

## Rare Pathological Entity: Niemann Pick Disease in Adults, about a Case

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**Abstract:** Niemann Pick is a rare lysosomal storage metabolic disease. It is a sphingomyelin-cholesterol lipidosis associated with the accumulation of foamy cells, inherited in an autosomal recessive manner. It is divided into 3 main types (A/B, C). The biological diagnosis of type A/B relies on the enzymatic assay of acid sphingomyelinase, while that of type C is based on the search for plasma oxysterols which serves as the initial screening test, confirmed by genetic testing. The differential diagnosis consists of excluding other lysosomal diseases (Gaucher, Wolman).

**Keywords:** Niemann Pick disease types A, B, and C - Acid Sphingomyelinase, Plasma Oxysterols.

### INTRODUCTION

Niemann-Pick disease (NP) is a rare hereditary storage disorder of autosomal recessive transmission. NP types A and B are caused by a total or partial deficiency of the lysosomal enzyme acid sphingomyelinase (ASM). Type C can occur due to defects in the Niemann Pick C1 (NPC1) transmembrane protein or the soluble Niemann Pick C2 (NPC2). The diagnosis is based on clinical and biological aspects, notably the myelogram and low enzymatic activity of acid sphingomyelinase or genetic testing. We report the case of a Niemann Pick diagnosed in a 57-year-old adult patient revealed by bone pain [1-3].

### OBSERVATION

This is a 57-year-old patient from a consanguineous marriage. He has a family history of a brother who was treated and died from tuberculosis. The patient was admitted for abdominal pain and a heaviness in the left hypochondrium radiating to the navel, progressively developing over the past year, associated with night sweats, occurring in a context of deterioration of the general condition. The clinical examination revealed splenomegaly and osteoarticular pain upon palpation.

A complete blood count was performed on our patient, showing thrombocytopenia at 4 G/L without other associated signs. In the face of thrombocytopenia, a blood smear was performed and did not show platelet aggregates or other abnormalities.

However, a myelogram was performed and highlighted numerous megakaryocytes with normal erythroid and granulocytic lineages. Upon examining this myelogram, many foamy cells of the Niemann Pick type were discovered incidentally. The myelogram showed a very rich marrow demonstrating a great number of megakaryocytes present at all stages of maturation. Presence of very large foamy cells with a sea-blue appearance, characteristic of Niemann Pick disease. Slight hyperplasia of the erythroid lineage without signs of notable dysplasia. The other lineages are well represented without signs of dysmyelopoiesis.

### Characteristic NP Cells in the Myelogram

The lipid profile showed a collapsed HDL cholesterol (< 0.05 g/l) with an LDL cholesterol (0.5 g/l) and elevated triglycerides (1.9 g/l), a total hyperbilirubinemia of 26.8 mg/L was noted, and the ALT and AST were normal.

The histological examination of a bone marrow biopsy revealed foam-like vacuolated histiocytes consistent with a lipid storage disease. In contrast, the biopsy of the accessory salivary glands showed no abnormalities.

The abdominal ultrasound showed a homogeneous splenomegaly, with two echogenic nodular lesions measuring 20 and 15 mm. The level of acid sphingomyelinase activity is normal. The genetic study was not conducted due to lack of resources.

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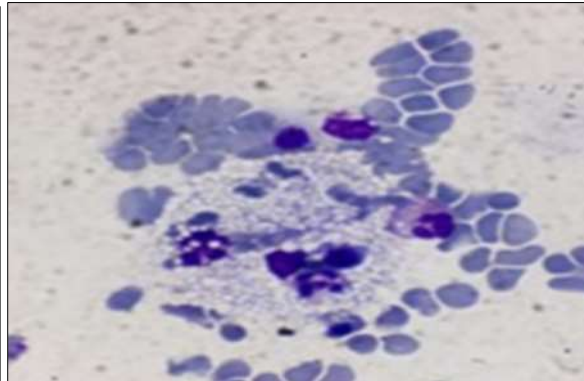
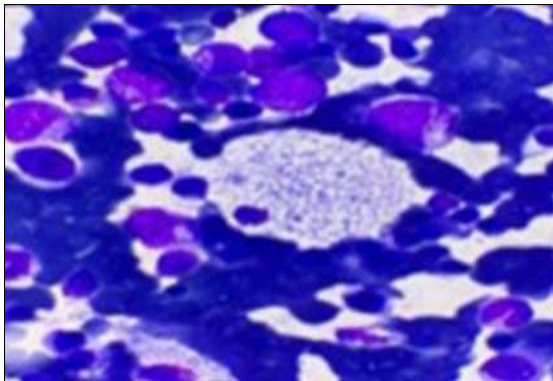
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## DISCUSSION

Niemann-Pick disease is a group of rare hereditary lysosomal disorders characterized by the

accumulation of lipids (sphingomyelin, cholesterol) in cells. It is divided into 3 main types (A/B, C), with distinct genetic causes and manifestations.



