European Journal of Case Reports in Internal Medicine

Gaucher Disease: One of the Few Causes of Massive Splenomegaly

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Doi: 10.12890/2022_003705 - European Journal of Case Reports in Internal Medicine - © EFIM 2022

Received: 01/12/2022
Accepted: 13/12/2022
Published: 19/12/2022

How to cite this article: Garça M, Correia S, Goulart A, Ávila P. Gaucher disease: one of the few causes of massive splenomegaly. *EJCRIM* 2022;**9**: doi:10.12890/2022_003705.

Conflicts of Interests: The authors declare there are no competing interests.
Patient Consent: The patient consented to the use of her images for scientific or educational purposes.

ABSTRACT

Gaucher disease (GD) is a rare, autosomal recessive genetic disease caused by deficiency of a lysosomal enzyme (glucocerebrosidase/-glucosidase) that leads to the accumulation of its substrate in lysosomal macrophages. GD remains rare and delayed diagnosis is common due its gradual onset. It is important to include this differential diagnosis in cases of massive splenomegaly and/or thrombocytopenia, in order to avoid potentially harmful splenectomy.

This case report describes a 25-year-old female patient with a 10-year medical history of anaemia and thrombocytopenia, who presented with symptoms of haemorrhagic dyscrasia, pancytopenia and massive splenomegaly. The differential diagnosis of massive splenomegaly included several conditions which were considered but ruled out. Because of a lack of resources, the patient was forwarded to a reference centre where the diagnosis of GD was made.

LEARNING POINTS

- Many diseases are associated with splenomegaly but massive splenomegaly is seen in only a few conditions.
- While some causes of splenomegaly are obvious (malaria, infection), the aetiological diagnosis of splenomegaly may involve extensive history taking, serum testing and imaging studies.
- Infiltrative disorders such as Gaucher disease are a rare cause of splenomegaly and should be considered when other more common causes have been ruled out.
- The authors hope to raise awareness of this diagnosis in order to encourage early treatment.

KEYWORDS

Gaucher disease, massive splenomegaly, pancytopenia

INTRODUCTION

Gaucher disease (GD) is a rare, autosomal recessive genetic disease caused by mutations in the GBA1 gene, which is located on chromosome 1 (1q21). It belongs to a group of heterogenous inherited lysosomal storage diseases which affect genes that encode the function of either the lysosomal enzymes required for the degradation of a wide range of complex macromolecules, or of specific transporters needed to export degraded molecules from the lysosomes [1].

The incidence of GD is around 1/40,000 to 1/60,000 births in the general population, but can reach 1/800 births in the Ashkenazi Jewish population [1]. The clinical presentation is variable, ranging from asymptomatic disease throughout life to early onset in childhood. The median age of diagnosis is 10–20 years of age [1, 2].

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In this paper, we report a case of GD in an adult woman who had been undiagnosed since the onset of symptoms more than 10 years previously. The diagnosis was by bone marrow biopsy, and subsequently confirmed biochemically with an enzymatic assay.

CASE DESCRIPTION

A female 25-year-old patient with a 10-year plus history of bicytopenia (anaemia and thrombocytopenia), presented with asthenia and haemorrhagic dyscrasia. She denied recent travel and other comorbidities other than slight bicytopenia, but mentioned that she had abandoned medical follow-up. She denied any complementary imaging studies. The patient's son is being studied because of his short stature.
Physical examination revealed skin pallor, gingival bleeding, multiple ecchymoses scattered on the upper and lower limbs at different stages of evolution, and a massively enlarged spleen occupying the left quadrants of the abdomen up to the iliac crest. No lymphadenopathy or signs of liver disease were observed.
The patient was admitted to hospital for a thorough evaluation.
A complete blood count (CBC) showed pancytopenia: haemoglobin was 8.4 g/dl, white blood cells (WBC) 3.53×10^9/l, platelets 18×10^9/l and reticulocytes 2.7% (0.5–2.5). No elevation of liver enzymes or coagulopathy was present.
The peripheral blood smear showed hypochromia and rare polychromatophilia. Peripheral blood flow cytometry revealed a T lymphocyte population of 24.90% and a B lymphocyte population of 4.18%, where monoclonality was excluded. JAK2 mutation analysis was negative.
The erythrocyte sedimentation rate was high, but acute and chronic infections including viral, bacterial, fungal, mycobacterial and parasitic diseases were ruled out. A complete autoimmunity study reported no changes.
No vitamin deficits or changes in iron kinetics were observed.
Abdominal ultrasound showed an enlarged liver with a homogeneous structure, measuring about 19.3 cm, and splenomegaly (26 cm in diameter) with a more heterogeneous texture and dispersed nodules, the largest being 5.4 cm in diameter.
Thoracic-abdominal-pelvic computed tomography revealed a liver with increased dimensions and a spleen (*Fig. 1*) with grossly enlarged dimensions with a heterogeneous texture due to the presence of several hypodense nodular lesions (*Fig. 2*).

