Case report

Gaucher's Disease: a rare disease with an unusual presentation

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Introduction

Gaucher's disease (GD) is the most common group of lysosomal storage disorders caused by defective activity of an enzyme β-glucosidase leading to accumulation of glucocerebroside in cells of macrophage lineage (1). Accumulation of glucosylceramide in tissues leads to multisystem organ involvement including liver, spleen, bone marrow, lungs and central nervous system.

The disease was first described by Gaucher in 1882, and the storage of glucocerebroside was first recognized by Epstein in 1924 (2). It has an autosomal recessive inheritance. GD includes three clinical subtypes (3). Splenomegaly is present in 95% of cases and it is often massive (1, 2). We report a case of GD presenting at infancy with an enlarged fatty liver. Although there was no obvious splenomegaly in this patient, Gaucher cells were seen during examination of the autopsy sections of the spleen.

Case report

A seven month old baby boy was brought to a tertiary care hospital for investigation of failure to thrive and recurrent infections since the age of 5 months. The baby had a poorly resolving cough and fever for which treatment had been obtained at a primary care unit on several occasions. The birth weight of the baby was 3300 g and normal development had been observed till the age of 5 months. He was the second baby of a consanguineous marriage. The first baby had died at the age of 6 months. Although medical records of the first baby were not available, the parents gave a history of yellowish discoloration of eyes with fullness of the abdomen of the first baby prior to death.

On examination, the baby was pale and febrile without peripheral lymphadenopathy. There was hepatomegaly. The spleen was not enlarged. The baby was drowsy on admission and later developed a convulsion. Examination

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of cerebrospinal fluid did not show any evidence of infection. The haemoglobin concentration and the platelet counts were low. The baby died a few days after admission.

At autopsy, the baby was 6200g in weight, pale and oedematous. A purulent exudate was observed at the nostrils. A normal amount of fluid was present in the body cavities. The heart was enlarged and both lungs were diffusely consolidated with purulent exudates in the airways and the lung parenchyma with abscess formation. The liver was enlarged, firm and yellow in colour. There were no nodules. The spleen was relatively small in size and showed a fine nodularity on cut surface. The other organs were macroscopically normal.

Microscopic examination of the liver showed fatty change with macrovacuoles in the hepatocytes pushing the nucleus to the periphery. Periodic acid Schiff (PAS) stain was negative. There was no evidence of hepatitis, cholestasis, Kuppfer cell proliferation or hyaline globules.

Microscopic examination of the spleen showed vague, pale staining nodules (Fig.1). The nodules comprised cells with eccentric nuclei, abundant bluish, fibrillary cytoplasm resembling wrinkled tissue paper (Fig. 2A). These cells were confirmed as Gaucher cells by a positive PAS reactivity (Fig.2 B).

Both lungs showed evidence of bronchopneumonia with abscess formation. There was no evidence of meningitis or focal lesions in the brain.

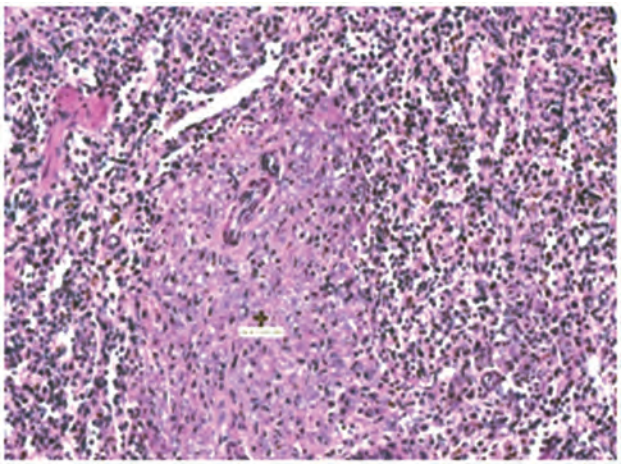

Fig.1. Pale staining nodules (indicated by black cross) in spleen. (H&Ex100)

