



A Case of Gaucher's disease presenting as Hemolytic Anemia

Authors

Sunil Kumar Agarwalla¹, Rina Meher²

¹Associate Professor, Dept. of Paediatrics, M.K.C.G. Medical College, Berhampur, Odisha, India

²Senior Resident, Dept. of Paediatrics, M.K.C.G.MC

Abstract

Gaucher's disease is an autosomal recessive and most common lysosomal storage disease characterized by glycosphingolipidase deficiency. The overall incidence is approximately 1:60,000 individuals. It is a multi-system disorder due to accumulation of glucosylceramide in tissues and organs and the main clinical features are Splenomegaly, Hepatomegaly, bone marrow infiltration leading to anemia, thrombocytopenia and leucopenia, and skeletal involvement leading to bone pain and pathological fracture. Serum β -glucosidase levels confirms diagnosis, Enzyme replacement being the only definitive treatment. We report a 1.5 yr Fch, case of Gaucher's disease presenting as Congenital Hemolytic Anemia.

Keywords: Gaucher's disease, anemia, hepatomegaly, splenomegaly.

Case Study

A 18month female child admitted to our ward with history of decreased appetite and abdominal distension for 1m, progressive pallor for 15days with past history of blood transfusion. There was no history of fever, cough and cold, loose motion, yellowish discolouration, convulsion, contact with Tuberculosis. She was a 2nd order child, 3rd degree consanguineous marriage with normal birth history. Elder sibling doing well. Child immunized as per age. BCG scar present. Weight was 10kg, length 72.5cm, MUAC 11.5cm, Head circumference 45cm, HT/age between -3SD TO -2SD. Patient was conscious, Severe Pallor, No Icterus, Cyanosis, Clubbing, Lymphadenopathy, Edema with Stable Vitals with Hepatomegaly 5cm, Splenomegaly 8cm, firm, with other systems being normal. Investigation reveals Hb 4.4mg/dl, TLC 15,290, TPC 27000, Reti count 2.25, Peripheral smear shows bicytopenia, MCV

80.1, MCH 21.4, MCHC 26.7, Sickling negative, MP(CT) neg, HPLC – HbF 1.4%, HbA2 2.5%, LFT and RFT normal.

Bone Marrow study shows bicytopenia with lipid laden macrophages suggestive of Storage disorder. Huge hepatosplenomegaly with persistent bicytopenia with PS not suggestive of hemolytic anemia indicates towards storage disorder. Fundoscopy shows Disc edema, No cherry Red spot. X-ray chest and limbs does not reveal any features of Osteopetrosis. Liver Biopsy study shows microvesicular fatty changes of hepatocytes. β -glucosidase activity level 2.2 (normal->4) confirmed our diagnosis. Blood transfusion given in 2 sittings and advised for regular intake of Folic Acid and proper nutritional advise. After explaining the prognosis patient referred to higher centre for definitive management.



Figure 1. Pt showing anemia with huge hepatosplenomegaly

characteristic Gaucher cells, macrophages engorged with lipids and eccentric nuclei⁽¹⁾.

Depending on the presence of central nervous system involvement, GD is classified into three types⁽²⁾.

Type 1 - Non neuronopathic form (presents in childhood or early adulthood): this accounts for 95% of cases. The main signs and symptoms are hepatosplenomegaly, bone lesions (painful crises caused by bone infarcts and osteonecrosis) and thrombocytopenia.

Type2 –Acute neuronopathic form (presents in childhood and is rapidly progressive and fatal): Early involvement (before the age of one year) of the brain stem and rapidly progressive (death before the age of 2 year), associated with organomegaly.

Type3 –Subacute neuronopathic form (presents in childhood but is slowly progressive): Progressive encephalopathy (oculomotor apraxia – epilepsy – ataxia) associated with the signs of type 1 disease in the child or adolescent. This brain involvement may be present from the beginning or occur later.

The presentation of the foetal form involves a reduction in foetal movements or even foetal immobility or anasarca. Definitive diagnosis is based on the demonstration of a deficiency of glucocerebrosidase enzyme activity (or acid β -glucosidase or glucosylceramidase (below 20-25%). It is usually carried out on the patient’s blood or during prenatal diagnosis, on total white blood cells or better on mononuclear cells, using synthetic substrates. If there is discrepancy between the clinical and biochemical findings, a skin biopsy must be made to obtain a fibroblast culture on which to check glucocerebrosidase enzyme activity.

Enzyme replacement therapy (ERT) with recombinant enzyme imiglucerase is highly effective form of therapy in reversing the hematological and visceral manifestations of Gaucher’s disease⁽³⁾.

Substrate reduction therapy (SRT) or Substrate Deprivation reduces the accumulation of the waste material in the first place, so that if an individual

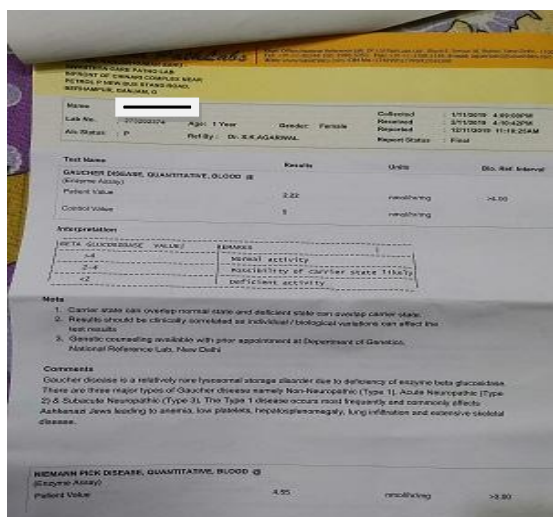


Figure 2 Report showing decrease GCS activity

Discussion

Gaucher’s disease is a rare autosomal recessive, potentially fatal disorder but most common type among lysosomal storage disorders⁽¹⁾. Gaucher’s Disease is caused by deficiency of an enzyme β -glucocerebrosidase that leads to accumulation of glucocerebrosides in cells of macrophage-monocyte system. The prevalence of GD is approximately 1/60,000 in the general population though this may reach 1/1000 in the Ashkenazi Jewish population. Its clinical expression is extremely variable, ranging from asymptomatic forms to lethal in-utero form.

GD leads to glycolipid accumulation and subsequent storage in cells giving rise to

has residual enzyme activity, the reduction in accumulation of substrate can mean that the patient's residual enzyme is capable of restoring substrate balance.

Our case is Type1 GD which is the most common type (95%).Anemia do occur in GD but presenting as congenital hemolytic anemia with history of multiple blood transfusion makes it a rare one.

Conclusion

Gaucher's disease is an inherited metabolic disease that presents as a multi-system disease. Three phenotypes have been described. Enzymatic activity level assay is diagnostic. Enzyme Replacement with recombinant enzyme is highly effective for treatment. But this ERT seems to be more theoretical than practical in our patients. Though a child of 1.5 yr presenting with HSM with h/o Blood transfusion points towards congenital hemolytic anemia like Thalassemia major but getting no evidence of hemolysis in PS, Normal reti count one has to bring the D/D of storage disorder like Gaucher disease, NPD, Taysach's disease.

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