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Value of the Myelogram in the Diagnosis of Gaucher Disease: Two Cases Report

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Abstract **Case Series**

Among the most common constitutional overload enzymopathies, Gaucher disease is a rare constitutional overload disease and often caused by lysosomal enzyme deficiencies in pediatric population more than adults. The cause of Gaucher disease is a deficiency of glucocerebrosidase resulting in an accumulation of glucocerebroside) in macrophages. These abundant macrophages are present in the lymphoid tissues (spleen, liver, marrow, lymph node), some of which have a characteristic morphological appearance (Gaucher cell) allowing the diagnosis to be suggested during myelogram. Reporting two cases of adult patients in whom the demonstration of overload cells in the myelogram allowed us to direct towards the diagnosis of Gaucher disease.

Keywords: Gaucher cell, enzymopathie, myelogram, cytology. Gaucher.

INTRODUCTION

Among the most common constitutional overload enzymopathies, Gaucher disease is a pathology first described by Philippe Charles Ernest Gaucher in 1882.

Constitutional overload diseases are rare and often caused by lysosomal enzyme deficiencies. Depending on the deficient enzyme there will be accumulation of certain types of sphingolipids which define the type of pathology (Gaucher disease, Niemann-Pick disease, Fabry disease, etc.), mucopolysaccharides (Hurler disease, Hunter disease, etc.) or both (mucolipidoses, gangliosidoses, etc.) [1].

The cause of Gaucher disease is a deficiency of glucocerebrosidase (b-glucosidase) resulting in an accumulation of glucocerebroside (glucoceramide) in macrophages. These abundant macrophages are present in the lymphoid tissues (spleen, liver, marrow, lymph node), some of which have a characteristic morphological appearance (Gaucher cell) allowing the diagnosis to be suggested [2, 3]. The first step for the diagnostic orientation of these diseases is the recognition of the cytological abnormalities. The myelogram remains an examination often prescribed in the context of an ethological assessment.

CASES REPORT

First Case

Mrs. Z.B, 31 years old, from the north of Morocco, treated in 2012 for non-Langerhansian Erdheim Chester type multi-systemic histiocytosis with osseous, hepatosplenic localization. Characterized by moderate thoracolumbar bone pain associated with an anemic syndrome, a CT scan showing lytic vertebral lesions with layered compressions, hepato-splenomegaly and an osteomedullary biopsy showing massive histiocytic CD68+ and anti-PS100 negative spinal cord infiltration.

The initial assessment after developing the diagnosis did not find any other location (pulmonary, cutaneous, neuro-pituitary, etc.). Patient was treated with corticosteroid therapy + alpha interferon at a dose of 9M per week divided into 3 injections every other day initially in hospital. Faced with the improvement in bone pain, the patient stopped her treatment after 3 months with a complete break in follow-up.

In July 2023, the patient was admitted to the internal medicine department of the Mohammed VI-Tangier university hospital center, for extensive purpura, predominantly sloping, with enormous splenomegaly which exceeds the umbilicus evolving in a context of apyrexia, night sweats and weight loss. The cardiovascular risk factors are none, with a Framingham score: <5%, no active or passive smoking. A history at age 10 of pulmonary tuberculosis treated for 06 months.

A myelogram is carried out to look for Gaucher cells with a karyotype study. The hemogram received with the myelogram reveals pancytopenia with leuko-neutropenia at 1.47 G/L in neutrophils, microcytic hypochromic anemia with hemoglobin at 8 g/dl and thrombocytopenia at 91 G/L. The complete blood count was checked on a blood smear taken manually with panoptic May Grunwald giemsa (MGG) staining, where cytopenia was confirmed and the absence of platelet aggregates was noted.

The spinal cord puncture of the left crest was received already spread on several slides in the laboratory and is colored in the same way as the blood smear. Observation at low magnification Gx10 shows a very rich marrow having numerous megakaryocytes with rare dystrophic elements, we also observe some large cells with a histio-macrophagic appearance with a barely visible blue-gray coloring. Observation at Gx100 magnification shows a granular neutrophil lineage at a very reduced percentage of 25% made up of Myelocytes: 05%, Metamyelocytes: 08% and neutrophils 12%. We note the presence of numerous erythrocyte islands with medullary erythroblastosis at 64%, we also note the presence of 05% of blasts, with a few histiocytes with pale blue gray cytoplasm streaked with numerous colorless fibrillar inclusions with a "peel-like" appearance. onion" evoking Gaucher cells, with rare images of cytophagy. The nucleus is most often single and repressed to the periphery, sometimes central. This diagnosis is confirmed by the enzymatic assay showing glucocerebrosidase deficiency. The genetic study is underway.

