However, during her stay she deteriorated neurologically (suggestive of lymphohistiocytic infiltration), for which she was treated with systemic high dose methylprednisolone (30 mg/kg/day for 3 days). She improved and was discharged. She got readmitted within a month with severe anemia and was again given packed red cell transfusions. However, she continued to deteriorate neurologically over the next few days and despite repeated courses of methylprednisolone, she succumbed to the disease within four months after diagnosis.



Fig. 1. The photograph shows the typical silvery gray hair, in this child with Griscelli syndrome.

Discussion

Griscelli, *et al.*(4) described two patients with partial albinism in 1978. As of January 2003, 60 cases have been reported(2). Most patients are diagnosed between 4 months and 7 years of age(1). The genetic defects include mutations in either MYO 5A or RAB 27A, both located on chromosome 15q21(5,6). It is characterized by partial albinism, variable cellular and humoral immunodeficiency and the occurrence of “accelerated phases” consisting of hemophagocytosis, pancytopenia, elevation of serum triglyceride levels, hypofibrinogenemia and hypoproteinemia. Dermatologic findings may be limited to hair, with skin and retinal pigmentation being occasionally affected. Microscopic examination of hair reveals uneven clusters of aggregated melanin pigment, accumulated

mainly in the medullary area of the shaft. Neurologic involvement with raised intracranial pressure, cerebellar signs, encephalopathy, hemiparesis, peripheral facial palsy, spasticity, hypotonia, seizures, psychomotor retardation and prog-ressive neurologic deterioration is known(7). Immunologic abnormalities include natural killer (NK) cell function defect with absent delayed type hypersensitivity(8). Secondary hypogammaglobulinemia can occur in accelerated phases, which are characterized by lymphohistiocytic infiltration of various organs mimicking hemophagocytosis. These are thought to be associated with EBV infection, although various other viral and bacterial pathogens have also been incriminated(8). They result from abnormal cytotoxicity function of T and NK cells resulting from inability to secrete cytotoxic granules when the RAB 27A is not functional. The differential diagnosis includes Chediak-Higashi syndrome (CHS) and Elejalde syndrome. CHS differs from GS by presence of abnormal giant cytoplasmic granules in leucocytes, more frequent cutaneous involvement, smaller, more evenly distributed pigment clumps in hair shafts and more consistent defective granulocyte activity(3). Elejalde syndrome, like GS has presence of spotty hair pigmentation, but incomplete melanization of melanosomes in skin, and no immunodeficiency(9). The prognosis of patients with Griscelli syndrome is grave. Curative hope is offered only by bone marrow or stem cell transplantation, which is more successful when, performed early in the course of the disease(8). Palliative management includes treatment of associated infections, and immunomodulatory therapy during accelerated phases (high dose systemic methylprednisolone, etoposide, intrathecal methotrexate, cytosine arabino-side and prednisone, or ATG, cyclosporine and steroids)(8,10).

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REFERENCES

1. Mancini AJ, Chan LS, Paller AS. Partial albinism with immunodeficiency: Griscelli syndrome: Report of a case and review of literature. *J Am Acad Dermatol.* 1998; 38: 295-300.
2. Scheinfeld NS, Johnson AM. Griscelli syndrome (emedicine website. Available at <http://www.emedicine.com/derm/topic926.htm>, Updated October 2003).
3. Gogus S, Topcu M, Kucukali T, Akcoren Z, Berkel I, Ersoy F, *et al.* Griscelli syndrome: report of three cases. *Pediatr Patholo Lab Med.* 1995; 15: 309-319.
4. 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.
5. Sanal O, Ersoy F, Tezcan I, Metin A, Yel L, Menasche G *et al.* Griscelli disease: genotype-phenotype correlation in an array of clinical heterogeneity. *J Clin Immunol* 2002; 22: 2337-2343.
6. Aksu G, Kutukculer N, Genel F, Vergin C, Omowaire B. Griscelli syndrome without hemophagocytosis in an eleven-year-old girl. Expanding the phenotypic spectrum of RAB27A mutations in humans. *Am J Med Genet* 2003; 116A: 329-333.
7. Hurvitz H, Gillis R, Klaus S, Klar A, Gross-Kieselstein F, Okon E. A kindred with Griscelli

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- disease: spectrum of neurologic involvement. *Eur J Pediatr* 1993; 152: 402-405.
8. Klein C, Philippe N, Le Desit F, Fraitag S, Prost C, Durandy A, *et al.* Partial albinism with immunodeficiency (Griscelli syndrome). *J Pediatr* 1994; 125: 886-895.
 9. Elejalde BR, Holguin J, Valencia A, Gilbert EF, Molina J, Martin G, *et al.* Mutations affecting pigmentation in man: I, Neuroectodermal melanolyosomal disease. *Am J Med Genet* 1979; 3: 65-80.
 10. Gurgey A, Sayli T, Gunay M, Ersoy F, Kucukali T, Kale G, *et al.* High-dose methylpredisone and VP-16 in treatment of Griscelli syndrome with central nervous involvement. *Am J Hematol* 1994; 47: 331-338.

Juvenile Idiopathic Osteoporosis

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Juvenile idiopathic osteoporosis (JIO) is a very rare condition of primary bone demineralisation that presents in childhood. Most pediatricians are unfamiliar with this condition owing to the difficulty in recognition and a long list of differential diagnosis. We report an 8-year-old girl who presented with generalized severe osteoporosis. Diagnosis of JIO was made by excluding other common causes of osteoporosis in this age.

Key words: *Childhood osteoporosis, Juvenile idiopathic osteoporosis.*

Juvenile idiopathic osteoporosis (JIO) is a rare condition of unknown etiology,

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characterized by prepubertal onset and spontaneous remission with progression of puberty(1). It is an important differential diagnosis for conditions causing generalized osteoporosis in childhood and is diagnosed by excluding other causes. In the present communication, we report a case of JIO along with an approach to generalized osteoporosis in childhood.

Case Report

An 8-year-old girl born to a noncon-sanguineous married couple presented with complaints of pain in both feet on walking and inability to get up from sitting position since the age of 3 years. Child was apparently normal till that age, when she had an accidental fall and sustained fracture of left femur, following which her movements were restricted for 6 months. The examination of the child revealed scoliosis, angulation deformity of the right arm and tenderness over both feet. Examination of other systems was essentially normal. Routine blood counts, urine examinations were normal. Creatinine-phosphokinase (CPK) level was within normal limits. A radiological skeletal survey was done which showed pencil-thin cortices of long bones, angulation of right humerus