

in children and adolescents with knee pain or monoarthritis with atypical features and/or a poor response to treatment.<sup>5,7,9</sup>

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## A Case Report of Gaucher Disease<sup>☆</sup>



### Enfermedad de Gaucher: a propósito de un caso

To the Editor,

Gaucher disease (GD), described in 1882 by Philippe Charles Ernest Gaucher, is a progressive, rare hereditary disease, with an autosomal recessive inheritance pattern.<sup>1</sup> Included in the group of lysosomal storage diseases, it is characterized as being the most prevalent, with an estimated frequency of 1 per 50,000 to 1 per 100,000 population, with the exception of the Ashkenazi Jewish ethnicity in which the incidence is estimated to be 1 per 850 births.<sup>2,3</sup> It produces a deficiency in the activity of the enzyme acid  $\beta$ -glucosidase (GBA), provoking an accumulation of glucocerebroside in the lysosomes of different cells,<sup>4</sup> causing cytopenias, hepatosplenomegaly, changes in the central nervous system (CNS) and skeletal manifestations, the latter being one of the most disabling aspects. Depending on the clinical expression, different types can be distinguished: type 1 (adult non-neuronopathic), the most common form, occurring frequently in Ashkenazi Jews, with variable manifestations, and not involving the CNS; type 2 (acute neuronopathic), infrequent, with no ethnic-related dominance, fatal after birth and involvement of the CNS; and type 3 (subacute or chronic neuronopathic),<sup>4</sup> beginning during childhood, adolescence or adulthood, with involvement of the CNS. Given the variety of conditions associated with bone pain, we consider it appropriate to report the case of our patient.

The patient was a 53-year-old man with no significant family or personal history. He was being studied because of neutropenia and thrombocytopenia with a duration of 10 years, as well as bone pain that had started 3 years earlier. He reported no hemorrhagic diathesis, infections or abdominal pain. Physical examination revealed splenomegaly, but the rest was normal. The results of

laboratory tests included a leukocyte count of 3400 mm<sup>3</sup>, neutrophils at 1200/mm<sup>3</sup> and platelets at 93,000 mm<sup>3</sup>; findings regarding hemoglobin, reticulocytes, coagulation, serum electrolytes, liver function, vitamin B<sub>12</sub>, folic acid, tumor markers (carcinoembryonic antigen, alpha-fetoprotein, CA 19-9, CA 15-3, prostate-specific antigen),  $\beta_2$ -microglobulin, rheumatoid factor, erythrocyte sedimentation rate, antinuclear antibodies, immunoglobulins, protein profile and lymphocyte populations were normal. Serologic tests for hepatitis B and C viruses and human immunodeficiency virus were negative. Plain radiography of distal femur and thoracolumbar spine were normal. However, lumbar magnetic resonance showed a homogeneous hypointense signal in the vertebral bodies on T1 and T2-weighted sequences. Splenomegaly was confirmed by abdominal ultrasound and osteoporosis by bone densitometry (T-score femur:  $-2.9$  standard deviations (SD); T-score spine:  $-2.8$  SD). Bone marrow aspirate/biopsy (BMA/BMB)

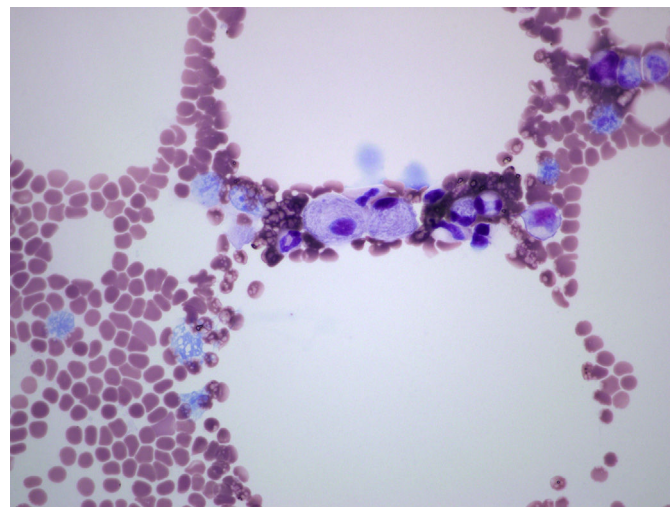


Fig. 1. Gaucher cells.

