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Case Report

Challenges in the Diagnosis and Management of Gaucher's Disease in a Young Adult Libyan Arab Female

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Abstract

Gaucher's disease is a rare lysosomal storage disease that can present with a wide range of clinical symptoms according to type and severity, ranging from mild general wellbeing, organomegaly, pancytopenia, neurological symptoms, lung involvement, and even death, making the diagnosis and work up challenging to reach a diagnosis. We report a Libyan Arab female presented with bruises after minor trauma, bone aches, and fatigue. A 35-year-old female from Libyan–Arab ethnicity attended the hematology clinic complaining of bruises after minor trauma, bone aches, and undue fatigability. She mentioned and evident from her medical record that she has been suffering from these complaints for 5 years and does not have any definite diagnosis. Mild splenomegaly was the only finding on clinical examination this time. There was no fever and no lymphadenopathy. Thrombocytopenia with a platelet count 90 × 10 and quot; 3/ml, and splenomegaly of 16 cm was found on investigations. She was diagnosed with cryptogenic thrombocytopenia, and she was advised for a follow-up visit. Our patient attended a follow-up visit twice in the next 18 months with similar complaints of manageable bruising, bone pain, and fatigability. Hematology reports showed thrombocytopenia in each visit. An ultrasonogram of the abdomen revealed a gallbladder stone and spleen have a size of 17 cm. Bone marrow biopsy was done, and a blood test confirmed glucocerebrosidase enzyme deficiency. Considering the diagnosis of Gaucher's disease, treatment with imiglucerase infusion was started. Unfortunately, she failed to continue the treatment due to a shortage of supply of the medication. A few months later, she got pregnant and developed threatened abortion, which ended with a miscarriage. This case illustrates the need to consider this disease in the differential diagnoses when dealing with unexplained thrombocytopenia, anemia, hepatomegaly, and splenomegaly. There are several challenges in the diagnosis and treatment of Gaucher's disease, particularly in resource-limited settings.

Keywords: Delayed diagnosis, Gaucher's disease, Libya, treatment challenges

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Introduction

Gaucher's disease is a lysosomal storage disorder. A defect glucosylceramidase beta (GBA) gene located on chromosome 1q22 results in a decreased level of glucocerebrosidase enzyme, which is present on the first chromosome (1q22). Gaucher's disease is characterized by hepatosplenomegaly associated with anemia, thrombocytopenia, coagulation abnormalities, and bone and lung disease. There are three types of the disease. Central nervous system is involved in type 2 Gaucher's disease and is the most severe form.[1-3]

Nevertheless, many patients with Gaucher's disease have few symptoms and do not need any treatment, and they can expect a normal lifespan.[1-3] The estimated life expectancy at birth for people with type 1 Gaucher's disease is 68 years, as mentioned in one study where the general population was expected to live up to 77 years. Patients with type 2 Gaucher's disease usually die within the first few years of life.

Philippe Charles Ernest Gaucher (July 26, 1854– January 25, 1918) was a French dermatologist born in the department of Nièvre, France [Figure 1a]. He described the disease in 1882 in a 32-year-old woman with enlarged liver and spleen in his thesis [Figure 1b].[4].

Case Report

A 35-year-old female patient from Libyan–Arab ethnicity attended the hematology clinic complaining of bruises after minor trauma, bone aches, and undue fatigability. She mentioned and evident from her medical record that she has been suffering from these complaints for 5 years and does not have any definite diagnosis. Mild splenomegaly was the only finding on clinical examination this time. There was no fever, no lymphadenopathy. Thrombocytopenia with a platelet count of 90 × 103/ml and splenomegaly of 16 cm was found on investigations. The diagnosis of cryptogenic thrombocytopenia was made, and she was advised to return for a follow-up visit to monitor the condition. Our patient attended a follow-up visit twice in the next 18 months with similar complaints of easy bruising, bone pain, and fatigue. Hematology reports showed thrombocytopenia

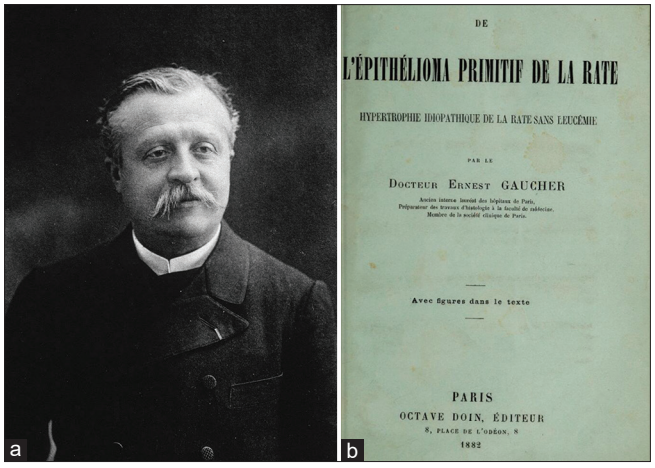

Figure 1: Gaucher and his disease. The portrait of Ernest Gaucher (a) and the cover page of his thesis on the condition (b). Both images are available in the public domain in several sources

