GRISCELLI SYNDROME A CASE REPORT

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Abstract:
Griscelli syndrome is a rare autosomal recessive disorder characterized by partial albinism with variable immunodeficiency. Silvery grey hair with large, clumped melanosomes on microscopy of hair shafts is diagnostic. A 5 month old male child presented with complaints of fever, refusal of feeds, convulsions, jaundice, malena of 2 days duration and progressive abdominal distension for the past 4 months. 3 elder siblings had succumbed to similar illness. Examination revealed pallor, icterus, fair skin, silvery hair over scalp, eyebrows and eye-lashes, distended abdomen with dilated veins and hepatosplenomegaly. Other systems were normal. A provisional diagnosis of Silver hair syndrome was made and investigated. The hemoglobin was 6gmdl, total leucocyte count 3200 cells/mm3 with polymorphs 34, lymphocytes 63, oesinophils 2 and monocytes 1. Platelets count was 1.4 lakh/mm3. Peripheral smear showed microcytic hypochromic anaemia, large intracytoplasmic granules were not seen in leucocytes (presence of intracytoplasmic granules in leucocytes is diagnostic of Chediak Higashi syndrome). Serum bilirubin was 5mgdl, Serum proteins 3gmdl, alkaline phosphatase 664 UL, GGT 488 IUL, prothrombin time was 58 seconds and APTT 1 min 28 seconds. Lipid profile revealed hypertriglyceridemia- 650mgdl. Chest X ray and ECHO were normal. Ultrasonogram of abdomen showed hepatosplenomegaly with thin rim of fluid in hepatorenal pouch. Blood cultures were sterile, mantoux test, urine screening and viral markers were negative. Bone marrow aspiration showed hypocellularity. Light microscopic examination of hair revealed uneven aggregations of large pigment granules and skin biopsy showed increased pigment in the basal skin layer containing melanocytes with poor pigmentation of adjacent keratinocytes. MRI brain showed T2 hyperintensities in the periventricular white matter, peritrigonal region and optic radiation. EEG was abnormal. The child was treated with antibiotics, blood components and anticonvulsants. The child's general condition deteriorated with worsening of jaundice, progressive hepatosplenomegaly, bleeding manifestations and succumbed.
to pulmonary haemorrhage after a month. Liver and splenic biopsy done after death revealed inflammation and early cirrhotic changes in the liver and haemorrhagic areas in the spleen. Bone marrow transplant is the only hope for cure when performed before the development of accelerated phase. Induction of remission with high dose methylprednisolone, etoposide, intrathecal methotrexate, cytosine arabinoside and prednisolone can also be tried. 

