Gaucher Disease: A Rare Case Report

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Introduction

Gaucher disease is a rare autosomal recessive disease. The disease is caused by mutations in the GBA1 gene located on chromosome 1(1q21) that markedly decrease the activity of glucocerebrocidase enzyme. The accumulation of the substrate glucosylceramide in the macrophages, induce their transformation into Gaucher cells in the reticuloendothelial system which act as protagonist factor in the disease symptoms.

Case Report

A specimen of spleen weighing 1100 gm, of 06 years old boy was received in Armed Forces Institute of Pathology. The baby is the only son of non consanguineous parents without any known family history. He had a history of progressive abdominal distention since age of 1.5 years with normal developmental milestones. On USG at the age of 03 years patient had hepato-splenomegaly and diagnosed as a case of Gaucher disease on bone marrow examination.

Histopathological examination of the sections from the spleen reveals diffuse infiltration of Gaucher cells having abundant fine, fibrillary eosinophilic granular cytoplasm resembling wrinkled tissue paper. The Gaucher cells are found PAS positive , PAS-D resistant and CD68 positive. On electron microscope, Gaucher cells show membrane bound inclusion bodies, filled with intracellular tubular structures composed of glucocerebrosides.

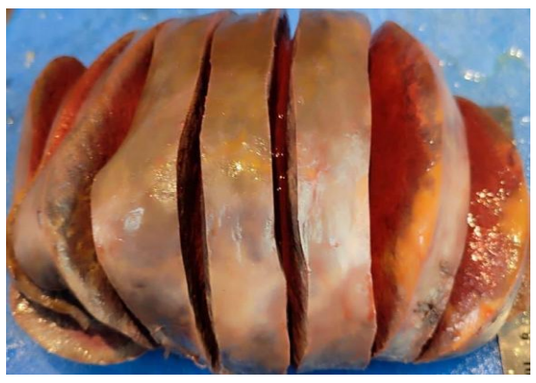

Figure 1: Gross appearance of the specimen.

Discussion

Gaucher disease (GD) was first described by the French physician Philippe Charles Gaucher in 1982 . During the preparation of his doctoral thesis, Gaucher performed the autopsy of a 32-year-old patient who had died after presenting a prominent splenomegaly, describing it as "Idiopathic Hypertrophy of the Spleen without Leukemia" . Later, in a similar case reported in, the disease was named Gaucher disease.[2]

Epidemiology

Gaucher disease is the most prevalent among Lysosomal storage diseases, with an incidence of 1 case per 40,000–60,000 births in the general population. [3]

Types

Three clinical sub types of Gaucher disease have been distinguished [1]:
1. Type I or chronic non-neuronopathic form
2. Type II or acute neuronopathic form
3. Type III , intermediate between type I and type II

