A Rare Case of Infantile Gaucher Disease - A Case Report
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ABSTRACT
A 3-month old male child weight 3.2 kg presented was with anaemia (Hb 3.1 mg/dl) and massive hepatosplenomegaly. His respiratory and CVS systems were normal. Osmotic fragility and G6PD spot test were normal. Hb electrophoresis showed HbA-86.02%, HbF 2.8% and HbA2 3.9%. Bone marrow aspiration and biopsy showed typical Gaucher cells. This case was diagnosed as an infantile Gaucher’s disease.

KEYWORDS: An infantile Gaucher’s disease, Acute neuropathic form Hepatosplenomegaly, Gaucher cells, Glucocerebrosidase, Thrombocytopenia, Acidphosphotase

INTRODUCTION
With an overall incidence of approximately 1 in 50,000 to 1 in 100,000 live births, Gaucher’s disease is the most prevalent lysosomal storage disorder[1,5]. It is the most prevalent among Ashkenazi Jewish in whom the disease genotype occurs at a rate of approximately 1 per 1000 births[7,13,14].

Gaucher’s disease is an autosomal recessive lipid storage disorder due to deficient or defective production of a normally occurring lysosomal enzyme glucocerebrosidase[3]. Enzyme deficiency leads to accumulation of glucocerebroside in large quantities in lysosomes of reticuloendothelial cells, i.e. macrophages of many organs primarily liver, spleen and bone marrow, but rarely the brain, central nervous system, lungs, kidneys, skin, lymphnodes, etc.[1,9].

This condition was first described on 1882 by French Medical Student Philippe Charles Earnest Gaucher. It was a case report as a thesis for his degree of medicine. Based on these large spleenic cells he thought it was a primary neoplasm of spleen[1,34]. In 1906, Merchand proposed that the disease was caused by storage of some material in the reticulo-endothelial cells and, in 1934 Aghion showed that the material was glucocerebroside, or a glycocyl ceramide[10].

In 1965, the primary defect was detected as a deficiency in enzyme glucocerebrosidase, which leads to inability to degrade glucocerebroside[3,11]. GD is sporadic worldwide with an estimated incidence of 1:60-80,000 individuals[7]. Gaucher’s disease gene is located on chromosome 1 at band q21 with a total length of 7 kb. Both the active gene and a homologous (96%) pseudogene (downstream from the active gene) have been cloned and sequenced. This is useful for molecular diagnoses of GD. There are more than 300 mutation causing GD. Most of these are point mutations[7,12]. The five most common mutations account for approximately 97% of the alleles in the Jewish population but only for approximately 75% of the alleles in the non-Jewish population[7,14,15],

There are three major phenotypes of GD have been recognised clinically: type-I (adult), type-II (acute infantile neuropathic) and type-III (juvenile)[8]. Here

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we reported a rare case of acute infantile neuropathic
Gaucher’s disease: type-II first time at our Institute of
Gandhi Medical College, Hyderabad, Telangana, India.

CASE REPORT

A 3-month old male child was presented with
complaining of dry cough, low grade fever, and not
responding to superficial and deep stimuli, with severe
hepatospleenomegaly. There was no lymphadenopathy
and petichial rash all over the body, no icterus and was
not accepting oral feeds. The boy was born from a
non-consanguineous marriage and elder sibling died
with same complaint at the age of 6 month.

The child was moderately nourished with pallor; on
abdominal examination revealed distension, palpable
liver and spleen. His liver was enlarged by 5 cm below
the right costal margin and spleen was enlarged by 6
cm below the left costal margin. No abnormality was
detected in his CVS and respiratory systems. The child
died on the seventh day of his hospital admission.

INVESTIGATIONS

X-ray of chest showed no active lung parenchymal
lesion. Abdominal ultrasonography revealed
homogenous hepatospleenomegaly.

Haematological Parameters

Blood analysis showed thrombocytopenia (platelet count
33,000/ml), leucocytopenia (total leucocyte count in the
range of 900-1500/ml), and anaemia (Hb 6.5 g/dl).
Peripheral blood film showed microcytic, hypochromia.
WBC showed few hyper segmented neutrophils. The
liver enzyme levels were within normal range. HIV
testing for this child was negative.

