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Splenomegaly and Gaucher Disease

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Authors' contributions

All authors contributed to the conduct of this work. They also declare that they have read and approved the final version of the manuscript.

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Case Report

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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-oldmalewith 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. The histological study showed the accumulation of substances called glucocerebrosides inside the lysosomes of cells in the macrophagic system.

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1. 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 bloodcell 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.

2. CASE PRESENTATION

A 45-year old male, without any particularpathological 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, no rcollateral 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 adecreased hemoglobin at11, 4 g/dl, white bloodcells increased to 18,2× 10^9/L and thrombocytopenia with platelets at 9 ×10^9/L, the patient was transfused with three units of platelets before the surgical act.The value of C-reactive protein (CRP) was at 12mg/l. Amyelogram detected a polymorphic rich marrow, with the presence of Gauchercells. 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).

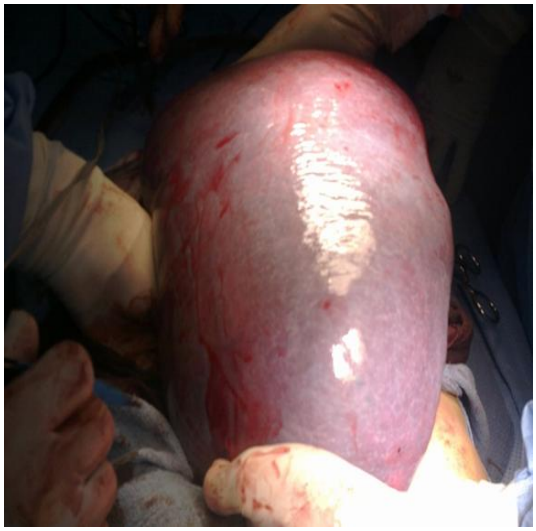

Fig. 1. Intraoperative image of the voluminous spleen

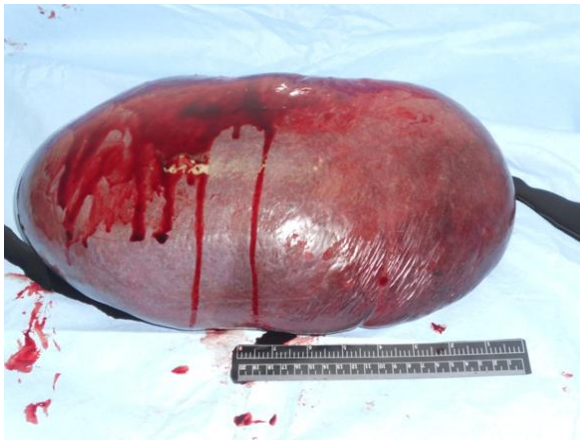

Fig. 2. Image of the total splenectomy

The postoperative follow-up was simple and his platelets increased to 287×10^9/L in 7 postoperative days, the bloodcells decreased to 8, 2 ×10^9/L after antibiotictherapy based on Peni V.

The anatomopathological study of the operating piece confirmed that the spleen measured 38 cm from the major axis and weighed 5 kg with atypical Gaucher large macrophages expressing granula rand fibrillar distented cytoplasm of "wrinkled tissue paper" appearance and eccentric nucleiin splenic localization. Our patient was given a modified form of the enzyme, glucocerbrosidase, by intravenous injection every two weeks. One year's hindsight, our patient had no signs of hemorrhage and improvement in his arthralgia.

3. DISCUSSION

Gaucher diseaseis a sphingolipidosis resulting from a deficiency of glucocerebrosidase, leading to the deposition of glucocerebroside. Despiteits rarity, itis the most common lysosomal storage disease [2]. It is an autosomal recessive genetic disease due to an enzyme deficiency in glucocerebrosidase [3.4].

Its pathophysiologyis explained by mutations in the GBA1 generesponsible for an accumulation of its substrate, glucosylceramide, in the lysosomes of macrophages, leading to their transformation in Gaucher cells [5.6]. These cells infiltrate the liver, spleen, bone marrow, but also the 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 commonin 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 maybe responsible for hypersplenism leading to thrombocytopenia, which is manifested by epistaxis, easy bleeding and hematomas and, more rarely, severe bleeding [9]. Hepatomegaly is presentin 60 to 80% of cases and vesicular lithiasis is found in 32% [10]. Chronic arthralgiais 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 [11]. Type 3 is of very heterogeneousclinical expression, the onset occurs at any time during childhood, in addition to type 1, there are also subacute neurological signs [12].

The diagnosis of Gaucher disease is based on DNA and/or enzyme analysis of white bloodcells. 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, lymphnodes, bone marrowor brain), which have a crumpled paper-like appearance, are pathognomonic [6,9].

Thrombocytopenia is commonin 90% of cases, anaemia is presentin 56% of cases, leukopeniais

rare, plasma protein electrophoresis and immunofixation show polyclonal hypergammaglobulinemia in 25 to 91% of cases [8,9].

Imaging is important to study the morphology of organs that maybe affected such as the spleen, liver, and long bones, but the use of abdominal CT scanning is limited because of therepeated 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 [8,12].

There are currently 2 specific treatments, enzyme replacement therapy (ERT),which is the reference treatment, and substratereductiontherapy (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.

4. 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.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

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

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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