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SHORT REPORT

Subclinical course of adult visceral Niemann–Pick type C1 disease. A rare or underdiagnosed disorder?

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Summary We present the third case of Niemann–Pick disease type C without neurological symptoms. The patient was a 53-year-old woman without significant prior health problems who died of acute pulmonary embolism. Autopsy findings of hepatosplenomegaly, lymphadenopathy and ceroid-rich foam cells raised the suspicion of the visceral form of acid sphingomyelinase deficiency (Niemann–Pick disease type B; NPB) or a much rarer disorder, variant adult visceral form of Niemann–Pick disease type C (NPC). To verify the histopathological findings, *SMPD1*, *NPC1* and *NPC2* genes were analysed. Two novel sequence variants, c.1997G > A (S666N) and c.2882A > G (N961S) were detected in the *NPC1* gene. No pathogenic sequence variants were found either in the *SMPD1* gene mutated in NPB or in *NPC2* gene. The pathogenicity of both *NPC1* variants was supported by their location in regions important for the protein function. Both variations were not found in more than 300 control alleles. Identified sequence variations confirm the diagnosis of the extremely rare adult visceral form of Niemann–Pick disease type C, which is otherwise dominated by neurovisceral symptoms. Although only three patients have been reported, this (most probably underdiagnosed) form of NPC should be considered in differential diagnosis of isolated hepatosplenomegaly with foam cells in adulthood.

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SHORT REPORT

Homozygosity for the double D409H+H255Q allele in type II Gaucher disease

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Summary Homozygosity for D409H has been associated with a unique type III subtype of the disease with a phenotype dominated by severe cardiovascular involvement, whereas neurological findings, if present, are restricted to oculomotor apraxia and features such as visceromegaly are either minimal or absent. Using PCR amplification followed by restriction enzyme analysis, 3 patients (1 Greek, 2 Albanians) were identified with the D409H/D409H genotype. All shared a very severe early-onset neurological phenotype that classified them as type II. Amplification and sequencing of the full coding region of the *GBA* gene revealed that all three patients were homozygous not only for D409H but also for H255Q. Both mutations were present on the same allele, as shown by analysis of the parental DNA. The double D409H+H255Q allele was found in heterozygosity in Greek, Bulgarian and Argentinian patients but was not identified in any Spanish patients carrying the D409H mutation.

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