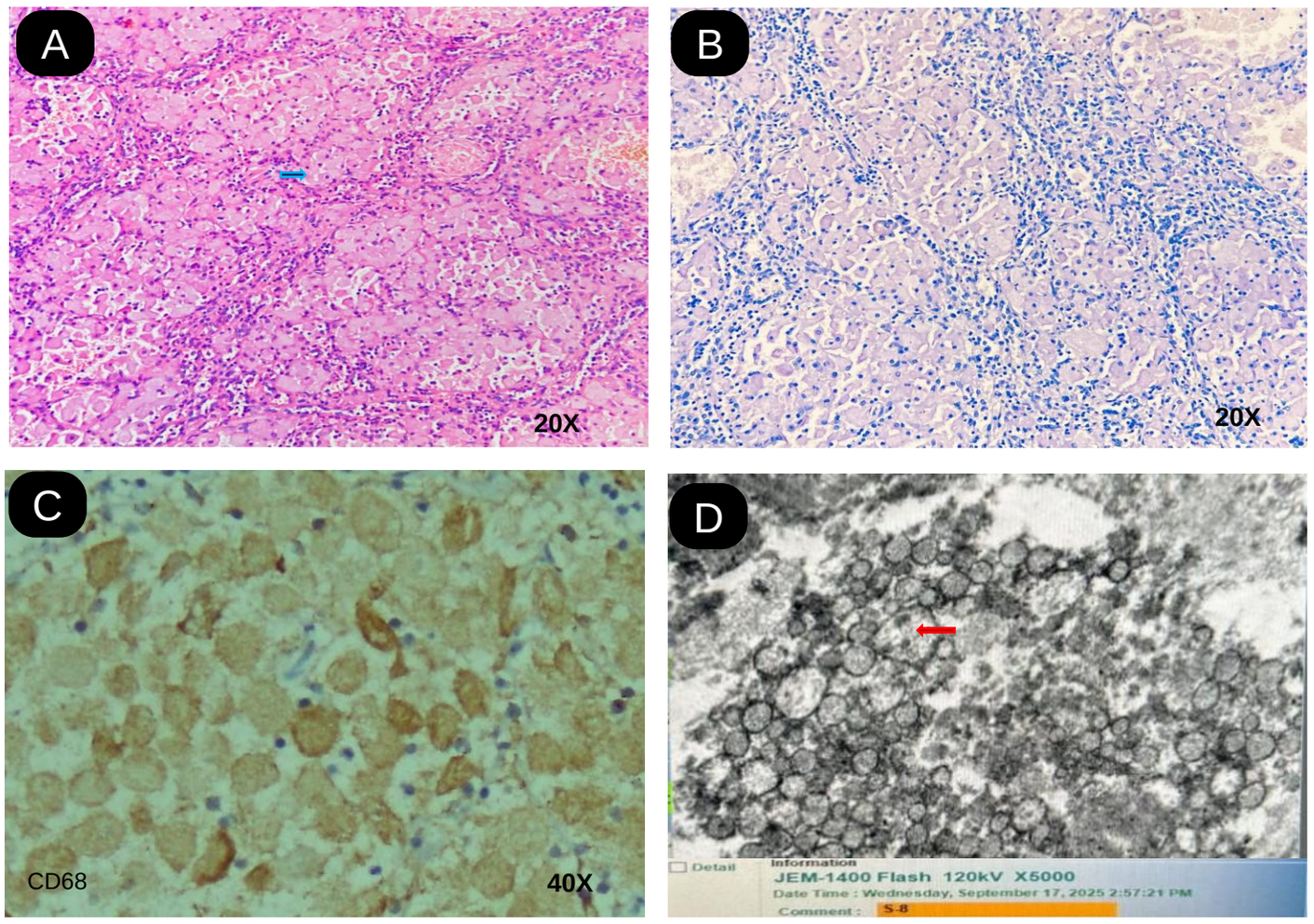

Figure 2: Microscopic features- **A**: H&E stained sections showing Gaucher cells having "crumpled tissue paper" cytoplasmic appearance.(blue arrow) **B**: PAS stained sections-Gaucher cells are PAS positive. **C**:Gaucher cells are positive for CD68 immunostain **D:** Electron microscopic view showing intracellular misfolded protein (Red arrow)

