GAUCHER'S DISEASE

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Introduction

Gaucher's disease is a rare inborn error of metabolism inherited as autosomal recessive disorder. It is a lysosomal storage disorder occurring due to deficiency of Beta-glucosidase. The incidence of Gaucher's disease is 1 in 10,000. Only a few cases have been reported from India, as the confirmation of diagnosis through enzyme assay has been available only since recently, while it is much more common among Jews [1].

Case Report

This 18-month-old boy, the second child of nonconsanguineous parents was brought with progressive pallor and abdominal distension noticed since the last six months. Findings on examination-Weight 9kg, height-86 cm, pallor, hepatomegaly 5cm, splenomegaly-6cm. On investigation-Hb 6 gm%, peripheral smear-microcytic hypochromic anaemia. Hemolytic screen including Hb electrophoresis was normal. Bone marrow examination revealed infiltration with large cells with wrinkled eosinophilic cytoplasm suggestive of Gaucher's disease (Fig 1). X-ray both femur showed metaphyseal widening suggestive of Gaucher's disease (Erlenmeyer flask deformity) (Fig 2). Leucocyte enzyme as-

Fig. 1 : Photomicrograph showing Gaucher's cells in bone marrow

say for Beta Glucosidase enzyme was markedly reduced-0.5 nmol/hr/mg of protein (Normal-9.6 nmol/hr). The enzyme assay was done fluorometrically using substrate 5 mM 4 methyl umbelliferyl-B-D-glucopyranoside, in 0.2% sodium tauroglycocholate. Aryl sulfatase enzyme levels were-94 nmol/hr/mg of protein (normal). Based on the above reports a diagnosis of Gaucher's disease (Type 1) was made in view of the absence of CNS involvement. The patient is being given symptomatic therapy and efforts are on to obtain recombinant Ceredase enzyme for enzyme replacement therapy. Gene therapy now promises hope for Gaucher's disease.

Discussion

Gaucher's disease was first described in 1882 by PCE Gaucher. Fifty years later Agihon reported that

Fig. 2 : X-ray of both femur showing Erlenmeyer flask deformity

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Gaucher's disease was due to accumulation of glucocerebroside. Brady in 1964 demonstrated that Gaucher's disease was due to Beta glucosidase deficiency. Enzyme replacement therapy was started in 1990 with good effect and gene therapy initiated since 1995 [2]. Reports from India are few [1], Gaucher's manifests in three forms. Type I is the commonest and manifests with hepatosplenomegaly, anaemia & orthopaedic involvement in the form of aseptic necrosis, fractures & pain. Yellow patches on the sclerae (pingueculae) are seen in 25% of the cases & abnormal pigmentation of the face, neck, hands or shins may occur. Associated immunoglobulin abnormalities are reported & transient changes in Factor IX may contribute to bleeding problems [3]. Type II (acute or infantile form) presents with neurological involvement in the form of strabismus, dysphagia, opisthotonos posturing and features of 'pseudobulbar palsy'. Most patients die by 6-12 months of age. Type III (Norbottnian type), named after the region in Sweden where it is prevalent, is a subacute neuronopathic type. They show gradually increasing dementia during middle to late childhood, often with behavioural changes, seizures, extrapyramidal and cerebellar signs. Organomegaly is mild [3].

Diagnosis of Gaucher's disease is confirmed by Beta glucosidase enzyme levels in leucocytes assay. In patients with bone involvement acid phosphatase levels are raised. The deficiency of Beta glucosidase enzyme leads to accumulation of glucocerebroside in tissue leading to the manifestations of the disease [3].

There is a 25% chance of recurrence in future offspring. Prenatal diagnosis is possible in cell culture

from amniotic fluid. The gene for beta glucosidase has been mapped to chromosome 1 q21 [4]. Splenectomy offers relief from anaemia and hemorrhagic manifestations but should only be pursued when the symptoms are severe. Bone marrow transplant provides a cure when successful but is associated with risks. Enzyme replacement with recombinant beta glucosidase (cere-dase) is a new form of therapy. The enzyme is administered 40 IU/2 weekly & produces symptomatic relief & regression of bone pains, nose bleeds & splenomegaly. The biochemical parameters also return to normal [5]. The recent introduction of *chitotridase* measurements has provided a valuable indicator of cellular burden of storage cells. Serial measurements are useful for monitoring disease progression & response to therapy [6]. Enzyme therapy is to continue life long & is exorbitantly expensive.

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