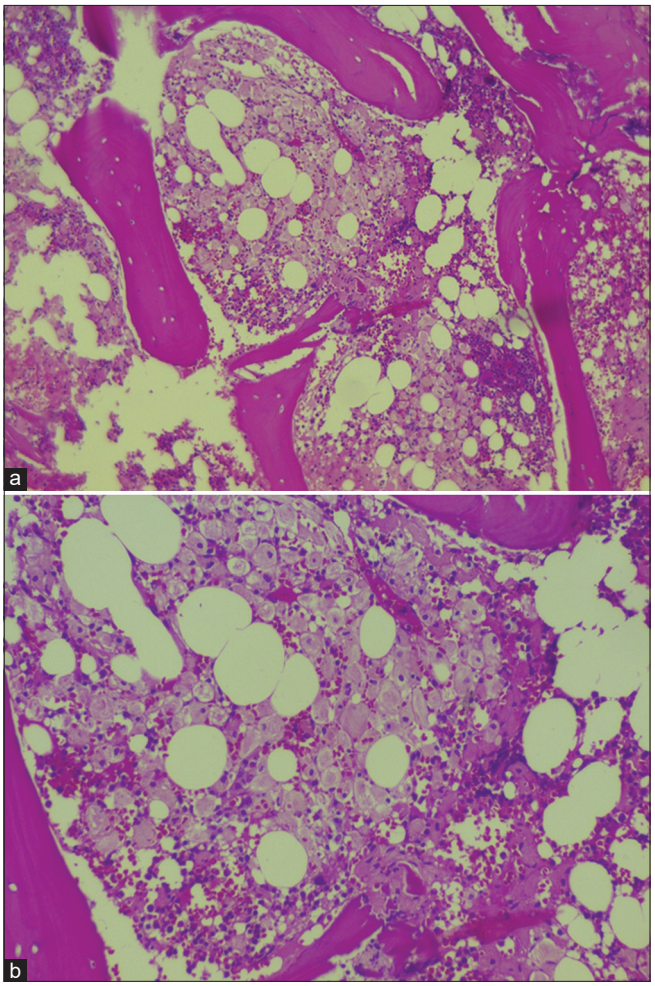

Figure 2: Bone marrow tissue using hematoxylin and eosin stain. The upper panel (a) demonstrates diffuse replacement by ovoid histiocytes with abundant, finely fibrillar, pale blue gray cytoplasm that is crinkled or wrinkled paper-like and the lower (×100) and panel (b) demonstrates Gaucher cells are typically enlarged, with eccentric nuclei, condensed chromatin and cytoplasm with a heterogeneous "crumpled tissue paper" appearance (×100) cropped and enlarged

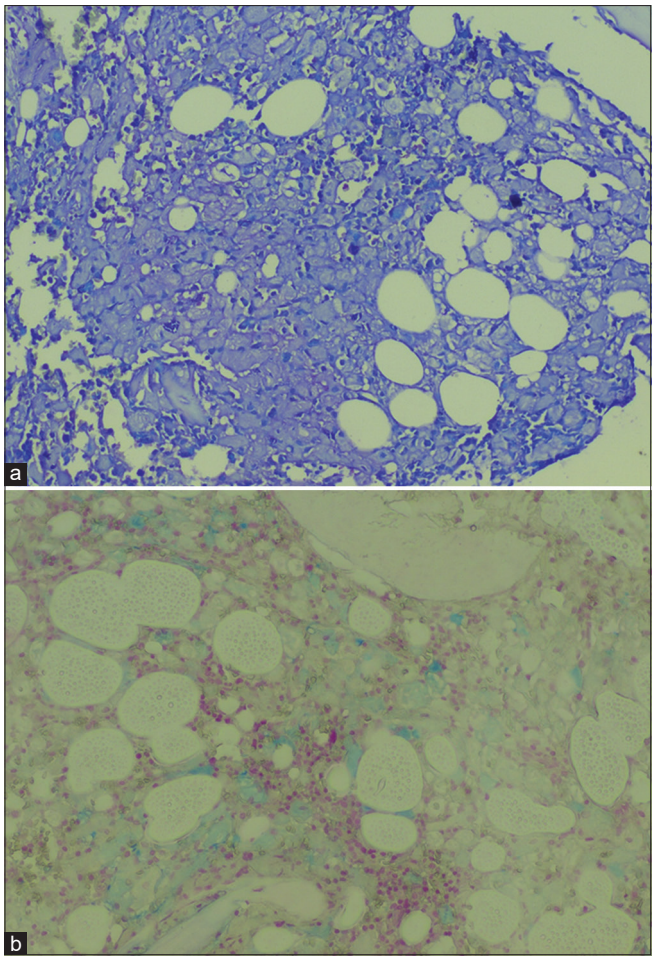

Figure 3: Bone marrow tissue using special stains. (a) (×200 Wright Giemsa stain) in high magnification (×200) shows bland histiocytes with voluminous cytoplasm with a lightly eosinophilic, crumpled tissue paper appearance and (b) is using Iron stain. Pearl's stain (×200)

in each visit. An ultrasonogram of the abdomen revealed a gallbladder stone and spleen have a size of 17 cm. Ct scan abdomen and pelvis showed mild hepatosplenomegaly and a small right ovarian cyst.

