Fibrous splenomegaly and Gaucher disease

Abstract

Gaucher disease is an autosomal recessive genetic disorder caused by a deficiency of a lysosomal enzyme, β-glucocerebrosidase, which is responsible for the accumulation of glucosylceramide in the lysosomes of macrophages in the liver, spleen and bone marrow. Clinical expression is highly variable from cytopenia, osteoarticular to neurological manifestations, resulting in delayed diagnosis. Diagnosis can be made by measuring the activity of β-glucocerebrosidase, the myelogram or osteomedullary biopsy, and treatment is essentially medical, based on enzyme replacement therapy.

Splenectomy is considered in situations where haematological complications are in the foreground, such as hypersplenism, haemorrhagic syndrome, or a symptomatic large splenomegaly.

We report the case of a 45-year-old patient with arthralgia and a large spleen whose myelogram and osteo-medullary biopsy was in favour of Gaucher disease. In the face of hypersplenism and symptomatic enlarged spleen, a total splenectomy was performed.

Introduction

Gaucher disease is a rare autosomal recessive disease. This condition is secondary to a deficiency in the activity of the lysosomal enzyme glucocerebrosidase, which is responsible for the degradation of glucosylceramide resulting from the breakdown of red and white blood cell membranes (1). Glucosylceramide accumulates in monocyte and macrophage cells, this accumulation leads to hepatomegaly, splenomegaly and bone manifestations (2). Hypersplenism and symptomatic nodular splenomegaly indicate the need for splenectomy although the treatment is mainly medical.

We report the case of a patient with this condition whose splenectomy was indicated in the context of a symptomatic spleen with hypersplenism.

Keywords Gaucher disease, splenomegaly, hypersplenism

Case Presentation

A 45-year-old patient, without any particular pathological history, was consulting for minimal epistaxis, with chronic arthralgia and generalized abdominal pain of variable intensity for 1 year, without neurological signs without transit disorders, in a context of apyrexia and preservation of general condition, The clinical examination found a conscious patient hemodynamically stable, slightly discoloured conjunctivae, abdominal palpation revealed a voluminous splenomegaly with a lower pole of the spleen palpated in the left iliac fossa, no hepatomegaly, nor collateral circulations, the ganglionic areas were free. Neurological examination was without impairment. The osteoarticular examination was unremarkable.

Abdominal ultrasound and abdominal CT scan showed a large nodular splenomegaly, the liver is normal in appearance, with a lithiasis gallbladder.

Blood counts found a decreased hemoglobin at 11.4 g/dl, white blood cells increased to 18200 ele/mm3, and thrombocytopenia with platelets at 9000 /mm3. A myelogram detected a polymorphic rich marrow, with the presence of Gaucher cells. Osteomedular biopsy showed histiocyte sheets with pale eosinophilic cytoplasm, the nuclei were hyper chromatic angular. This morphological aspect was suggestive of an overload disease, particularly Gaucher disease. Enzyme assay was not performed. In view of the large size of the spleen and the hypersplenism the patient was operated on by median laparotomy and splenectomy was performed as well as cholecystectomy (Figs. 1 and 2).

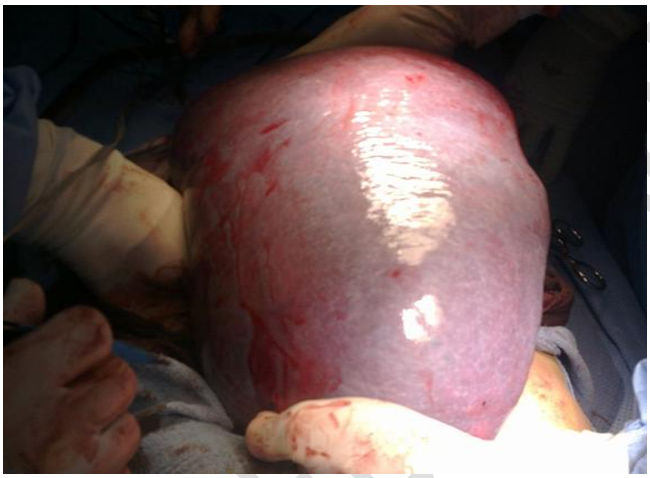

Fig. 1: Intraoperative image of the voluminous spleen.

