Gaucher's Disease- A case report

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Abstract

A 3 years old immunized girl of consanguineous parents presented abdominal distension with hepatosplenomegaly. she was moderately anemic ,moderately wasted and stunted. Neurological examination was normal. Musculoskeletal system examination revealed no abnormality. Diagnosis was supported by typical bone involvement in X-ray film (thin cortex in limb bone) and gaucher cell in the bone marrow and also in the splenic aspiration. There are three subtypes Type1: Non neutropathic form. Type 2: Acute neuropathic form. Type 3: Chronic neuropathic form. However some cases do not fit precisely into one of these categories. All forms of Gaucher disease are autosomal recessively inherited. So, this patient more or less correlates with Gaucher disease type 1. Treatment option for type 1 and 3 include medicine and enzyme replacement therapy, which is usually very effective.

Key words: Gaucher's cell, lipid storage disease, ERT.

CBMJ 2014 July: Vol. 03 No. 02 P: 45-48

Introduction

Gaucher's disease is the lipid storage disease, an autosomal recessive disorder caused due to deficient or defective production of a naturally occurring lysosomal enzyme glucocerebrosidase (GD). Failing enzymatic degradation, there is accumulation of glucocerebroside (a glycolipid) in large quantities in lysosomes of reticulocendothelial (RE) cells i.e, macrophages of many organs, primarily liver, spleen and bone marrow but rarely the brain & nervous system, lungs, kidneys, skin and lymph nodes etc.

This condition was first described in 1882 by a French medical student Philippe Charles Ernest Gaucher who wrote a descriptive case report as a thesis for his degree of medicine. He considered large splenic cells that now bear his name as a manifestation of primary neoplasm of spleen[1].

1906 Merchand proposed that the disease was caused by storage of some material in the reticuloendothelial cells and ultimately in 1934 Aghion showed that the material was glucocerebroside, a glucosyl ceramide[2]. In 1965, the primary defect was detected as a deficiency in the enzyme glucocerebrosidase resulting in inability to degrade glucocerebroside[3,4].

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The severity of the disease is widely varies. Some patients present in childhood with virtually all the complication of gaucher disease, whereas other remain asymptomatic upto eighth decade of life.

The clinical manifestations of GD are produced by the accumulation of 'Gaucher cells' in various organs as mentioned earlier. There is great variability in the severity of all types of GD. Type I (adult type) disease may be entirely asymptomatic, discovered during population survey[5]. In the symptomatic patients, the spleen massively enlarged producing pressure symptoms. Skeletal disorders and bone lesions that may cause pain are common in type I, occasionally present in type III and usually absent in type II disease. Widening of the distal femur may give rise to a typical "Erlen-Mayer flask deformity".

Since the disease is rare, in non-endemic population a case of huge splenomegaly or hepatomegaly will obviously, non raise the suspicion of GD from the outset rather it may point to some other locally prevalent parasite or infectious diseases like malaria, kala azar (visceral leishmaniasis), schistosomiasis, brucellosis etc. or other medical problems associated with organomegaly.

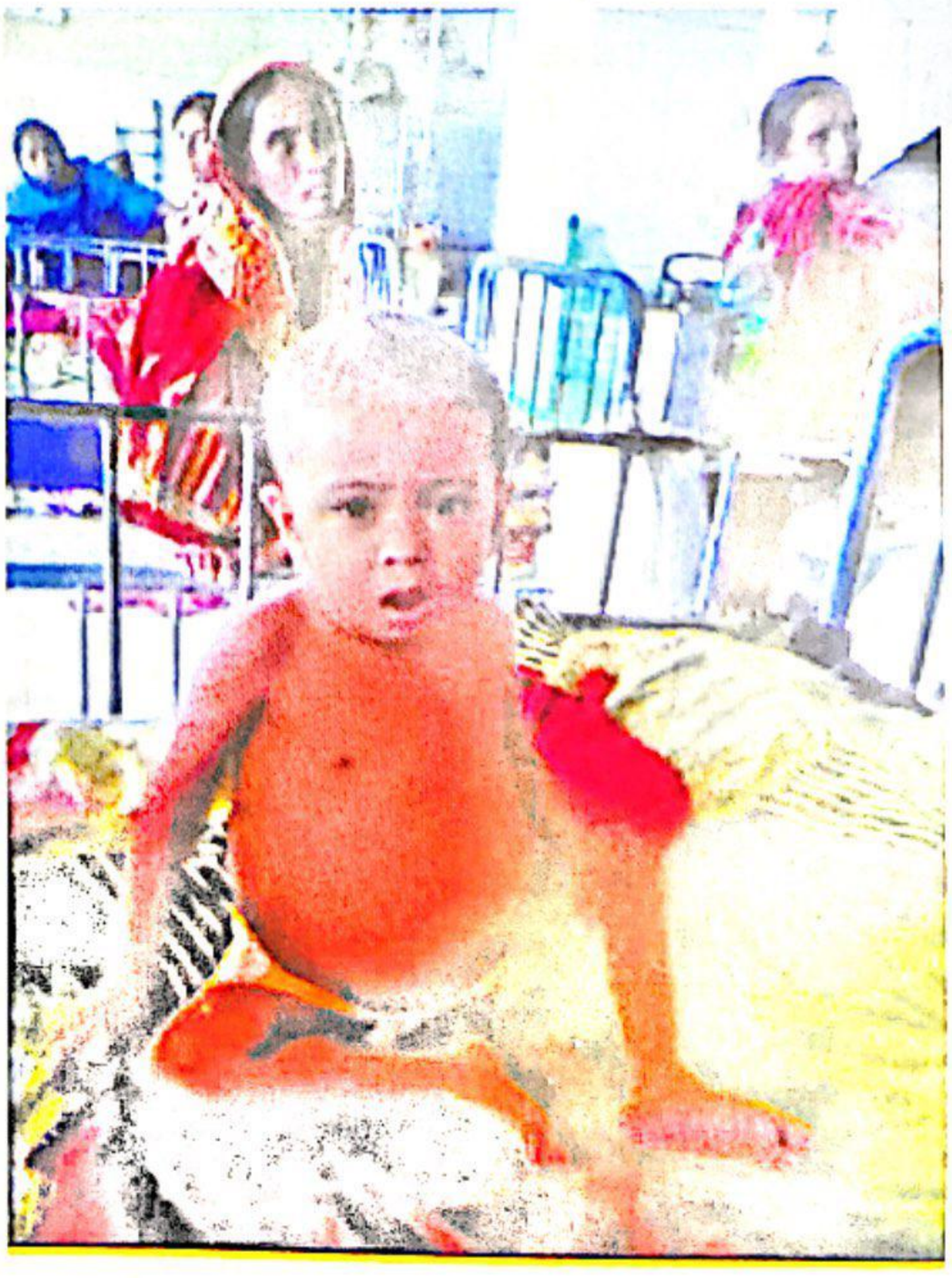
The diagnosis Gaucher's disease mainly confirmed based on findings of Gaucher cell on bone marrow and other tissue. Assay of enzyme glucocererosidase is not possible due to unavailability of the test in our country and the patient could not afford to get it done as well from abroad.

Treatment option for type 1 and type 3 include medicine and enzyme replacement therapy. There is no good treatment for brain damage[6]. Successful bone marrow transplantation cures the non neurological manifestation of the disease. Splenectomy may be required on rare occasions if the patient is anemic or mechanical discomfort. Bisphosphonates for bone lesion and liver transplant may require. Gene therapy may be a future step[7].

So far we know, this is the second reported case in Bangladesh.

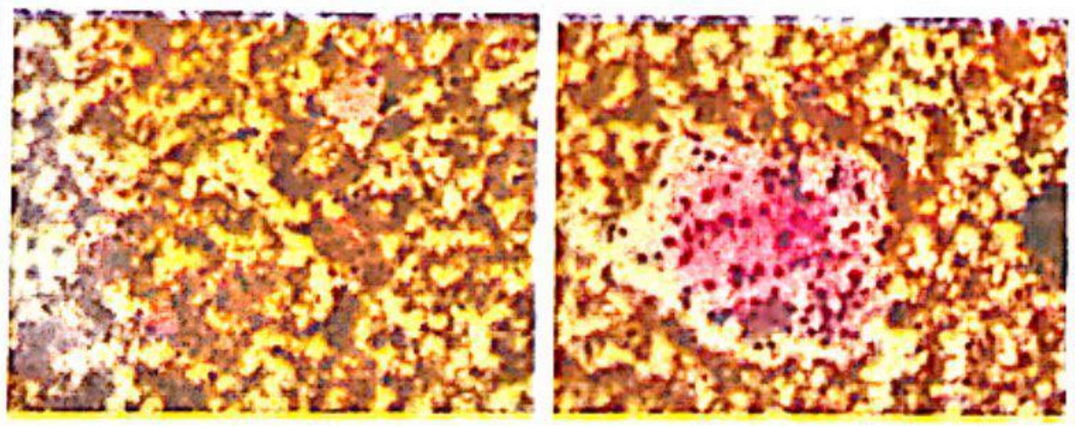
Case report

Miss Samia 3 years old immunized girl of consanguineous parents hailing from Trishal Mymensingh admitted on 21/8/14 with the complaints of abdominal distension since one year of age. Birth history is uneventful. He has no history of delayed crying after birth and no delayed milestone of development. Dietary history reveals normal. Other family members in her family are healthy. She is moderately anemic, moderately stunted (Height for age 87.3% of NCHS). She has hepatosplenomegaly, liver is 9 cm from right costal margin and spleen is 16 cm from left costal margin along the long axis but having no evidence of ascites. She has subnormal intelligence but motor and sensory function is normal. All the cranial nerves are also intact. Bony survey shows back and spine normal and no joint deformity is detected.

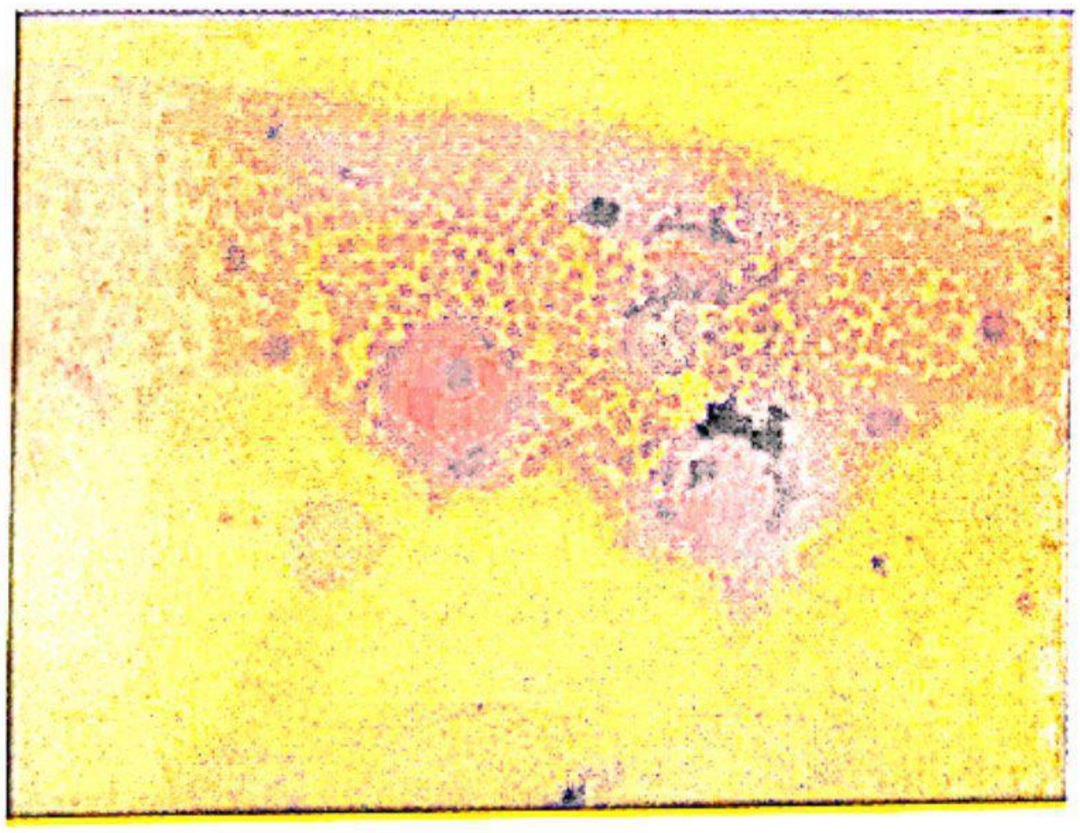


Picture-1: Patient of Gaucher's disease

Fundoscopy findings reavels no abnormality. Examination shows all the vital signs within normal limit. Other systemic examination shows no abnormality. Complete blood counts reveald total count of WBC is 8,400/cmm of blood. Platelet count 1,50000/cmm of blood, Polymorph-36%, Lymphocyte-59%, Eosinophil- 02%, Monocyte-03%, Basophil-00%, Hemoglobin-9.1gm/dl and peripheral blood film shows microcytic hypochromic anemia. Liver function test is within normal limit. ICT for Kala-azar is negative. Random blood sugar 4.2 mmol/L. X-ray limb shows thin cortex. Report on examination of Bone marrow puncture and splenic aspiration – smears show gaucher cell.



Picture-2: Slpeenic smear shows Gauchers cell.



Picture-3: Bone marrow smear shows Gaucher's cell.

Discussion

GD is an autosomal recessive disorder it is not gender specific and may affect both sexes equally.Type I disease is heterogenous and may manifest at any age starting from childhood to the old age with variable presentations from entirely asymptomatic incidentally discovered disease during population survey[8] with normal life expectancy to severally affected cases with organomegaly and cytopenia resulting in early death. Our patient presented at the age of about 3 years and although he had huge hepatosplenomegaly, there were no cytopenias but pressure symptoms only. Hepato-splenomegaly may occur as a result of various pathological factors like reactive increase of white pulp in inflammation and infection, congestive expansion of the red pulp compartment(in case of spleen only) increased blood pool, increased macrophage function, proliferative cellular infiltration, extramedullary haemopoiesis, storage disease, cysts and solid tumors etc[10].

The relative incidence of the cause of hepato-splenomegaly is subject to geographical variations. In the western countries haematological disorders come first while in the tropics parasite infections like malaria, leishmaniasis and schistosomiasis are of immediate concern. In Bangladesh, a case of huge hepato-splenomegaly brings in mind various differential diagnoses like visceral leishmaniasis, tropical splenomegaly syndrome (TSS), thalassaemias & haemogobinopathies, cirrhosis of liver with portal hypertension, lymphoma, collagen diseases (e.g., SLE) and lastly, storage diseases etc. In our case, haematological disorders were excluded straightway by normal blood counts and normal blood film findings. Absence of anaemia and lack of past history of malaria attacks excluded the possibility of TSS. Moreover, negative immunological tests for leishmaniasis exclude kala-azar. However, in our finding presence of typical Gaucher cells in the bone marrow and spleen smears in an otherwise unremarkable marrow made the diagnosis of Gaucher's disease more or less straightforward. Enzymatic assay of Beta-glucosidase activity in leucocytes[11] or cultured fibroblasts[12] is diagnostic of GD when aow value is detected. The test is not available in Bangladesh nor could our patient afford to get it done from abroad. Prenatal diagnosis of GD may be established by examining amniocentesis cells

for their beta glucosidase activity[12] or chorionic villus DNA for prevalent mutations.Type I GD seems particularly suitable for enzyme replacement thereby (ERT)because of the lack of the central nervous system involvement. ERT was tried by various workers since mid 1970s its successful and regular clinical use started only in 1990s when a mannose terminated of the enzyme extracted from human placenta was marketed commercially by the name alglucerase (Ceredase)[13-15]. It has been replaced soon by imiglucerase (Cerezyme), the recombinated product.Successful bone marrow transplantation cures the non neurological manifestation of the disease. Splenectomy may be required on rare occasions if the patient is anemic or mechanical discomfort. Bisphosphonates for bone lesion and liver transplant may require. Gene therapy may be a future step[7].

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