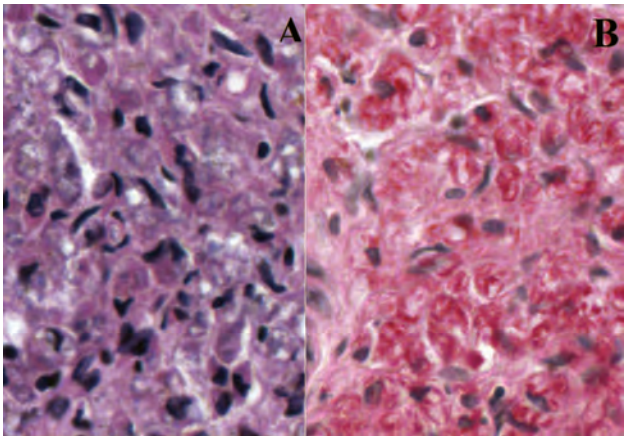

Fig.2. Gaucher cells in spleen.
A) H & E x400. B) PAS stain x400

Discussion

Depending on the presence of central nervous system involvement, GD is classified

into three types. Type 1 is a non neuropathic form presenting in childhood or early adulthood. Type 2 is an acute neuronopathic form presenting in childhood which is rapidly progressive and fatal. Type 3 is a chronic neuronopathic form presenting in childhood but is slowly progressive (1). The current case fits into type 2 as the patient presented in infancy with neurological manifestations and an acute clinical course.

Type 2 GD is the rarest and most severe form, occurring in 1/100,000 to 1/500,000 live births without ethnic predisposition (4). This acute, neuropathic form presents in both perinatal and infantile groups, with symptoms notable by 6 months of age. The clinical course of type 2 GD is inevitable despite the time of presentation and is characterized by rapidly progressive neurologic degeneration and organ failure. The average lifespan of an infant with type 2 GD is 9 months (4).

The most common signs and symptoms noted in GD are splenomegaly (95%), hepatomegaly (87%), radiological bone disease (81 %), thrombocytopenia (50%), anemia (40%), growth retardation (34%), bone pain (27%), and bone crisis (9%) (2,5). Splenomegaly has been the most common presenting sign of GD even though splenomegaly was not present in this baby.

Hepatomegaly is reported in 50-87% (1,2) of the cases with Gaucher disease with the presence of Gaucher cells in the liver. However, Gaucher cells were not evident in this case. Fatty liver has also been reported in GD, accounting for 5.8% cases of cases of fatty liver due to metabolic causes. However, other metabolic diseases like Wilson disease, glycogen storage disorder, galactosaemia and tyrosinaemia are more common causes of fatty liver in childhood than GD (6,7).

Although GD is usually diagnosed by demonstrating Gaucher cells in the bone marrow, definite diagnosis requires absence of serum level of β-glucosidase as pseudo-Gaucher cells are reported in the bone marrow and lymph nodes in acute lymphoblastic leukemia, plasmacytoid lymphoma, CML, type II congenital dyserythropoietic anaemia, thalassemia, Hodgkin lymphoma, multiple myeloma, Waldenström macroglobulinemia, atypical mycobacterial infection and AIDS (2,3,8,9). The literature also shows an association between Gaucher disease and Non-hodgkin lymphoma (3).

As serum β-glucosidase enzyme assay is not available in Sri Lanka, morphological differentiation of Gaucher cells from pseudo-Gaucher cells is important and the diagnosis should be made in an appropriate clinical context. In the presence of cytopenia related symptoms, hepatosplenomegaly and typical Gaucher cells in the bone marrow, the diagnosis of Gaucher disease is not difficult. Pseudo-Gaucher cells are

reported to be smaller than Gaucher cells, stains negative with PAS and lack the characteristic "wrinkled tissue paper appearance" that is seen in Gaucher cells (9).

In conclusion, a high degree of suspicion is required for GD especially in infants as the typical clinical presentation of splenomegaly may not be present. Although GD is mostly diagnosed by hematologists by identifying Gaucher cells in the bone marrow, histopathologists should also be aware of the morphology as the disease can occur in solid organs.

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