The evolution was marked by the patient's improvement after hospitalization and her discharge on the fourth day.

Second Case

Mrs. E.N 50-year-old patient, with a history of undocumented anemia treated with iron, presents an abdominal mass that has been evolving for 20 years with a recent increase in volume for 2 years with notion of a similar case in the sister, admitted for general deterioration in the internal medicine department. The clinical examination reveals enormous splenomegaly reaching the pelvis, and punctiform purpura of both legs. The biological assessment reveals pancytopenia with a profound leukopenia at 0.87 G/L associated with normochromic normocytic anemia with a hemoglobin at 8.8 g/dl and a major thrombocytopenia at 27 G/L. The hemolysis assessment is positive, the ultrasound shows spleno-hepatomegaly with absence of lymphadenopathy of significant size with a doubt about a thrombosis of a small portal bronchus associated with a perfusion disorder and hepatic lesions of wise VIII, the result concluded an appearance suggestive of Gaucher disease.

The spinal puncture at the level of the left crest was received spread over several slides, and was stained in the laboratory by MGG. Observation at magnification Gx10 shows a very rich marrow having numerous megakaryocytes with rare dystrophic elements. We note the presence of numerous activated macrophages with histiocytomacrophage cells which rarely phagocytize the marrow cells. The neutrophilic granular lineage is at 29% with discreet signs of dysgranulopoiesis; there is hyperplasia of the erythroblastic lineage at 65% which shows signs of dyserythropoiesis. Presence of 03% of lymphocytes, 03% of eosinophils. Presence of very rare histiocytes suggestive of overload histiocytes such as probable Gaucher cells. An enzymatic assay was carried out with the aim of confirming the diagnosis of Gaucher disease which is in progress.

One month later, given the persistence of symptoms, protein electrophoresis revealed a suspicious aspect of hypogammaglobulinemia, with the presence of kappa and lambda light chains, raising suspicion of a monoclonal gammopathy. Despite the low percentage of plasma cells 05% at the marrow level, the two diagnoses (Gaucher disease and gammopathy) were retained.

DISCUSSION

Classically there are three types of Gaucher disease, the recognition of which depends mainly on the presence or absence of neurological damage associated with the visceral disease.

Type 1 Gaucher disease, represents 95% of cases, manifests itself mainly in its visceral form. However, type 2 Gaucher disease, present in less than 1% of patients, often leads to death before the age of 2 due to serious acute neurological damage. To type 3 gaucher disease, concerns approximately 5% of cases, with signs of subacute neurological damage, it is often associated with a progressive encephalopathy of variable severity with typical clinical manifestations of type 1 disease [4]. In type 1 of gaucher disease, we do not observe neurological damage (as observed in our cases), this form constitutes the predominant form, it is more frequently observed in the Jewish population [5]. The clinical presentation of this form is very varied, manifesting largely as hepatosplenomegaly, bone disorders, thrombocytopenia, and occasionally neutropenia. It should be noted that forms of the disease diagnosed in adulthood are relatively common in this category.

The Diagnosis

Historically, the diagnosis was established by the observation of Gaucher histiocytes during a myelogram, and more rarely by a spleen or liver biopsy [4]. Although it is difficult for a novice cytologist to distinguish these typical Gaucher cells (figure 1) from the "pseudo-Gaucher" cells observed in certain hematological pathologies (figure 2) such as in contexts where cell regeneration is rapid, without enzyme deficiency, such as in chronic myelogenous leukemia and thalassemia syndromes [6].

