GAUCHER’S DISEASE- A RARE CASE REPORT
AZEEM AHAMED
Department of General Medicine,
MADURAI MEDICAL COLLEGE AND HOSPITAL

Abstract :
Gaucher’s disease is a rare autosomal recessive lysosomal storage disease due to deficiency of acid beta glucosidase enzyme. The disease frequency varies from 1 in 1000 in Ashkenazi Jews to 1 in 1,00,000 in other populations (5). All patients with Gaucher’s disease have non uniform infiltration of bone marrow by lipid laden macrophages termed Gaucher’s cells(5). We present here a case of Gaucher’s disease in a 17 year old patient who presented with anaemia, growth retardation, seizures, poor scholastic performance and excessive fatiguability. Bone marrow biopsy showed the characteristic Gaucher’s cell and serum enzyme estimation was done to confirm the disease.

Keyword : Gaucher’s disease, Gaucher’s cell, acid beta glucosidase.

Introduction:
Gaucher’s disease is an autosomal recessive lysosomal storage disorder that results from deficiency of acid beta glucosidase enzyme which was first recognised by a French doctor Philippe Gaucher in 1882. Deficiency of the enzyme leads to buildup of glucocerebroside which infiltrates the bone marrow, spleen, liver and even brain. Disease variants are classified based on the absence or presence and progression of neurologic involvement. There are three types of Gaucher’s disease. Type 1 is a non- neuropathic disease that presents in childhood to adulthood as visceral disease. Type 2 is a rare, severe CNS disease that leads to death by 2 years of age. Type 3 disease has highly variable manifestations in CNS and viscera.

CASE REPORT:
A 17 year old male presented with c/o easy fatiguability, growth retardation and breathlessness on exertion and poor scholastic performance in the past. History of absence seizures present for last 2 years and episodes of transient unawareness lasting nearly 5 mins. No history of aura or automatisms. No history of trauma, incontinence of urine or faeces. No history of jaundice, bleeding manifestations or bone pain. History of one episode of generalised tonic clonic seizures present during the stay in the hospital, post ictal state lasted around 10 minutes.

History of frothing from the mouth and tongue bite was present. The patient was treated with blood transfusion, iron supplementation and anti epileptics and other supportive measures while in hospital.

The patient was born of a second degree consanguineous marriage. Antenatal history was uneventful. There is history of delay in attaining developmental milestones and also poor scholastic performance. No history of other systemic illnesses.

On Clinical Examination: Patient had pallor, short stature and sparse axillary and pubic hair. Massive splenomegaly was present. Detailed neurological examination was done. There was borderline Intellectual impairment. There was no focal neurological deficit.

Blood Investigations:
Hb – 7.6 g % RBC count – 2.5 lakh/cu.mm. Platelets - 1.5 lakh/cu.mm. RDW – 20.6% MCV – 79.4fL MCH – 24.4 pg. MCHC – 23.4g/dl. PCV – 40. ESR – 25 mm/hr. WBC – 4700/ cu.mm [ DC – P 60 L 35 E4 M1] Hemoglobin electrophoresis – normal study Peripheral smear : RBC – anisopoikilocytosis, hypochromic microcytic, normochromic normocytic. WBC – count and morphology normal. Platelets - count and morphology normal. Renal function, liver function and thyroid function tests were normal and urine analysis was within normal limits. S. acid phosphatase was 6.4 units and was elevated.(o -4.7 Units) S.Iron – 17.4 microg/dl. S. ferritin – 3.25 nanog/ dl HBsAg – negative. IgM Anti HCV Ab – negative. HIV ELISA – negative.

ECG - LVH present.
USG abdomen-Hepatomegaly and massive splenomegaly present. Ophthalmologic evaluation – no evidence of Kayser-Fleischer ring EEG was done - B/L paroxysmal epileptiform discharges- abnormal record.
Psychiatric evaluation – I.Q. 75 – Borderline intellectual impairment seen.

