Case Report

Gaucher Disease: A Case with Unexplained Splenomegaly

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ABSTRACT

A 5 years old male child presented with fever, repeated chest infection, short stature and developmental delay. On examination; he had massively enlarged spleen measuring 10 cm below left costal margin. He was advised bone marrow examination by pediatric consultant to find out the cause for splenomegaly. Bone marrow examination revealed hypercellular marrow with numerous mononuclear storage cells having fibrillary cytoplasm, morphologically resembling Gaucher cells. The bone marrow trephine biopsy also revealed heavy infiltration in the form of sheets of storage cells both interstitial and paratrabecular in distribution. These cells showed strong PAS positivity confirming the diagnosis of Gaucher disease.

Key Words: *Enzyme Replacement Therapy, Gaucher Disease, Glucoceribrosidase, Splenomegaly.*

Introduction

Gaucher disease is the most common sphingolipidosis. It was first described by Philippe Gaucher in 1882 in a patient with massive splenomegaly. Gaucher disease is the most prevalent form of lysosomal storage disorders with autosomal ressesive mode of inheritance. It is caused by deficiency of enzyme glucocerbrosidase leading to accumulation of its substrate; glucocerebroside in recticuloendothelial cells of the body, also called glucosylceramide.[1] There are three phenotypic presentations of Gaucher disease; Type1 Non-neuropathic is the most common form. It should be considered in all cases of unexplained splenomegaly and hepatomegaly. Pancytopenia may occur due to bone marrow suppression.[2] Gaucher disease type-2and type-3 are characterized by neurological involvement.[1]

Case Report

Mr Muhammad Ali Ahmad 5 years old boy presented in paeds OPD of Railway Hospital Rawalpindi with complaints of fever and repeated chest infection. He had short stature and developmental delay. He was 1st child of consanguineous marriage. He was born at full term by spontaneous vaginal delivery. He had history of strabismus for which he was operated upon about one and half year ago. There was no family history of similar illness in other siblings. On examination he was afebrile. His occipito-frontal circumference was 40.5cm. He had short neck with 13kg body weight and 96 cm height. Spleen was 10 cm enlarged. He was advised bone marrow examination to find out the cause of splenomegaly His blood complete picture showed hypochromia and microcytosis. The X-ray wrist joint showed radiological bone age of 32±06 months. The X-ray skull, chest and pelvis showed no abnormality.

Bone marrow examination revealed hypercellullar marrow with numerous storage cells mostly mononuclear with occasional binucleated forms; having fibrillary cytoplasm, morphologically resembling Gaucher cells. Bone marrow trephine biopsy showed moderately hypercellular marrow. There was marked infiltration in the form of sheets of storage cells having granular pink cytoplasm and strong PAS positivity; confirming the diagnosis of Gaucher disease. In some of the areas the infiltration was in the form of group of cells with interstitial as well as paratrabecular pattern.

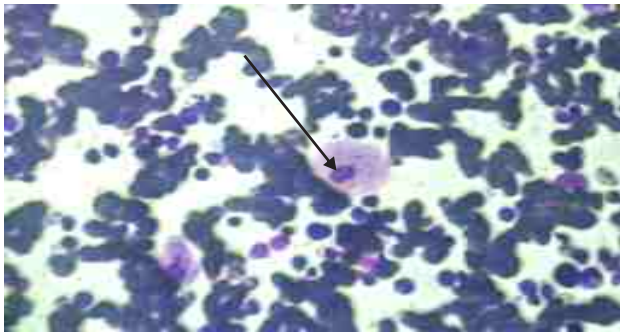

Fig 1: Bone Marrow Aspiration Smear Showing Gaucher Cells

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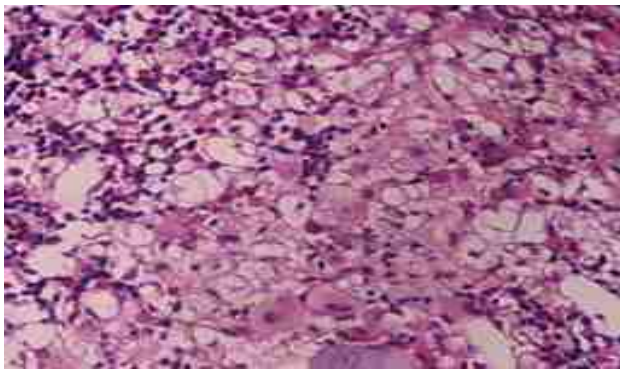

Fig 2: Bone Marrow Trephine Biopsy Showing Sheets of Gaucher Cells

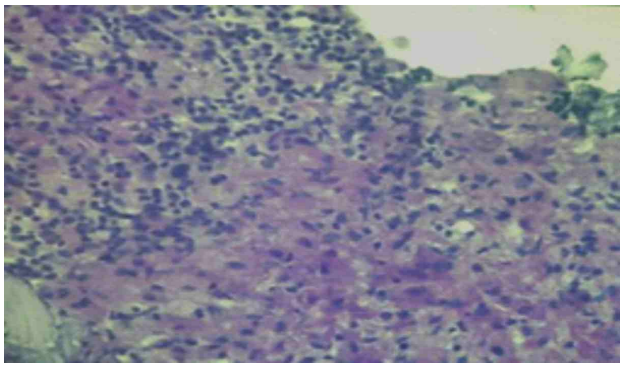

Fig 3: Bone Marrow Trephine Biopsy Showing Gaucher Cells with Diffuse PAS Positivity

Discussion

Gaucher disease is the most prevalent form of lysosomal storage disorders with autosomal recessive inheritance. Its prevalance is around 1/40,000 to 1/60,000 births in general population. The highest incidence is in Ashkenazi Jews, 1 in 850 individuals. [1] It is characterized by accumulation of glucocerebroside in the macrophages due to deficiency of enzyme β-glucoserebrosidase. 90% of the Gaucher disease patients present with moderate to massive splenomegaly.[3]

The molecular genetics of Gaucher disease involves GBA1 gene, located on chromosome 1 (1q21). More than 400 mutations have been found in the GBA1 gene. The common mutations in Ashkenazi Jews comprised of N370S, L444P and 84GG.[1] The N370S allele is also prevalent in other population of Europe, North America, and Israel.[4] L444P mutation in homozygous state is strongly associated with neuropathic Gaucher disease type-2 and type-3.[1]

In the past the diagnosis of Gaucher disease was made by the presence of Gaucher cells in the bone marrow aspiration and trepine biopsy. The classical features of these storage cells include a diameter of 20–100µm with eccentrically placed nucleus and striated cytoplasm having "wrinkled tissue paper appearance.[5] The Gaucher cells show strong Periodic acid-schiff positivity. Enzyme assay for β-glucoserebrosidase deficiency is the present day gold standard method for the diagnosis of Gaucher disease.[5] Other investigations include, blood complete picture, liver function tests , serum ferritin levels, ultrasound abdomen, chest X-ray, X-ray lower limbs and Magnetic Resonance Imaging (MRI) of bone and abdomen.[5] Imiglucerase as enzyme replacement therapy (ERT) is available for Gaucher's disease, but is expensive.[6]

Conclusion

Gaucher disease should be one of the differential diagnoses in all age group patients with unexplained splenomegaly.[7] Bone marrow transplantation is the only curative option in these patients with gene therapy as the future therapeutic modality.

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