An enzyme study showed very low levels of enzyme
glucocerebrosidase (<19% of the normal level) which
confirmed our diagnosis of Gaucher’s disease. Genetic
study was planned for this patient; it could not be done
due to non-availability.

Bone Marrow Aspiration

A bone marrow aspiration was done for this patient on

bone marrow aspiration, H and D stained smears
revealed the presence of few large cells with abundant
foamy cytoplasm and small round nucleus (Gaucher
cells). These cells were showing positivity with a special
stained PAS (periodic acid shiff) technique (Figures 1
and 2).

DISCUSSION

Gaucher’s disease is very rare. Three clinical forms
of the disease are known: the adult type (type-I), acute
infantile neuropathic (type-II) and the juvenile (type-
III).

Type-II and III involve the central nervous system and
are very rare; they do not occur predominantly in
Jewish families and are characterised by rapid
neurologic deterioration and lead to early death[8], with
null or severe mutations[16].

Figure 1: H and E stained bone marrow biopsy imprint

Figure 2: PAS stained bone marrow biopsy imprint
Type-I (the adult type): is a non-neuropathic form but pulmonary involvement widely reported in this type of Gaucher’s disease. Soumya patra et al. reported a case with pulmonary involvement (type-I) which is very rare with mild one mutation [4,17,18].

Type-II (acute infantile): Gaucher’s disease is so low growing disease that does not occur in Jewish families [8]. These abnormal cells accumulate in the CNS. This is the acute infantile neuropathic form of Gaucher’s disease, which presents in early infancy with neurological complications. The infantile variety is the severest form leading to organomegaly and CNS involvement usually manifesting by six months and ending totally by two years.

Only six such cases have been reported so far in Indian literature. Rao et al. also reported a case of infantile Gaucher’s disease [6].

Type-III GD (juvenile): By the absence of primary neurological symptoms, Hepatospleenomegaly is usually common to all three types. Type-III is a less well-defined subacute neuropathic disorder which will later have onset of neurological symptoms (from 2 to 20 year) and with better prognosis. Type-III is a prototype of Norrbottonian (Northern Sweden) disease. It has been subdivided into three further subtypes: a, b, and c [19].

The glucocerebroside laden enlarged RE cells with eccentrically placed nucleus are called Gaucher’s cells, which accumulate in many organs causing organomegaly with dysfunction and also marrow replacement with cytopenias [1,15,20]. In our case the presence of characteristic Gaucher’s cells in bone marrow supports our diagnosis.

Gaucher cells in routinely stained preparation have cytoplasm with crinkled, striated, onion-skin or crumpled-up paper like appearance. The cytoplasm stained with the periodic acid shiff (PAS) technique showed positivity for acidphosphotase. Electron microscopy reveals spindle or rod shaped membrane bond inclusion bodies 0.6-4 mm in diameter. These bodies consist of plenty, small tubules 130-750 Å in diameter [21,22].

Neurologic symptoms are the hallmark of type-II and type-III disease. Mostly symptoms are: acculomotor abnormalities, hypertonia of neck muscle with extreme arching of neck (opisthotonus), bulbar signs, limb rigidity and seizures [24], severe neonatal ichthyosis (colloidin babies) described infants with acute neuropathic Gaucher’s disease [23].

In the literature, stated Gaucher cells have been found in a colonic polyp [25], and the maxillary sinus [36]. Skeletal lesions are often seen patchy areas of bone demeniralisation and areas of infarcts are found and widening of the distal femur gives rise to a typical ‘Erlenmeyer flask deformity’ [26]. Bone pain is important clinical manifestation in this type.

Neoplastic disorders somewhat more common in GD are lymphoprolifrarative disease [27], including CLL [28,29,31], lymphoma [39] and Hordkin’s lymphoma [37,38]. The definitive diagnosis was established by determining leukocyte [32] or cultured fibroblast [33], b-glucosidase activity or by demonstrating mutations in the patients DNA 10. Prenatal diagnosis was done by examining cultured amniocentisis for this b-glucosidase activity [33] or amniocentisis or chorionic villus DNA for mutations.

CONCLUSION

Infantile Gaucher’s disease is very rare. Routine bone marrow aspiration in children with anemia and hepatospleenomegaly, in the absence of hemolysis will help to rule out this diagnosis.

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