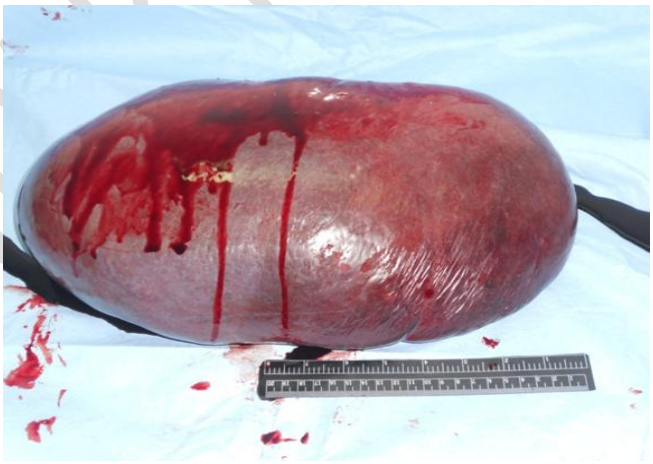

Fig.2. image of the total splenectomy

The postoperative follow-up was simple and his platelets increased to 287,000 /mm3 in 7 postoperative days. An anatomopathological study of the operating piece confirmed that the spleen measured 38 cm from the major axis and weighed 5 kg with a morphological aspect of

Gaucher disease with splenic localization. Our patient was given a modified form of the enzyme, glucocerbrosidase, by intravenous injection every two weeks.

Discussion

Gaucher disease is a sphingolipidosis resulting from a deficiency of glucocerebrosidase, leading to the deposition of glucocerebroside**.** Despite its rarity, it is the most common lysosomal storage disease (2) . it is an autosomal recessive genetic disease due to an enzyme deficiency in glucocerebrosidase (5).

Its pathophysiology is explained by mutations in the GBA1 gene responsible for an accumulation of its substrate, glucosylceramide, in the lysosomes of macrophages, leading to their transformation in Gaucher cells (6,8). These cells infiltrate the liver, spleen, bone marrow, but also other organs resulting in organomegaly, bone fragility and even osteonecrosis (7). The clinical presentation is very heterogeneous, ranging from the asymptomatic to the lethal form. There are 3 types, which vary in terms of epidemiology, enzymatic activity and manifestations. Type 1 Gaucher disease is the most common in 95% of cases, and can occur from the age of 2 years to adulthood (3). Splenomegaly is one of the main clinical signs in more than 90% of cases, and may be responsible for hypersplenism leading to thrombocytopenia, which is manifested by epistaxis, easy bleeding and hematomas and, more rarely, severe bleeding (9). Hepatomegaly is present in 60 to 80% of cases and vesicular lithiasis is found in 32% (10). Chronic arthralgia is reported in 80% of cases, especially in the spine and lower limbs (9). Our patient was considered a type I carrier of the disease due to its symptomatology.

Type 2 Gaucher disease is often discovered in infants between 3 and 6 months of age and, in addition to hepato-splenomegaly, associates signs of acute neuropathy and the progression is fatal before the third year of life (12). Type 3 is of very heterogeneous clinical expression, the onset occurs at any time during childhood, in addition to type 1, there are also subacute neurological signs (11).

The diagnosis of Gaucher disease is based on DNA and/or enzyme analysis of white blood cells. Carriers are detected and types are distinguished by molecular biology. Although biopsy is unnecessary, Gaucher cells (lipid-laden tissue macrophages found in the liver, spleen, lymph nodes, bone marrow or brain), which have a crumpled paper-like appearance, are pathognomonic (8,9).

Thrombocytopenia is common in 90% of cases, anaemia is present in 56% of cases, leukopenia is rare, plasma protein electrophoresis and immunofixation show polyclonal hypergammaglobulinemia in 25 to 91% of cases (3,9).

Imaging is important to study the morphology of organs that may be affected such as the spleen, liver, and long bones, but the use of abdominal CT scanning is limited because of the repeated irradiations for these patients under long-term follow-up (13). The risk of Parkinson's disease, the incidence of hepatocellular carcinoma, melanoma, pancreatic cancer, and multiple myeloma appears to be increased in patients with Gaucher disease (3,11).

There are currently 2 specific treatments, enzyme replacement therapy (ERT), which is the reference treatment, and substrate reduction therapy (SRT). Symptomatic (analgesics...), orthopaedic, and rehabilitative measures necessary for patients must be undertaken(13)). Splenectomy can be useful in cases of anaemia, leukopenia or thrombocytopenia or when the size of the spleen is troublesome (9), such as in the case of large splenomegaly to note patient.

Conclusion

The rarity of Gaucher disease and the variability of its clinical picture explain its late diagnosis. It is important to include this disease in the diagnostic decision tree in cases of splenomegaly and/or thrombocytopenia and to treat patients before the onset of complications with disabling sequelae.

ETHICAL APPROVAL

As per international standard written ethical approval has been collected and preserved by the author(s).

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