P-084 - DIAGNOSIS OF HEXOSAMINIDASE A DEFICIENCY THROUGH WHOLE EXOME SEQUENCING: REPORT OF TWO NORTHERN BRAZILIAN CASES

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**INTRODUCTION:** The diagnosis of Hexosaminidase A (HEX A) deficiency relies on the demonstration of absent to near-absent HEX A enzymatic activity in the serum, white blood cells, or other tissues from a symptomatic individual in the presence of normal or elevated activity of the beta-hexosaminidase isoenzyme. However, Whole Exome Sequencing (WES) has been an effective technology with remarkable impact in diagnosis of metabolic and neurologic diseases. **OBJECTIVE:** To report two patients diagnosed with HEX A deficiency through WES.

**METHODOLOGY:** WES exams were performed before biochemical assays, searching for variants related to metabolic and neurologic diseases. **RESULTS:** Patient 1: D.S.S, a 13-year-old male, third child of a non-consanguineous couple, started with neuropsychomotor regression at the age of 6. His older sister developed similar clinical presentation when she was 4 years old and died of uncontrollable seizures at the age of 12. He was referred to Medical Genetics evaluation because of worsening of ataxia/incoordination, speech, life skills, cognitive decline, spasticity and seizures. Ophthalmological evaluation was normal and CT scan showed reduced attenuation of the cerebral white matter. A homozygous pathogenic variant c.556G>A p.(Arg189His) was identified in exon 5 of HEXA gene. Then, complementary measurement of HEX A activity showed extremely low result (>0,09µmol/l/h; Ref.: >= 2 µmol/l/h). Patient 2: BSB, a 5-year-old male, second child of a non-consanguineous couple whose first son died at the age of 7 from a “demyelinating disease with progressive neurological deterioration”. He had normal neuropsychomotor development until the age of 4 when he started with ataxia, speech/cognitive decline and seizures. MRI showed deep white matter demyelination and ophthalmological evaluation was normal. A homozygous pathogenic variant c.533G>A p.(Arg178His) was identified in exon 5 of HEXA gene. HEX A activity measurement (493,5 nmol/h/mL) was lower than normal reference range (550,0 to 1675,0 nmol/h/mL). He has been using levetiracetam with partial improvement of seizures. His parents decided to try acetyl-DL-Leucine as off-label use. They refer a slight improvement of ataxia. **CONCLUSIONS:** WES can be used as a single test to diagnose metabolic disorders. Confirmation of the defect by a second measure (metabolites, enzyme assay etc) should also be performed.