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Bone Marrow smear – Normocellular marrow, active erythropoiesis predominantly microcytic normoblastic and occasional megaloblastic maturation .Leucopoiesis – normal pattern of maturation .Megakaryocytes – seen

Bone marrow biopsy report– Mature trabeculae of bone tissue with bone marrow material showing erythroid and matured myeloid series with GAUCHER cells.

Impression : Plenty of large cells with fibrillary cytoplasm and peripheral nuclei -GAUCHER CELLS are seen. Suggestive of Gaucher’s disease.

The beta glucosidase enzyme assay showed levels of 2nmol/hr/mg(normal reference range >4 nmol/hr/mg). Thus bone marrow biopsy and enzyme assay confirmed the diagnosis of Gaucher’s disease.

Gaucher’s cell seen in high power view of bone marrow biopsy specimen of patient.

**DISCUSSION:**

Gaucher’s disease is a rare autosomal recessive disease that results from decreased activity of acid beta glucosidase enzyme also called glucocerebrosidase (GBA) with the gene on chromosome 1q21. Disease variants are classified on the basis of absence or presence and progression of neuronopathic involvement .There is a vast phenotypic variation in the disease presentation.(1)

Various combinations of partially active or null-GBA alleles could lead to variable levels or thresholds of GBA activity and, hence, differing phenotypes.(3 )

There are three major types .Type 1 disease is non neuronopathic and can present in children or adults as visceral disease .Type 2 disease is a rare severe CNS disease that leads to death by 2 years of age .Type 3 disease has variable manifestations in the CNS and viscera .It presents in early childhood as rapidly progressive massive visceral disease and slowly progresses to static CNS involvement, in adolescence with dementia and in early adulthood with rapidly progressive uncontrollable seizures and mild visceral disease .Visceral disease in Type 3 is nearly identical to that in Type 1 but generally more severe .Early findings in CNS may be limited to defects in lateral gaze tracking .This variant is more frequent among individuals of Swedish descent.(5 )

The common finding reported in each patient was slowed horizontal saccadic eye movements (4 ). In some, the eye movement abnormality was described as mild, and in the others the finding was not documented at the time of diagnosis (1). However, on subsequent neuro-ophthalmologic evaluations, the saccadic abnormality was ultimately detected, in some cases several years after the initial diagnosis. Usually the onset of seizures was within a few years after the clinical diagnosis of Gaucher ‘s disease, although few patient develop clinical seizures significantly later, at age 18. EEG findings included a diffuse encephalopathic pattern and generalised epileptiform activity.

All patients with Gaucher’s disease have non-uniform infiltration of bone marrow by lipid laden macrophages termed Gaucher’s cells leading to marrow packing and cortical bone destruction and even vertebral collapse. Interestingly, Gaucher-like cells are well described in various haematological malignancies unrelated to Gaucher’s disease, including Hodgkin’s disease, non-Hodgkin’s lymphoma, multiple myeloma (MM) and chronic myeloid leukaemia(2).

Regular enzyme replacement therapy is currently the treatment of choice in significantly affected patients and efficacious in patients with bone marrow involvement and hepatosplenomegaly. Adult patients may benefit from bisphosphonates to improve bone density.(6 ) Other approaches to stabilize the enzyme in order to improve enzyme function called pharmacologic chaperone therapy are under investigation(7). The visceral but not the CNS involvement responds best to enzyme therapy (5). Splenectomy is another mode of therapy in severe disease(8). Bone marrow transplantation may be required in severe advanced cases.(8)

**CONCLUSION:** This patient had features of visceral disease in the form of massive splenomegaly and bone marrow involvement. Besides he had neurologic involvement in the form of seizures which was confirmed by EEG and he also had intellectual impairment. The presence of neurologic involvement in Gaucher’s disease is quite rare. This case is presented due to its rarity.

**REFERENCES:**


