P-041 - NOVEL MUTATION IN NAGLU GENE CAUSES SANFILIPPO SYNDROME TYPE B IN A CUBAN PATIENT.

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INTRODUCTION: Mucopolysaccharidosis IIIB (MPS IIIB) is an autosomal recessive disorder caused by an enzyme deficiency of alpha-N-acetyl-glucosaminidase, resulting in excess intralysosomal accumulation of heparan sulfate. The clinical spectrum varies, but is usually characterized by developmental delay, behavioral abnormalities and sleep disturbance in early childhood. Homozygous or compound heterozygous conditions in the NAGLU gene (NM_000263.3) are the cause of this syndrome. More than 100 mutations in this gene have been reported. Purpose: The aim of this presentation is to describe the clinical, biochemical and molecular findings of a Cuban patient with MPS IIIB, which have a novel pathogenic variant in NAGLU gene and unusual clinical signs.

METHODOLOGY: The diagnosis was performed by clinical findings suggestive of MPS, qualitative chemical tests and Thin Layer Chromatography (TLC) for urinary glycosaminoglycans, enzyme assay for N-α-acetylglucosaminidase and Sequence analysis of IDUA gene. The silico functional prediction was performed using Mutation Taster and mutalyzer 2.0.28.

RESULTS: The male patient was born after 38.5 weeks of gestation by normal vaginal delivery. He had a healthy birth weight of 3.28 kg and a length of 50cm. The early clinical characteristics observed by the parents were recurrent infections and diarrhea. During the first years the patient presents frequent respiratory infections, autistic and hyperactive behavior and neurological deterioration. He also experiences an occasional sleep disorder. Currently the patient has a slightly coarse facie, sinofris, progressive neurological deterioration, conduct disorder, language delay, regression and loss of acquired skills. Ulcerative colitis and intestinal polyps has being diagnosed. The biochemical assays showed an elevated heparan sulfate urinary excretion, and very low intralysosomal enzymatic activity. In the molecular study of NAGLU gene we detected the novel mutation c.640dupC; p.L214Pfs*59. The patient was a homo-zygote for the mutation and it was also seen in the Sanger sequence chromatogram of his parents. This variant was classified as disease causing during “in silico” evaluation.

CONCLUSION: The suggestive clinical findings and the enzymatic activity levels allowed the patient diagnosis as Sanfilippo B syndrome. The molecular study confirmed the presence of a novel mutation associated with this disorder.