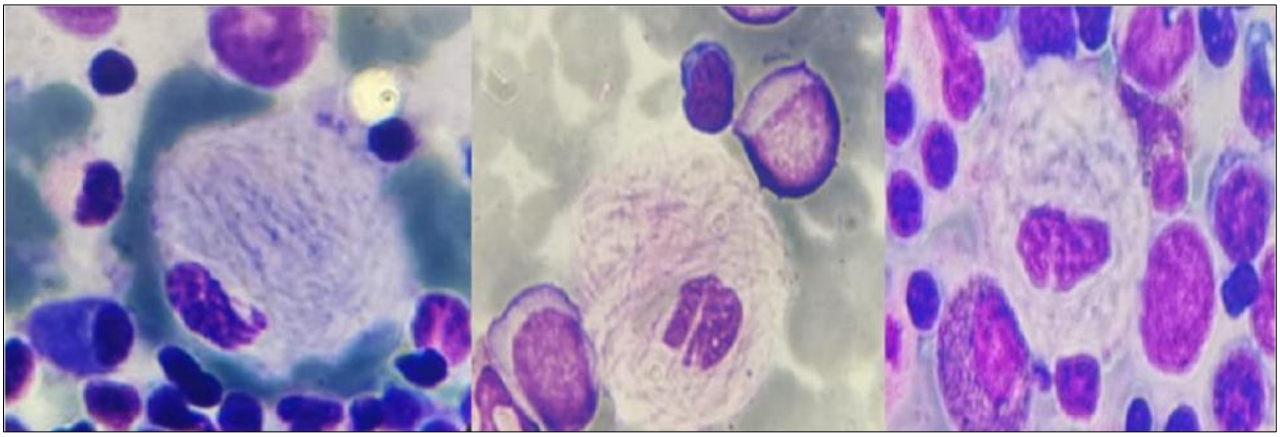

Figure 1: Examples of typical Gaucher cells. Bone marrow smear (May-Grunwald Giemsa stain). (Gx 100.) Hematology and immunohematology laboratory of CHU-Mohammed VI-Tangier.

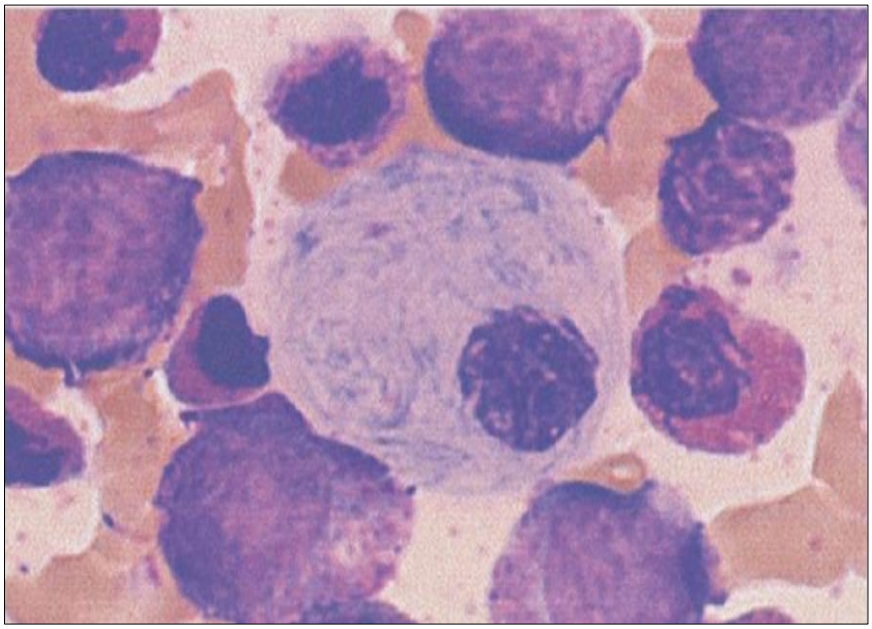

Figure 2: Example of a Gaucher-type overload cell on a chronic myelogenous leukemia marrow.

When there is a clinical suspicion, the myelogram is no longer as indicated today as was before. The reference examination lies in the demonstration the glucocerebrosidase deficiency in circulating leukocytes or skin fibroblasts in culture. There are also molecular diagnostic techniques. The search for mutations, especially in the GBA1 gene, the chromosome 1 [1q21]), genotyping remains an essential step; it can provide prognostic information through phenotype-genotype correlations, particularly in children to demonstrate whether they are at risk of developing a neurological form of the disease [6].

The Treatment

The classic treatments were symptomatic treatments such as transfusions, analgesics, and very often we resorted to total or partial splenectomy, this type of treatment has become obsolete, because of the hepatic, infectious and bone complications that it caused (due to the relocalization of Gaucher histiocytes). These treatments are currently replaced by administrations of modified placental glucocerebrosidase and especially recombinant glucocerebrosidase [7].

Clinically, in the presence of thrombocytopenia associated with splenomegaly, it is important to consider

Gaucher disease, regardless of the patient's age group and medical history, and to perform a myelogram analysis. In order to detect the presence of overload cells. It is in this context that the diagnosis was made in our patients.

CONCLUSION

In our patients, the clinical presentation marked by enormous splenomegaly raises suspicion of Gaucher disease, especially with the signs of bone damage in the first patient.

The myelogram was indicated for these patients given the thrombocytopenia associated with the enormous splenomegaly. The study of the medullogram made it possible to highlight the presence of numerous Gaucher histiocytes, making it possible to guide the diagnosis, for the performance of an enzymatic dosage in order to confirm it.

Acknowledgement

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