P-106 - DEVELOPMENTAL DELAY-HYPOTONIA-THROMBOCYTOPENIA: SUSPECTED FROM MITOCHONDRIAL DISEASE DUE TO HETEROPLASMIC VARIANT ON MTCYB GENE

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INTRODUCTION: Mitochondrial diseases has a wide clinical spectrum, it may involve an alteration on mitochondrial structure or function that implicate a pathogenic mutation on the inherited mitochondrial or nuclear DNA. Heteroplasmic mtDNA have tissue segregation patterns than vary widely, for example, muscle have higher levels of the mutant mtDNA, whilst levels in blood decrease over time. OBJECTIVE: Describe clinical-molecular correlation of heteroplasmic variant in MTCYB gene

METHODS: Retrospective analysis of clinical history and molecular results of a pediatric case with developmental delay, hypotonia and thrombocytopenia.

RESULTS: A 2-year-old girl, during first trimester had a subchorial hematoma and caesarean delivery due to podalic position and umbilical artery restriction to 37 weeks of gestation. Parents non-consanguineous, healthy father and mother refers constant fatigue. During first year she shows mild hypotonia, retarded motor and language development. However, at 18-mo she presented small bruises on lower limbs secondary to thrombocytopenia with normal-sized platelets (92.000 plateles/\text{uL}), mild splenomegaly and unilateral hypoplasia renal. Acquired or medication induced platelet dysfunction were excluded. Bone marrow aspirate was normal. Whole exome sequencing (WES) identifies genetic “likely pathogenic” variant on MTCYB gene (m.15246G>A,p.Gly167Asp) in heteroplasmy (52% in blood). Alls known genes causing of congenital thrombocytopenia were normal. She continues clinical follow up, physical therapy, speech therapy and variable count of platelets; occasionally, low or normal levels.

CONCLUSIONS: We analyze the hypothesis if variant on MTCYB gene explain signs and symptoms like hypotonia and neurodevelopmental delay in this case. Because, the clinical spectrum of mitochondrial disease is broad and poorly understood, consequently, long-term prognosis are difficult to predict. MTCYB gene encoded subunit of respiratory complex III located within the mitochondrial inner membrane. Phenotypes describe by mutations in MTCYB are broad: hypotonia, retarded motor and language development, exercise intolerance, gait ataxia, cerebellar hypoplasia, seizures, hypertrophic cardiomyopathy and parkinsonism onset since childhood until adulthood. Usually, high mutation load is associated with more severity, however, variation in percentage heteroplasmy levels in tissues is common and change with age, for this reason is relevant genetic counseling and detailed clinical follow up.