Clinical report

New mutation in a young woman diagnosed with Niemann–Pick disease type C

Ana Lario a,∗, Carlos de Miguel a, Emilio Ojeda a, Santiago Gil a, María J. Coll b, Pilar Alfonso c

a Servicio de Hematología y Hemoterapia, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
b Centro de Diagnóstico Biomédico, Hospital Clinic, Barcelona, Spain
c Departamento de Bioquímica y Biología Celular y Molecular, Universidad de Zaragoza, Zaragoza, Spain

ABSTRACT

Background and objective: To describe a new molecular variant of Niemann–Pick disease type C (NPC) in a 27-year-old patient with splenomegaly and abolition of osteotendinous reflexes.

Material and methods: NPC1 is the main gene with described mutation in NPC disease. Here we report a case with a new mutation, p.N916S, not described before in a patient diagnosed with NPC.

Results: p.N916S was described as a cause of NPC disease by predictive programmes Mutation Master, PolyPhen2 and SIFT.


© 2016 Elsevier España, S.L.U. All rights reserved.

Nueva mutación descrita en una mujer joven con esplenomegalia, diagnostica da de enfermedad de Niemann-Pick tipo C

RESUMEN

Fundamento y objetivo: Describir una nueva variante molecular del Niemann-Pick tipo C (NPC) en una paciente de 27 años con esplenomegalia y abolición de reflejos osteotendinosos.

Material y métodos: NPC1 es el principal gen mutado en el NPC. Presentamos un caso con una nueva mutación, p.N916S, no descrita previamente en pacientes con NPC.

Resultados: p.N916S fue descrita como causa de la enfermedad de NPC por los programas predictivos Mutation Master, PolyPhen2 y SIFT.


© 2016 Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

Niemann–Pick disease is part of a group of metabolic diseases classified as lysosomal storage disorders with autosomal recessive inheritance. They comprise two distinct entities: the first includes types A and B, with a sphingomyelinase deficiency, and the second, Type C,1 in which there is a LDL cholesterol processing and transport abnormality.

Among the Niemann–Pick disease, the most common clinical form is Niemann–Pick Type B disease, which is not associated with neurological symptoms. However, the occurring of neurological symptoms is a frequent form of presentation in types A and C. The splenomegalia is a common finding in all variants of Niemann–Pick disease.

The suspected diagnosis is based on clinical presentation and morphology of the bone marrow. In types A and B, the final diagnosis is established by enzymatic studies (sphingomyelinase

Please cite this article as: Lario A, de Miguel C, Ojeda E, Gil S, Coll MJ, Alfonso P. Nueva mutación descrita en una mujer joven con esplenomegalia, diagnosticada de enfermedad de Niemann-Pick tipo C. Med Clin (Barc). 2016;146:494–496.

∗ Corresponding author. E-mail address: ana.lario@gmail.com (A. Lario).

2387-0206/© 2016 Elsevier España, S.L.U. All rights reserved.
deficiency), and in Type C, by documenting the accumulation of unesterified cholesterol at intracellular level (fibroblast culture or filipin test)\(^2\) or by molecular biology techniques (NPC1 and NPC2 gene mutations).\(^3\) The oxysterols test\(^5\) can be a support in diagnosis.

The enzyme replacement therapy with recombinant acid sphingomyelinase is not yet an established procedure in Niemann–Pick Type B (phase 2 of the clinical trial has not started yet). Miglustat,\(^6\)\(^–\)\(^10\) a glucosylceramide synthase inhibitor, has recently been approved in Europe – in 2009 – and in Japan in 2012 in specific cases of Niemann–Pick Type C to prevent the progression of neurological symptoms.

**Patient and results**

We report the case of a 27-year-old female patient who had an asymptomatic splenomegaly discovered after an ultrasound was performed due to a recurrent urinary tract infection. She had no individual or familial medical history. All developmental milestones during childhood occurred normally and never had behavioural or school problems.

The patient had mild thrombocytopenia as the only blood test abnormality (platelets \(127 \times 10^9/L\)); the rest of the CBC results were normal. Biochemical determinations were normal except for a slight increase in total cholesterol (223 mg/dl), while HDL cholesterol was normal (53 mg/dl); moreover, the values of LDL cholesterol and triglycerides were 150 mg/dl and 101 mg/dl, respectively. Serological tests were normal. An abdominal MRI ruled out vascular disorders and confirmed splenomegaly (Fig. 1). Bone marrow aspirate and biopsy showed the presence of multiple large size histiocytic cells with abundant and foamy cytoplasm, along with sea blue histiocytes with a tendency to form small groups that were evenly spread in the aspirate (Fig. 2). The cytochemical behaviour of these cells were positive for acid phosphatase and TRAP, showing intracellular lipid deposits (Sudan Black and Oil Red).\(^11\) In immunohistochemistry, these cells had an intense multifocal reactivity for histiocytic differentiation markers (CD68 and CD163).

With high suspicion of a deposition disease, an enzyme study was performed, showing normal activity of acid glucocerebrosidase (6.4 nmol/mg prot/hr, ruling out Gaucher disease), similar to acid sphingomyelinase (0.394 nmol/mg prot/hr, ruling out the Niemann–Pick disease, types A and B). Chitotriosidase levels were elevated (653 nmol/ml × h [3–32 nmol/ml × h]), but not within Gaucher disease range (considering the range and determination), indicating that we were facing a probable deposition disease. A whole body MRI was also performed without relevant findings or neurological involvement data, except for the already known splenomegaly (19 cm long).

She was evaluated by Neurology and Ophthalmology and the Neuro-ophthalmologic examination was described as: normal psychomotor/cognitive development and normal birth; without neurological symptoms (there were no crisis, dystonia, ataxia, cranial nerve involvement or psychiatric symptoms). The neurological examination was normal (strength, sensitivity, cranial nerves,
دانلود مقاله

http://daneshyari.com/article/3806123

امکان دانلود نسخه تمام متن مقالات انگلیسی ✓
امکان دانلود نسخه ترجمه شده مقالات ✓
پذیرش سفارش ترجمه تخصصی ✓
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله ✓
امکان برداخت اینترنتی با کلیه کارت های عضو شتاب ✓
دانلود فوری مقاله پس از برداخت آنلاین ✓
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات ✓