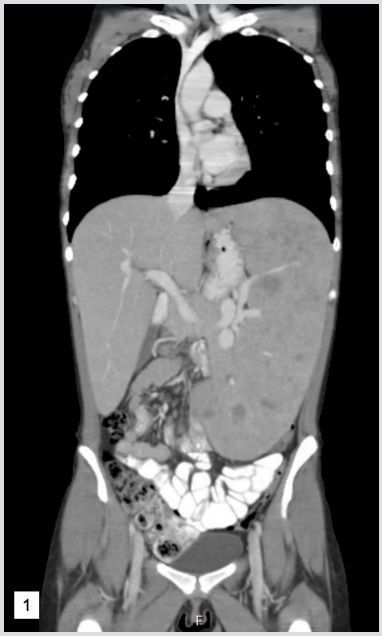

Figure 1. Thoracic-abdominal-pelvic computed tomography (coronal view), showing massive splenomegaly

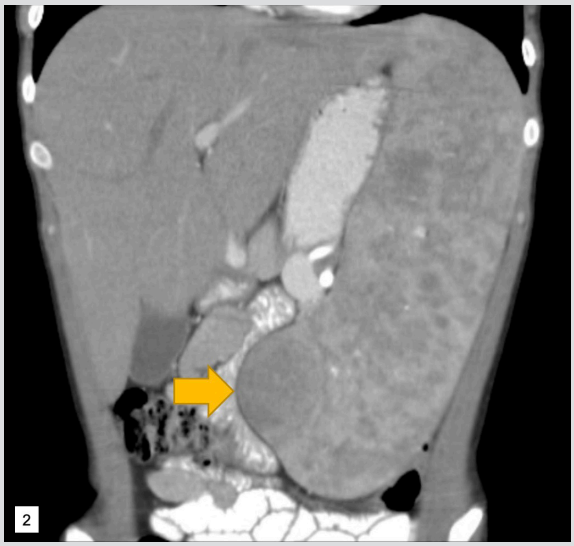

Figure 2. Abdominal-pelvic computed tomography (coronal view). The spleen has a heterogeneous texture due to the presence of multiple hypodense intraparenchymal nodular lesions of variable dimensions, the largest measuring 33 mm in diameter, suggestive of Gaucheroma (arrow)

The most common aetiologies of massive splenomegaly include infectious diseases, autoimmune diseases, vascular congestion, haematological disorders and infiltrative conditions, most of which had been excluded.

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Bone marrow aspiration and bone marrow biopsy were performed but were unsuccessful with no evaluable cellularity. Due to the inconclusive results, the failure to exclude haematological disease and the high suspicion of infiltrative diseases which required differentiated evaluation or, ultimately splenectomy, the patient was sent to a referral centre.

A new bone marrow biopsy was performed, with difficulty due to fibrotic bone. The results suggested lysosomal storage disease, that is, GD. The enzyme assay showed a deficit of β-glucosidase activity and a significant increase in the enzymatic activity of β-D-chitotriosidase. The results were compatible with a diagnosis of GD. Genetic testing is underway.

Currently, the patient is undergoing follow-up with specialised consultation and awaiting therapeutic guidance.

DISCUSSION

Massive splenomegaly is usually defined when the spleen reaches the iliac crest, crosses the midline or weights more than 1500 g [3].

A wide variety of conditions are associated with splenomegaly, but massive splenomegaly is seen in only a few diseases. Conditions to consider in the differential diagnosis of massive splenomegaly include infectious disease (malaria, leishmaniases), haematological disorders (leukaemia, lymphomas) and infiltrative conditions (GD) [3].

In a young adult presenting with visceromegaly, bone pain, bleeding and fatigue, storage disorders must be part of the differential diagnosis[2].

Three major phenotypic presentations of GD have been identified: type 1 is the most common and generally presents without neurological damage, while types 2 and 3 are characterised by neurological impairment. Type 1 is the adult type and typically presents with splenomegaly (95% of reported cases). Indeed, splenomegaly may be the only clinical sign, leading to unnecessary tests if GD is not considered. In children, growth retardation and delayed puberty are common.

Bone marrow aspiration is not mandatory to confirm a diagnosis of GD.

Treatment modalities include enzyme replacement treatment (ERT), substrate reduction therapy, bone marrow transplantation and splenectomy if needed [2].

There were a few clinical findings in our case that could have pointed to the diagnosis, such as the growth retardation of the patient's son. Diagnosis is frequently delayed since it requires resources and procedures such as enzyme activity assays, molecular diagnosis, and pathological biopsy performed in reference centres.

With this case report, the authors have highlighted the need to consider lysosomal storage disease as a differential diagnosis in cases of massive splenomegaly for early diagnosis and prompt treatment to promote a better prognosis.

REFERENCES

1. Nguyen Y, Stirnemann J, Belmatoug N. Gaucher disease: a review. *Rev Med Interne* 2019;**40**(5):313–322. Available from: https://pubmed.ncbi.nlm.nih.gov/30638965/
2. Kannauje PK, Pandit V, Wasnik PN, Gupta AK, Venkatesan N. Gaucher's disease in an adult female: a rare entity. *Cureus* 2021;**13**(8):e17318. Available from: https://pubmed.ncbi.nlm.nih.gov/34557364/
3. Chapman J, Goyal A, Azevedo AM. Splenomegaly. Treasure Island, FL: StatPearls; 2022. Available from: https://pubmed.ncbi.nlm.nih.gov/28613657/