**Type A and B: Deficiency in acid sphingomyelinase (ASM), genetic causes with the SMPD1 gene (chromosome 11p15.4) and autosomal recessive inheritance. Type C: Cholesterol transport defect, genetic causes with the NPC1 gene (95%) or NPC2 (5%) and autosomal recessive inheritance. Clinical manifestations depend on type A/B or C**

For type A (Acute neuro-visceral form): Begins in infants (3-6 months), multiple symptoms: severe hepatosplenomegaly, severe psychomotor delay, progressive neurological degeneration (from hypotonia to spasticity), cherry-red spot upon eye examination, with death before age 3.

For type B (Chronic visceral form): Begins in childhood/adolescence), multiple symptoms: Hepatosplenomegaly (liver fibrosis, cirrhosis), pulmonary involvement (infiltrates, recurrent infections), osteoporosis/bone pain, absence of major neurological signs, with survival to adulthood.

For type C (Lipid transport disorder), it presents a variable onset (from infancy to adulthood), and a characteristic triad: Neurological involvement (supranuclear vertical gaze palsy, dystonia, seizures, dementia, psychiatric disorders in adults); Visceral involvement (moderate hepatosplenomegaly); Psychiatric involvement (psychosis, hallucinations in adult forms) [1-3].

The biological diagnosis of NP disease is based on specific tests that vary according to the main type (A/B, C). Here are the key methods: Niemann-Pick Disease Types A and B (ASM deficiency - Acid Sphingomyelinase) [1-5].

### Enzymatic Dosage:

On a sample of peripheral blood (leukocytes) or skin biopsy (fibroblasts), measuring the activity of acid sphingomyelinase (ASM) in leukocytes or skin fibroblasts. An activity < 10% of normal confirms the diagnosis.

Genetic analysis by sequencing the SMPD1 gene to identify pathogenic mutations, useful for genetic counseling and prenatal diagnosis. Niemann-Pick

Disease Type C (Cholesterol transport defect - NPC1 or NPC2 genes).

Test of Filipin staining, fibroblast staining with filipin to visualize the accumulation of unesterified cholesterol under UV. Complex technique, subjective interpretation, possible false negatives.

Measurement of plasma oxysterols, which are key markers, has become the first-line screening test, through measurement of 7-ketocholesterol (7-KC) and cholestane-3 $\beta$ ,5 $\alpha$ ,6 $\beta$ -triol. Non-invasive (blood sample), high sensitivity/specificity (>90%).

Genetic analysis, through sequencing of the NPC1 genes (95% of cases) and NPC2 (5% of cases). Essential to confirm the diagnosis after biochemical tests. Other complementary diagnostic steps are used:

- Bone marrow biopsy showing 'sea-blue histiocytes' (non-specific) spumous cells.- Imaging/Electrophysiology: brain MRI (atrophy), abnormal evoked potentials (type C).-Prenatal diagnosis: enzyme or genetic testing on chorionic villi/amniocytes.

### Genetically:

Autosomal recessive disease (25% risk if both parents are carriers). Family screening is done by enzymatic or genetic testing in relatives, while prenatal diagnosis looks for mutations on chorionic villi or amniocytes.

For an accurate diagnosis, specialized care at a reference center for lysosomal diseases is recommended.

The only discrepancy lies in the enzymatic dosage, which should be of low activity in type B and is normal in our patient. Nevertheless, this result does not eliminate the diagnosis according to the literature. The

differential diagnoses in types A and B include Gaucher's disease, Wolman's disease, and mucopolysaccharidoses. Meanwhile, in type C, it is differentiated from other neurodegenerative disorders, such as Wilson's disease and gangliosidoses.

Therapeutic management includes symptomatic treatments, based on respiratory physiotherapy (type B), anticonvulsants, and antidystonic drugs (type C), as well as possibly a liver transplant (type B complicated).

Specific treatments according to the form of the disease, thus in type B, Olipudase alfa (enzyme replacement therapy approved in 2022) is used, and in type C, Miglustat (synthesis inhibitor of glycosphingolipids) is used, allowing for the slowing of neurological progression.

#### **Other Treatments are Currently Under Research:**

Gene therapy (preclinical trials for types A/B); Pharmacological chaperones for type C. The prognosis varies according to the type of disease, with death before 3 years for type A, a life expectancy between 20 and 60 years for type B, and variable from childhood to adulthood for type C. The key prognostic factors also vary according to the type of disease. In type A, it depends on rapid neurological degeneration, in type B, it depends on the severity of pulmonary and hepatic involvement, and in type C, it depends on the age of onset of neurological symptoms [6-8].

#### **CONCLUSION**

Niemann-Pick disease: a hereditary, rare overload pathology. Two distinct entities in terms of genetics and metabolism: type A and B and type C. The symptoms, rate of progression, and life expectancy are

variable. The clinical context and a careful hematological examination of the blood and bone marrow are therefore a fundamental step in the diagnostic orientation and early detection of Niemann-Pick disease.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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