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detected cells with eccentric nucleus, basophilic cytoplasm with the appearance of tissue paper, suggestive of Gaucher cells (GC) (Fig. 1). The GBA enzyme activity was determined in leukocytes by spectrofluorometry, which confirmed that it was lacking. The molecular genetic study showed double heterozygosity for the L444P and p.Tyr244Cys mutations.

This observation constitutes a representative example of the clinical, biochemical and genetic characteristics of type 1 GD.<sup>5</sup> The fact that our patient had a history of years of bone pain can make diagnosis more difficult, when these manifestations are associated with other signs of the disease like cytopenias or organomegaly. Extra-articular manifestations are useful for reaching a correct diagnosis, avoiding incorrect diagnoses of inflammatory and/or autoimmune diseases. The BMA confirmed GD, which is accountable for an accumulation that generates substances responsible for bone resorption, producing pain, deformity and functional disability.<sup>6</sup> Radiographic examination reveals manifestations such as abnormal bone remodeling (disclosing the Erlenmeyer flask deformity, which was not found in our patient), spontaneous fractures, osteopenia, osteonecrosis and osteolysis. However, the development of osteoporosis of unknown cause, whether or not it is associated with thrombocytopenia and splenomegaly, should lead us to suspect GD. These findings were significant and enabled the quantification of GBA activity, and led us to request a genetic study to confirm the disease.<sup>6</sup> A high index of suspicion and initial biochemical studies are needed to verify the diagnosis and begin enzyme replacement therapy to revert, establish and improve the clinical prospects of the patient.

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## The Great Unknown, Whipple's Disease<sup>\*</sup>



### Enfermedad de Whipple, la gran desconocida

To the Editor,

Whipple's disease was first described by George Hoyt Whipple in 1907. It is a multisystem infectious disease, produced by *Tropheryma whippelii*, which was identified for the first time in 1991. The name is of Greek origin (*trophe* nutrient + *eryma* barrier) and is related to the defective absorption of nutrients characteristic of this disorder. The clinical signs include arthralgia, weight loss, diarrhea and abdominal pain, although the clinical manifestations can vary widely. Thus it may take up to 6 years to be diagnosed. We report 2 cases in which the final diagnosis was Whipple's disease.

#### Case no. 1

The patient was a 47-year-old man, a farmer, who had a 15-month history of polyarthritis in knees, ankles and hands. He was admitted by the gastroenterology department because of abdominal pain, vomiting and fever. Physical examination revealed pain in left abdomen and there appeared to be a mass on palpation. Ancillary tests showed an erythrocyte sedimentation rate of 100 mm/h and normochromic anemia, and thoracoabdominal computed tomography (CT) disclosed mesenteric infiltration and lymph nodes in the jejunal loops. Exploratory laparotomy was performed, as was biopsy of the lymph nodes and bowel mesentery. The pathological study resulted in a diagnosis of Whipple disease, with the

presence of periodic acid Schiff (PAS)-positive macrophages with intracellular inclusions. The patient was treated with cotrimoxazole for 2 years, accompanied by tetracycline for the first 3 months. Twenty years later, the patient is asymptomatic.

#### Case no. 2

This patient was a 63-year-old man with systemic hypertension, renal failure, arthritis and a 9-year history of low back pain, with a diagnosis of spondyloarthritis. He had posterior uveitis and vitritis affecting right eye and had had 3 episodes of pancreatitis requiring hospital admission in the gastroenterology department. Computed tomography revealed nonspecific mesenteric lymph node enlargement (Fig. 1). Gastroscopy, during which a specimen was removed for biopsy, disclosed erosive disease involving the duodenal bulb. One month later, the patient was readmitted in the gastroenterology department with fever, diarrhea and abdominal pain. According to a duodenal biopsy (Fig. 2) that had been carried out during the earlier hospital stay, the diagnosis was Whipple's disease. Treatment was begun with ceftriaxone and imipenem, and included cefixime during the first 2 months. He was subsequently treated for 2 years with trimethoprim/sulfamethoxazole.

Whipple's disease is frequently associated with rheumatic manifestations (60% of the cases), which precede the gastrointestinal signs in three fourths of the patients. They are often the first symptoms of the disease. They commonly appear in the form of polyarthritis, generally chronic, intermittent, seronegative and nonerosive,<sup>1</sup> although cases have been reported in which there are atypical rheumatic symptoms such as spondylodiscitis,<sup>2</sup> erosive arthritis,<sup>2</sup> and even osteonecrosis of the hip. The joints most frequently affected are the carpi and large joints of the lower limbs. When the diagnosis is uncertain, it is important to rule out this disease in patients with seronegative arthritis and signs

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