P-086 - NIEMANN PICK DISEASE: CLINICAL, BIOCHEMICAL AND MOLECULAR CHARACTERIZATION OF ARGENTINEAN PATIENTS AND THE REPORT OF A NOVEL MUTATION.

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INTRODUCTION: Niemann-Pick disease (NPD) is a group of rare autosomal recessive lysosomal storage disorders. NPD has been divided into two distinct entities: a) acid sphingomyelinase deficiencies (ASMD) (including NPD types A and B) activity coded by SMPD1 gene, and b) NPD type C (including C and D), produced by deficiency of either the NPC1 or the NPC2 transport proteins. Type A NPD is a fatal neurodegenerative disorder of infancy: type B NPD is a less severe form, the most patients have little or no neurologic involvement and survive into adulthood. Type C NPD is a complex lipid storage disorder caused by defects in cholesterol trafficking, resulting in a clinical presentation dominated by neurologic involvement. AIM: to report the clinical, biochemical and molecular studies for the characterization of patients, in the context of a systematic clinical research protocol of this pathology in Argentina. METHODOLOGY: We present a diagnostic algorithm for NPD consists: I- compatible patient selection II- histological and biochemical studies III- enzymatic determinations (acid sphingomyelinase and chitotriosidase) IV- filipin test in fibroblast culture V- molecular analysis. RESULTS: we studied three nosological defined patients with NPD: two type B NPD and one type C NPD. The type B NPD, patients of nonconsanguineous parents with hepatosplenomegaly, however they did not present any neurological symptoms. Bone marrow biopsy show foam cells. The plasma chitotriosidase was slightly increased. ASM activity level was lower. The SMPD1 gene sequencing revealed that the patient 1 is homozygous for the mutation p.R608del, patient 2 is compound heterozygous, allele1 p.Ser147LeufsTer19 and allele 2 a novel mutation (p.Lys578Thr). The type C NPD, patient presented ataxia, mental and motor retardation and language impairment with seizures and hepatosplenomegaly. The plasma chitotriosidase was slightly increased. Functional studies in fibroblasts with Filipin were positive. The NPC1 gene sequencing indicated that the patient is homozygote for the missense mutation p.R1186H. As regards the other CONCLUSION: Patients with NPD present with a large phenotype spectrum of nonspecific disease manifestations that can lead to considerable diagnostic delay and missed cases. Early diagnosis of NPD is priority for appropriate management.