Pathophysiology

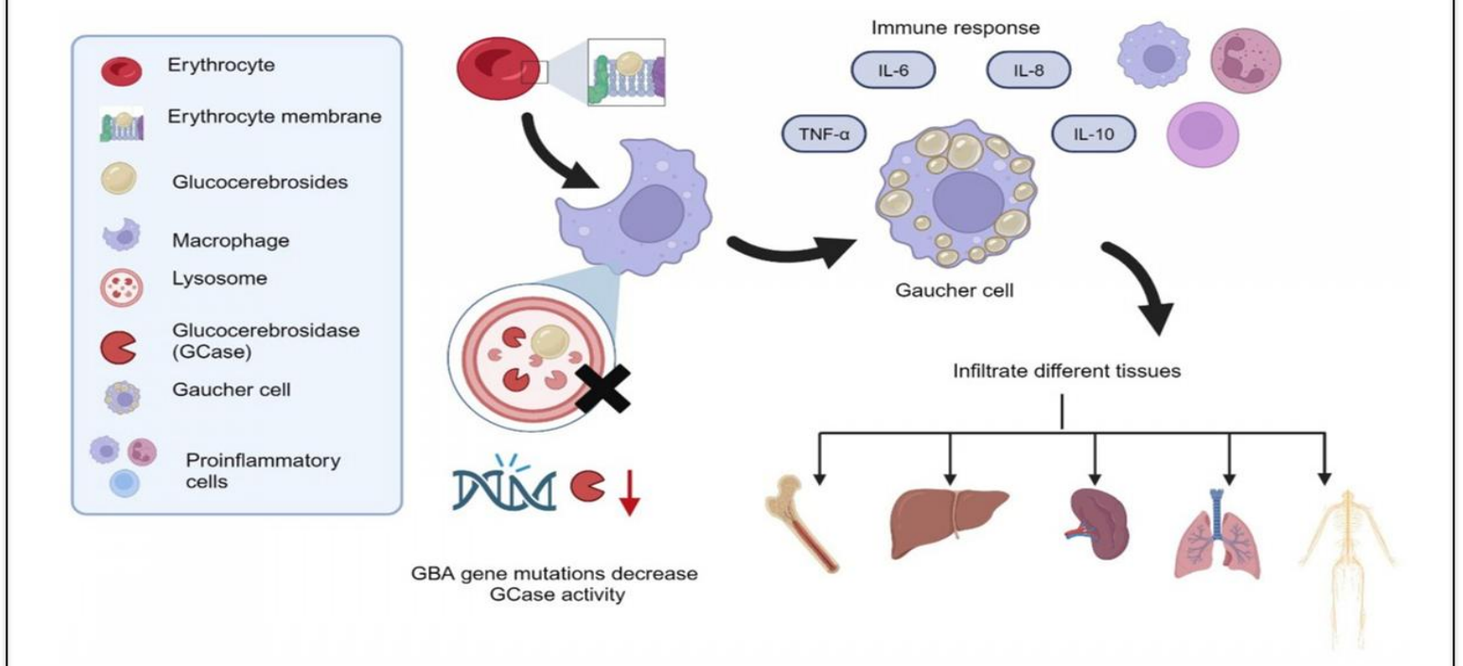

Figure 3: Pathophysiology of Gaucher disease.[2]

Patients with Gaucher disease have a 20-fold higher risk of developing Parkinson disease as these two diseases share common mutations in genes involving protein folding mechanisms of the cell.[1,4]

Diagnosis

Definitive diagnosis is made by deficient Glucocerebrocidase enzyme activity and characteristic mutation in GBA gene (L444p mutant allele). Although genotype-phenotype correlation is not uniform in all patterns of the disease [4]. Biopsies of the affected organ may identify Gaucher cells. Bone marrow aspiration (not recommended) is done to rule out other diseases[6] . Elevated serum ferritin, chitotriosidase, ACE and Lyso-Gb 1 supports the diagnosis[6]. Prenatal diagnosis is implemented in familial cases [4].

Treatment

Treatment of Gaucher Disease focuses on managing the symptoms as there is no cure. These include enzyme replacement therapy, substrate reduction therapy, Chaperone therapy etc [1,4,6]. Allogenic hematopoietic stem cell transplantation can be curative [1].

Prognosis

The disease has variable prognosis depending on its type - ranging from near normal life expectancy with appropriate therapy to death in early childhood [1,2].

Conclusion

The main histopathological finding in Gaucher disease is the presence of enlarged glycolipid laden macrophages called Gaucher cells found in the reticuloendothelial systems. Although histopathological findings must be interpreted in the context of clinical and biochemical tests as several other diseases like leukemia and multiple myeloma represent 'pseudo-Gaucher' like cells [5].

Take home messages

- Gaucher disease is common among population where consanguineous marriage rate is high.
- The clinical presentations and the complications of the disease are variable in different patients.
- A multidisciplinary approach is important for the early diagnosis of the disease, monitoring of the treatment regimen, and anticipation of potential complications to prevent irreversible damage.

References:

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