**Keyword**: Silver hair syndrome, Griscelli syndrome, accelerated phase

**CASE REPORT:**
A 5 month old male child presented with complaints of fever, abdominal distension, refusal of feeds, convulsions, jaundice and malena of 2 days. The abdominal distension had been gradually progressing for the past 4 months. 3 siblings aged 9 months, 1 ½ years and 2 days succumbed to similar illness. One elder sibling aged 9 years was alive and healthy. Examination revealed pallor, icterus, fair skin, silvery hair over scalp, eyebrows and eyelashes (Fig 1). The abdomen was distended with dilated veins and hepatosplenomegaly. Other systems were clinically normal. A provisional diagnosis of Silver hair syndrome was made and proceeded with investigations. The hemoglobin was 6gm/dl, total leucocyte count 3200 cells/cumm with polymorphs 34%, lymphocytes 63% eosinophils % and monocytes 1%. Platelets count was 1.4 lakhs/mm^3. Peripheral smear showed microcytic hypochromic anaemia, leucocytes with normal morphology, large intracytoplasmic granules were not seen in leucocytes (presence of intracytoplasmic granules in leucocytes is diagnostic of Chediak Higashi syndrome). Liver function tests and coagulation profile were abnormal with serum bilirubin 5mg/dl, serum pro teins 3gm/dl, alkaline phosphatase 664 U/L, GGT 488 IU/L, a prolonged prothrombin time 58 seconds and APTT 1 min 28 seconds. Lipid profile revealed hypertriglyceridemia 650mg/dl. Chest X ray and ECHO were normal. Ultrasonogram of the abdomen showed hepatosplenomegaly with thin rim of fluid in hepatorenal pouch. Blood cultures were sterile, mantoux test, urine screening and tests for viral markers were negative. Serum immunoglobulins level were normal. Bone marrow aspiration showed hypocellularity. Light microscopic examination of hair showed uneven aggregations of large pigment granules and skin biopsy showed increased pigment in the basal skin layer containing melanocytes with poor pigmentation of adjacent keratinocytes (Fig2A & 2B). MRI of brain showed T2 hyperintensities in the periventricular white matter, peririgional region and optic radiation (Fig.3). EEG was abnormal. The child was treated with antibiotics, blood components and anticonvulsants. The child’s general condition deteriorated with increasing hepatosplenomegaly, reappearance of jaundice and bleeding manifestations and succumbed to pulmonary haemorrhage after a month of hospital stay. Liver biopsy and splenic biopsy were done after death which revealed inflammation and early cirrhotic changes in the liver and haemorrhagic areas in the spleen.
DISCUSSION:
The first description of Griscelli syndrome was made in 1978 and over 60 cases have been reported. Griscelli syndrome is a rare disorder caused by mutation in 3 different genetic loci on chromosome 15q21(1,2): the Myosin Va gene, RAB27A and the MLPH gene. Males and females are equally affected. Most of the cases are diagnosed during infancy. The youngest age at diagnosis is 1 month. At birth, nonspecific findings can occur which includes petechiae and hepatosplenomegaly. Clinical features include partial albinism of hair and skin, recurrent infections, fever, hepatosplenomegaly and an accelerated phase triggered by a viral infection caused by EBV or Hepatitis A virus. Accelerated phase is characterized by fever, hepatosplenomegaly, pancytopenia, hemophagocytosis (lymphohistiocytic infiltration of various organs) coagulopathy, elevated liver enzymes, hypoproteinemia and elevated triglycerides. However hemophagocytosis was not evident in bone marrow biopsy of our case. Immunological abnormalities include impaired NK cell activity, absent delayed hypersensitivity, impaired helper T cell function and hypogammaglobulinemia (3). Microscopic examination of hair shaft reveals uneven clusters of aggregated melanin pigments in the medullary area. Histopathological examination of skin shows hyperpigmented melanocytes with poorly pigmented adjacent keratinocytes (4). The present case had similar picture in microscopic examination of hair and skin biopsy. Neurological manifestations include raised ICT, seizures, psychomotor retardation, encephalopathy, bilateral basal ganglia involvement, hypotonia, bulbar poliomyelitis, hemiparesis and facial palsy (5).
Three types of Griscelli syndrome have been recognized. They manifest with silver grey hair accompanied by neurological abnormality (type 1), immunodeficiency (type 2) and no other abnormality (type 3). Our case is type 1 with neurological abnormalities. In 2003, Dinakar et al reported a 6-year-old girl from India with similar disease. Her brain was affected with Dandy Walker cyst unlike our case.

The differential diagnosis of Griscelli syndrome include Chediak Higashi syndrome, Eliejalde syndrome and Hermansky Pudlak syndrome. Chediak Higashi can be distinguished from Griscelli by the presence of intracytoplasmic granules in the leucocytes. In our case intracytoplasmic granules were not seen. A similar syndrome with dermatological findings and pigment abnormalities – Eliejalde Syndrome can be distinguished from Griscelli by the presence of immunodeficiency. However immunoglobulin levels were normal in our case. Hermansky Pudlak syndrome presents with albinism, visual defects, photophobia, strabismus, nystagmus and lifelong bleeding tendencies. Peculiar pigmented reticular cells in bone marrow, lymph node and liver biopsy readily differentiate this disease from Griscelli syndrome. Bone marrow of the present case revealed hypocellularity and no pigmented reticular cells favouring Griscelli syndrome. Prenatal diagnosis is possible at 20 weeks of gestation by examination of hair and skin biopsy. The mean patient age at the time of death is usually 5 yrs. In GS type 1 there is no definitive cure. GS type 2 also have a grave prognosis. Treatment with bone marrow transplantation is the only hope for cure when performed before the development of accelerated phase. Induction of remission with high dose methyl prednisolone, etoposide, intrathecal methotrexate, cytosine arabinoside and prednisolone have been tried. The prognosis of type 3 GS is good and no active intervention is required.

REFERENCES:


