CASE REPORT

Clinico-hematological profile of lysosomal storage disorders – a report of three cases

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Introduction

Gaucher's disease was first described by Gaucher in 1882 [1]. Gaucher's disease is an autosomally recessive inherited deficiency of the lysosomal beta glucosidase which is encoded by a gene on chromosome 1 [2, 3]. It is more prevalent among Ashkenazi Jewish individuals with an incidence of approximately 1 in 1000 [4]. The diagnosis is confirmed by demonstrating deficient beta glucosidase activity in isolated leucocytes or cultured fibroblasts. Neimann-Pick disease results from the deficiency of the lysosomal enzyme, sphingomyelinase and the subsequent accumulation of its substrate, sphingomyelin [5]. We report three cases of storage disorders who presented at Lady Hardinge Medical College and Kalawati Saran Children's Hospital within a month. In the first two cases, the diagnosis of Gaucher's disease was confirmed by lysosomal enzyme assay.

However, the third patient left against medical advice, so the diagnosis couldn't be confirmed. The clinical and hematological parameters of these cases are summarized in Table 1.

Discussion

Gaucher's disease is the most common lysosomal storage disorder. It is found principally in jews of European stock. There are three clinical subtypes. The most common accounting for 99% of cases is called type I, or the chronic non neuronopathic form. Splenic and skeletal involvement dominate this pattern of the disease with sparing of the brain. These patients have reduced but detectable levels of glucocerebrosidase activity, so the longevity is short but not markedly. Type II, or acute neuronopathic form is the infantile acute cerebral pattern. In these patients, there is virtually no detectable enzyme activity, leading to death at an early age. Very few cases of type II disease have been reported. Type III, the juvenile or Norrbotten form is intermediate between types I and II [6].

The pathologic hallmark in Gaucher's disease is the presence of the Gaucher cell in the monocyte macrophage system, particularly in the bone marrow. These cells, which are 20-100µm in diameter, have a characteristic wrinkled paper appearance. However, gaucher cells are not diagnostic, as pseudo-gaucher cells/ gaucher-like cells may be seen in various conditions like chronic granulocytic leukemia, acute leukemia, thalassemia major and occasional cases of myelodysplastic syndrome [7,8]. The diagnosis of homozygotes can be made by measurements of glucocerebrosidase activity in peripheral blood leucocytes or in extracts

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Table 1 Clinical and hematological parameters of the cases.

	Case 1	Case 2	Case 3
Age / Sex	9 months/ female	8 year/ male	5 months/ female
Lymphadenopathy	-	Generalized	-
Organomegaly	Hepatosplenomegaly	Splenomegaly	Massive Hepatosplenomegaly
Neurologic signs & symptoms	Seizures, deep tendon reflex-brisk, plantar-extensor	-	-
History of consanguinous marriage	-	Present	Present
Family history	No Sibling	Sibling Healthy	Sibling with similar complaints; expired at 6 months of age
Clinical diagnosis	? Cerebral palsy ? Storage disorder	? Leukemia ?? Kala-azar	? Thalassemia
Hemoglobin (g/dl)	10.3	8.3	9.6
TLC /cmm	7,400	12,400	11,000
Platelets /cmm	1,40,000	50,000	1,47,000
Bone marrow	Typical Gaucher cells, PAS positive	Large cells with foamy cytoplasm; similar cells in lymph node (fig 1)	Foamy histiocytic cells (fig 2)
Enzyme assay in peripheral blood			
β glucosidase (normal >4.0)			
Sphingomyelinase (normal 3-10)	0.60 nmol/hr/mg 8.0 nmol/hr/mg	0.72 nmol/hr/mg 10 nmol/hr/mg	Patient left against medical advice
Final diagnosis	Gaucher's disease	Gaucher's disease	? Niemann-pick's Disease

Fig. 1 Large cells with abundant vacuolated cytoplasm, (case 2) (Wright's stain, 400x) **Fig. 2** Two large histiocytic cells with abundant foamy cytoplasm (case 3) (Wright's stain, 1000x)

of cultured skin fibroblasts. Chitotriosidase, an enzyme synthesized by macrophages, is markedly elevated in patients with Gaucher's disease. It is a reasonably specific biomarker for Gaucher's disease because levels are only slightly elevated in other disorders affecting macro-phages [9].

Niemann-Pick disease types A and B are lipid storage disorders that result from the deficiency of enzyme, acid sphingomyelinase. Type A is the severe infantile form with extensive neurological involvement, marked visceral

accumulation of sphingomyelin, and progressive wasting and early death within the first 3 years of life. Type B patients have organomegaly but no CNS involvement [6].

In the past, management of patients was primarily symptomatic. Enzyme replacement therapy is being used for gaucher's disease, however such therapy is extremely expensive. Experimental and clinical experience with other approaches including substrate reduction therapy, pharmacologic chaperone therapy, gene and stem cell therapies

have identified their useful applications and limitations. However, despite these remarkable advances, significant hurdles still remain before the goal of treating all or most lysosomal diseases can be realized [10].

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