P-109 - LEIGH SYNDROME AS A MILD PRESENTATION DUE TO A RARE COMPOUND HETEROZYGOUS VARIANTS IN NDUFAF6 GENE.

Beltrán OI 1,2, Patiño JA 1, Garzón C 1

(1) Grupo de investigación BioGenEtica & BioDerecho-Facultad de Medicina Universidad Militar Nueva Granada. (2) Consulta de Genética, Carrera 9 N 103A-36, Bogotá-Colombia. beltran.orietta.gen@gmail.com

INTRODUCTION: Leigh syndrome (LS) it a disorder that affects directly the mitochondrial energy generation, this syndrome has a broad clinical and genetic spectrum, with wide and progressive neurodegenerative manifestations and early onset. Patients usually show global delay or developmental regression, hypotonia, ataxia, dystonia, and ophthalmologic abnormalities. All these clinical findings may be a manifestation of primary deficiency of the mitochondrial respiratory chain complexes. OBJECTIVE: The primary objective was to analyze the clinical and molecular diagnosis in a patient with LS. CASE DESCRIPTION: We present a 4 year colombian boy, first child of non consanguineous parents, delivery at 38 weeks by C-section owing to decelerations. During his first year he presented a normal neurodevelopment, after that he start to present expression speech delay that became a progressive situation. He came at age of 4 to consultation with height and weight according to age, clinical exam present mild ptosis, clenched hands, and flat foot. MRI and lab test were performed, showing bilateral and symmetric hyperintensity in putamen and increase lactate pyruvate ratio. A multigene sequencing panel was performed guided to mitochondrial diseases; identifying a missense heterozygote uncertain significance variant c.371T>C;p.Ile124Thr and missense pathogenic heterozygous variant c.532G>C;p.Ala178Pro in NDUFAF6 gene (clinvar rs201732170; clinvar rs201088736). CONCLUSIONS: LS has a enormous genetic heterogeneity, involving mutations in nuclear or mitochondrial DNA that affect the proper function of respiratory chain complexes. The biallelic mutations on the nuclear NDUFAF6 may generate a complex I deficiency, on literature research a single affected allele is not enough to cause disease, our hypothesis is that variant c.371T>C;p.Ile124Thr is pathogenic. Correlation clinical with genetic testing confirm the diagnosis of a mitochondrial disease by mutation in nuclear DNA with pattern of inheritance autosomal recessive and to guide optimal genetic counseling and management focused on nutritional interventions (diet rich in antioxidants) and rehabilitation for to preserve or even improve the patient's existing functioning.