LETTER TO EDITOR (VIEWERS CHOICE)

A RARE CASE OF GRISCELLI SYNDROME

Vignesh P, Poovazhagi V, Jeyachandran P

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An 8 years old girl presented with one day history of left focal seizures and lethargy. She had discolouration of hair with multiple skin nodules on and off from the age of one year and frequent hospitalizations for pneumonia from the age of six months. There was no significant family history. On examination, child was febrile with pallor. She had hypopigmented silvery grey hair (Fig 1), multiple non tender subcutaneous nodules over the lower extremities and hypopigmented macules over the forehead and trunk. On systemic examination, she had a firm hepatosplenomegaly. Her Glasgow coma scale was E1V3M3. Fundus showed a pale disc. Complete hemogram showed white blood cell count of 4800/cumm (61% polymorphs, 34% lymphocytes, 5% eosinophils), hemoglobin of 8.5gm/dl and platelets of 91,000/cumm. Peripheral smear showed neutrophilic leucocytosis, shift to left with toxic granules and thrombocytopenia. Renal and liver function tests were normal. Blood culture grew klebsiella. Cerebrospinal fluid analysis was normal. Her activated partial thromboplastin time was prolonged (44.6 sec). Serum triglycerides were 250mg/dl (Normal = 100 to 199mg/dl), Ferritin was 79.5 ng/ml (normal = 7 to 140 ng/ml), and fibrinogen was 1.0 g/L (normal = 1.5 to 2.77 g/L). Immunoglobulin profile revealed IgM 92 mg/dl (Normal: 40 to 90 mg/dl), IgG 810 mg/dl (Normal: 667- 1180 mg/dl), IgG1 486 mg/dl (Norma: 395- 710 mg/dl), IgG2 245mg/dl (Normal: 200- 355 mg/dl), IgA 102 mg/dl (Normal: 79-169 mg/dl), IgE 72 IU/ml (Normal < 100). Lymphocyte subset analysis and genetic analysis could not be done. CT brain showed calcified foci in subcortical region of both frontal lobes, bilateral sublentiform nuclei, head of caudate and left parafalcine. Skin potassium hydroxide (KOH) mount showed no fungal elements. Subcutaneous nodule biopsy showed dense lymphocyte infiltrate in lobules of adipose tissue with well-formed epithelial granuloma and occasional Langerhans giant cell. Bone marrow examination was normal. Hair examination revealed abnormal melanin aggregates predominantly in medulla (Fig 1). She was treated with antibiotics, anticonvulsants, anti-edema medications and supportive therapy. However, she succumbed to death after fourteen days of hospitalization.

Griscelli syndrome is a rare autosomal recessive disorder that results in pigmentary dilution of the skin and hair and immunodeficiency. It has been rarely reported in India.(1) It is caused by mutations in one of the three genes which are RAB27A, MYO5A and MLPH. Children with RAB27A mutation develop an uncontrolled T-lymphocyte and macrophage activation syndrome known as hemophagocytic syndrome which was not seen in our child.(2) In Griscelli syndrome caused by RAB27A defects, CT scan can show areas of coarse calcification in the globi pallidi, left parietal white matter, and periventricular and left brachium pontis as was seen in our patient.(3) Often the first manifestation of Griscelli syndrome is silvery hair.(4) Differential diagnosis includes Chediak Higashi syndrome and Elejalde syndrome.(5) Cytoplasmic granules in leucocytes characteristic of Chediak Higashi syndrome is not seen in patients of Griscelli syndrome.(3) Features include granulomatous lesions, partial albinism, generalized lymphadenopathy, hepatomegaly and jaundice.(3) Neurological impairment occurs as a result of central nervous system (CNS) lymphohistiocytic infiltration with erythrophagocytosis.(6) CNS disorder is stable and never regresses with time. The symptoms may be of obstructive hydrocephalus without hematological abnormalities or organomegaly, bilateral basal ganglia involvement(7), hypotonia, absence of coordinated voluntary movements, bulbar poliomyelitis, encephalopathy, hemiparesis, peripheral facial palsy, spasticity or seizures. Some have secondary hypogammaglobulinemia and functional granulocytic abnormalities.(8) Griscelli syndrome has large, clumped melanosomes in hair shafts in contrast to normal uniform distribution of melanin near the cuticle and this leads to silvery grey sheen as was seen in our patient.(9) Medical treatment of patients with Griscelli syndrome is difficult. For patients with defects in RAB27A, antibiotics and antiviral agents are used. Allogenic bone marrow transplant is an effective therapeutic option for patients with hemophagocytosis.(10) To suppress the accelerated phase of disease, immunosuppressive therapy is used. The prognosis for long term survival is relatively poor. Mean patient age at the time of death is 5 years.(1) Prenatal diagnosis of Griscelli syndrome has been accomplished by examination of hair at 21 weeks of gestation.(11) By cloning the Griscelli syndrome genes, direct mutation-based carrier detection and prenatal diagnosis currently appears possible in families with defined MYO5A or RAB27A gene mutations.(10)

Figure 1: The silvery grey hair and hypopigmented skin macules (left side), and the abnormal aggregates of melanin in hair shaft

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From: Department of Pediatric Intensive care, Institute of Child Health and Hospital for Children, Egmore, Chennai. India.

Address for Correspondence: Dr Poovazhagi V, 8/11 Manjolai street, Kalaimagal nagar, Ekkaduithangal, Chennai 600 032, India. Email: poomuthu@yahoo.com

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