Bone marrow biopsy was done [Figure 2 and 3], and Glucocerebrocidase enzyme deficiency by blood test was confirmed. A genetic study was not done for this patient because glucocerebrosidase enzyme deficiency was significantly low in her blood, supported by the bone marrow biopsy results. A beta-glucosidase leukocyte test will almost certainly show whether the patient has Gaucher's disease or not, as all patients with Gaucher's disease have low enzyme activity in their blood. Genetic testing is required to assess carriers who may occasionally have borderline low enzyme levels; hence, further genetic analysis is required to clarify whether they have Gaucher's disease.[5]

Therefore, bone marrow biopsy and the confirmed glucocerebrosidase enzyme deficiency were performed, and the results were in keeping with Gaucher's disease [Figures 2 and 3]. Considering the diagnosis of Gaucher's disease, treatment with imiglucerase injection was started. Unfortunately, she failed to continue the treatment due to a shortage of supply of the medication. A few months later, she got pregnant and developed threatened abortion, which ended with a miscarriage.

Discussion

Gaucher disease is a rare autosomal recessive disorder. The disease is also known as Cerebroside lipidosis syndrome.[1-3,6] The incidence reported is approximately 1:40,000 individuals. The condition is much more common among Ashkenazi Jews and also in the Afrikaner population. Gaucher's disease results from a deficiency of the glucocerebrosidase enzyme resulting from a GBA gene mutation.[2] Beta-glucocerebrosidase breaks down glucocerebroside into glucose, and deficiency of this enzyme causes accumulation of glucocerebroside within cells and resulting damage of cells and tissues. Gaucher disease is a multi-system disorder. The signs and symptoms of Gaucher disease vary widely among affected individuals. At least three types of Gaucher disease have been described in literature based on their characteristic features.[3,6]. Type 1 Gaucher disease is the most common type, and affected patients present with enlargement of the liver and spleen, anemia, thrombocytopenia, bone pain, and fractures. Central nervous system features predominate in type 2 and 3 Gaucher's disease. Differential diagnoses of Gaucher's disease include other lysosomal storage disorders and conditions where Gaucher-like cells can be found, such as chronic lymphocytic leukemia and lymphoma.[3,6-8]

The diagnosis is commonly made by the measurement of glucocerebrosidase levels in circulating leukocytes. A serum glucocerebrosidase level <15% of the mean regular activity confirms the diagnosis of Gaucher's disease. However, to confirm the diagnosis genotyping is usually required.[3,6-8]

Enzyme substitution therapy (using imiglucerase or velaglucerase) and substrate reduction

therapy (miglustat) are effective treatment options for type 1 and type 3 Gaucher's disease [allogeneic]. Bone marrow transplantation is also recommended for type 3 individuals. Type 2 Gaucher's disease patients can have only supportive therapy.

Gaucher's disease type 1 is more common in the western population and some Jewish populations. Type 2 and 3 Gaucher's disease is prevalent in non-Jewish Middle Eastern populations, India and China.[9] There are case reports reported from Maghreb countries, mainly from Tunisia, Morocco, and Algeria.[10,11] Several cases from South Africa are also published.[12] Our patient was from an ethnic background where Gaucher's disease is uncommon, which delays diagnosis. Differential diagnosis of Gaucher's disease must be kept while dealing with a combination of anemia, thrombocytopenia, with hepatosplenomegaly.[6-8]

Conclusions

Gaucher's disease can be treatable. However, its diagnosis and treatment can be challenging, particularly in resource-limited settings. Although the diagnosis was delayed in our case, further challenges were to confirm glucocerebrosidase enzyme deficiency, as we had to send the blood samples abroad. Unfortunately, we could not do the genetic testing as it had to be done abroad, and the patient could not afford to do both. Furthermore, providing expensive treatment imiglucerase was another challenge as it was not consistently available. This is an expected problem in low- and middle-income countries and civil and armed conflict zones.

Declaration of patients' consent

The authors certify that they had obtained the appropriate patient consent. The patient has given consent for images and other clinical information to be reported in the journal. The patient understands that no names and initials will be published, and all due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authors' contribution

All named authors were involved in the patient's clinical care, conception, drafting, and approval of the article.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

No prior ethics is required in our institution for single case reports, or short case reports provided the patient provided consent on an anonymous basis as stated above.

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