Gaucher's Disease in Adults

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Abstract

A case of Gaucher's disease diagnosed by bone marrow aspiration cytology.

Key words: *Gaucher' Disease, bone marrow aspiration*

Introduction

Gaucher's disease is an autosomal recessive lysosomal storage disorder of glucocerebrosidase in cells of macrophage lineage. Accumulation of glucosylceramide in tissues leads to multisystem organ involvement like liver, spleen, bone marrow, lungs and central nervous system. Serum β-glucosidase levels <15% of mean normal activity confirms the diagnosis.[1] It occurs in approximately 1/ 75,000 births worldwide, but is more prevalent in individuals of Ashkenazi Jewish descent. To the best of our knowledge only six cases of Gaucher's disease in adults have been reported from India so far.[1] Clinically, Gaucher's disease is classified into three major types. Type 1 is nonneuronopathic type also called the adult form. Type 2 disease is the acute neuronopathic form while Type 3 is sub-acute neuronopathic Gaucher's disease.[2] Advent of efficacious enzyme therapy, emphasizes the importance of early diagnosis and intervention to prevent morbid manifestations (organomegaly and osteopenia/ osteoporosis.)

Clinical Summary

A 40 year old man presented with history of abdominal discomfort, lump in abdomen and anorexia of almost 8 years duration. He was born of second degree consanguineous marriage. He did not have fever, jaundice, or bleeding from the gastroinstestinal tract at time of presentation. There was no past history of tuberculosis or blood transfusions. On clinical examination, he had pallor, massive splenomegaly and hepatomegaly with no other physical findings. Based on these findings, a differential diagnoses of tropical splenomegaly, storage disorder or haematological neoplastic disease was considered.

Investigations revealed Haemoglobin of 6.8 gm/dl, WBC count of 1500/ cubic mm and platelet count of 20,000/ cubic mm, with reticulocyte count of 1%. His renal functions and liver function tests were within normal limits. Ultrasonography of abdomen revealed hepatomegaly with coarse echo-texture and massive splenomegaly. CT scan of abdomen confirmed hepatosplenomegaly.

Pathological findings and treatment

Bone marrow aspirate showed normoblastic erythropoiesis and marked increase in reticulum cells, strongly positive for Periodic Acid Schiff stain. Bone marrow biopsy revealed lipid laden macrophages (Gaucher's cells) (Figure1and Figure2), peculiar to Gaucher's disease. Serum levels of β-glucosidase were found to be absent, there by confirming Gaucher's disease.

Enzyme replacement therapy with recombinant β-glucosidase could not be started in view of financial constraints. He was advised splenectomy, which he refused.

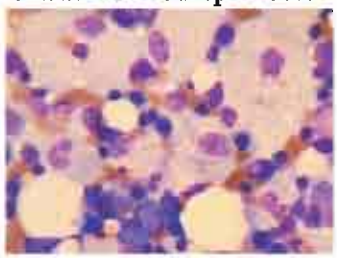

Figure 1 : Bone marrow imprints
(Gaucher cell showing crumpled paper appearance)

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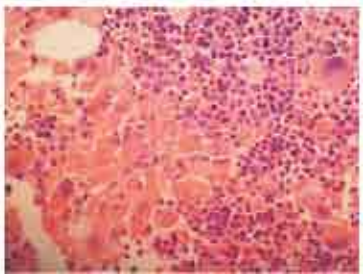

Figure 2 : Bone marrowTrephine biopsy (Showing Gaucher cells)

Discussion

Gaucher's disease is a genetic glycolipid storage disease characterised by glucocerebrocide in cells and certain organs due to defective activity of β-glucocidase. The disease is classified into 3 types:

Type 1: Is common and is non neuropathic. Hepatosplenomegaly, pancytopenia and skeletal involvement are specific features. Age at presentation is childhood or early adulthood.

Type 2: Is acute neuronopathic and rapidly progressive.

Type 3: Is chronic neuronopathic and slowly progressive.[1]

The disease is most prevalent in Ashkenazi Jews and transmitted as an autosomal recessive fashion.[1] Though Gaucher's disease manifests in infancy, it is also being diagnosed with greater frequency in the older population. The Gaucher's Registry shows that 7.7% of patients are 65 years and above.[3] Skeletal involvement occurs as bone pains, pathological fractures, and lytic lesions in long bones with premature osteopenia. Aseptic necrosis of femoral head is described as Erlenmeyer Flask Deformity.[1]

An increased risk of cancer in Gaucher's disease has been reported, especially haematological cancers.[3] Our patient did not have any haematological malignancy but he had splenomegaly, hepatomegaly and pancytopenia. Pancytopenia is usually due to presence of Gaucher's cells in bone marrow which compete with hematopoietic cell precursors.

Gaucher's disease can also occur in adults and the elderly. A high index of suspicion is required in such cases as clinical profile is different with involvement of lungs and other organs leading to pulmonary hypertension and sometimes Parkinsonism.[2]

Genetic testing is required for a definite diagnosis. Other laboratory studies like enzyme activity, increased serum Acetyl Cholinestrerase (ACE) levels and ferritin levels are helpful. DEXA scan may reveal the extent of osteopenia. Enzyme replacement therapy, Cerezyme (Imiglucerase) an analogue of human intracellular glucocerebrosidase is the treatment of choice for Types 1 and 3 Gaucher's diseases. Substrate reduction therapy, Zavesca (Miglustat) therapy of 100mg, 3 times daily is indicated for those patients with mild to moderate Gaucher disease, for whom enzyme therapy is not suitable. Supportive therapy like blood products and bisphosphonates can be administered to those patients who decline the above options.[5] Surgical options like splenectomy is indicated for multiple splenic infarcts or extensive splenic fibrosis.

Conclusion

A 40 year old man, born of second degree consanguineous marriage, presented with massive splenomegaly and hepatomegaly. On investigations serum β- glucosidase was found to be absent confirming a diagnosis of Gaucher's disease. Physicians need to be made aware that Gaucher's disease may present in adults, though rarely, and may remain symptomless for very long periods of time, as in our case. There have been many advances in treatment in the form of enzyme replacement therapy.

References

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