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Case Report

Gaucher's disease: a case report

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ABSTRACT

Gaucher's disease (GD) is an autosomal recessive disorder, characterized by lack of acid β-glucosidase (glucocerebrosidase) enzyme resulting in accumulation of glucosylceramide in different organs. This enzyme is encoded by a gene on chromosome 1. Accumulation of glucosylceramide in tissues leads to multisystem organ involvement viz. liver, spleen, bone marrow, lungs and central nervous system. It is common in Ashkenazi Jews but rare in India. Around five hundred cases are identified and diagnosed in India. Serum β-glucosidase levels <15% of mean normal activity confirms the diagnosis, enzyme replacement being the only definitive treatment. Here we report a case of Gaucher's disease.

Keywords: Gaucher disease, Glucocerebrosidase, Splenomegaly

INTRODUCTION

Gaucher disease (GD) is a lipid storage disease characterized by deposition of glucocerebroside in cells of the macrophage-monocyte system. It was first described by Gaucher in 1882, and the storage of glucocerebroside was first recognized by Epstein in 1924. The metabolic defect, which is the deficiency of the lysosomal hydrolase β-glucosidase, or β-glucocerebrosoidse, was identified by Brady et al. Its birth incidence in Ashkenazi Jewish is about 1 in 450.[1,2]

CASE REPORT

Index child is a 6-year-old female Hindu child born to a non-consanguineous marriage 4th in birth order presented with complain of weakness, pallor and progressive abdominal distension since age of 1 year. There was no history of easy bruising or prolonged bleeding on trauma, hematemesis, fever, night sweats, weight loss or bone pains.

There was history of 3 blood transfusion in the past starting at age of 1 year then every year thereafter.

Family history is remarkable as 1st two siblings both female had history of similar complain of abdominal distension and multiple blood transfusion. 1st sibling expired at age of 4 year and 2nd one at age of four and half year. Third sibling, Male, 14-year-old is healthy child with no similar complain. There was no similar history on paternal and maternal side.

On examination, the patient was pale and had massive splenomegaly and hepatomegaly with no icterus or lymphadenopathy or any other physical findings. There were no signs of ocular motor problems or other neurological abnormalities. Rest of systemic examination was essentially normal. On the basis of history and finding of massive hepato-splenomegaly and anemia, we considered a differential diagnosis of tropical splenomegaly, malaria, hemolytic anemia and storage disorder.

On investigation patient had hemoglobin of 6.8gm% (anemia), white cell count was 1570/mm^3 (leucopenia) and platelet count-52000/mm^3 (thrombocytopenia) with a reticulocyte count of 2.2%. His biochemical parameters (liver and renal function, blood sugar and electrolytes)

were normal. Hb electrophoresis was normal. Serum copper levels were also within normal limits. Ultrasound study of abdomen showed massive splenomegaly and hepatomegaly with coarse echotexture of liver.

To evaluate massive splenomegaly, bone marrow aspiration was performed which revealed Gaucher's cells in a background of normal erythroid, myeloid and megakaryocytic lineage cells (Figure 2). Confirmation of diagnosis for Gaucher's disease (type 1) was performed by β-glucosidase levels which was 0.77 nmol/hr/mg (normal levels >6.0nmol/hr/mg). Final diagnosis was GD (type-1).

Figure 1: Index case showing abdominal distension and hepatosplenomegaly.

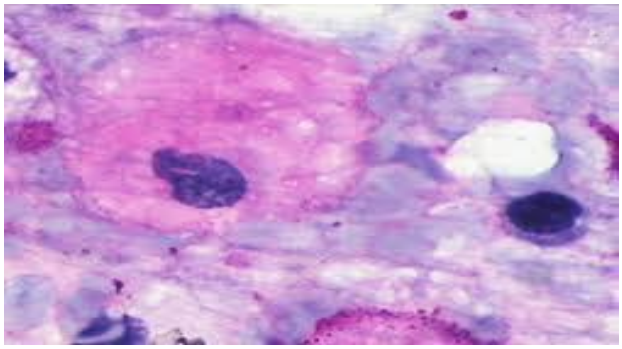

Figure 2: Bone marrow aspirate showing Gaucher's cell.

The 14-year-old third sibling was also examined and he did not show any evidence of GD on clinical and laboratory examination.

DISCUSSION

Gaucher's disease is a very rare genetic disease; occurring in 1 in 50,000 to 100,000 people in the general population. GD is equally common in both sexes. About 1 in 100 people in the United States are carrier of type 1 GD and in Ashkenazi Jews carrier state is 8.9% while the birth incidence is 1 in 450.[1]

Depending on the presence of central nervous system involvement, GD is classified into three types:

- Type 1 (non-neuropathic) is the commonest variety; neurological manifestations are absent and have a bimodal presentation, with peaks at 10-15 years and around 25 years.
- Type 2 (infantile, acute neuropathic) is the severe form with extensive visceral and brain involvement, seizure, spasticity, usually dies before the 3rd birthday.
- Type 3 (juvenile or Norrbotten form) is chronic milder variety. They may live early teen or adulthood. [2]

The disease severity and its various clinical courses depend upon the nature of the mutation in the glucocerebrosidase gene and its genotype/phenotype correlations.[3]

On enzyme activity testing finding less than 15 % of the mean normal activity of the enzyme is diagnostic. Genotype testing is helpful for diagnosis but PCR based test should be read cautiously as they can reveal the presence of recombinant alleles. Complete blood count and liver function test and other associated markers like increased serum ACE levels and serum ferritin levels may be present. Bone marrow aspiration reveals the classical finding of Gaucher's cells- glycolipid laden macrophages.

Enzyme replacement therapy (ERT) and substrate reduction therapy (SRT) are the backbone of the management. ERT causes a dramatic effect on organomegaly with a 25% of decrease in liver and spleen volume in first 6 months.[4] Hemoglobin rises by 1.5gm% in the first 4 to 6 months and platelet counts will double in the first year of treatment. However, many patients would still require surgical treatment in the form of splenectomy to correct their pancytopenia.[5]

Substrate reduction therapy (SRT) is a newer form of therapy uses agents that will inhibit the enzyme glucosylceramide synthatase and thus decrease the biosynthesis of glucocerebrosidase. One of the major advantages of SRT is its ability to cross the blood brain barrier and thus improve the neurological symptoms of GD. Advances in the management of this neglected, rare disorder continue to be hindered by high cost of therapy.

CONCLUSION

GD should be considered in the differential diagnosis of patients with unexplained splenomegaly especially with an extended period of time. Moreover, the early recognition of GD would lead to safe and effective

treatment with enzyme replacement which can decrease morbidity and reduce as far as possible the visceral and skeletal involvement.

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