P-070 - ATYPICAL PHENOTYPE OF NEURONAL CERIOD LIPOFUSCINOSIS TYPE 2: CASE SERIES OF SIX PATIENTS FROM ARGENTINA

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**INTRODUCTION:** Neuronal Ceroid Lipofuscinosis type 2 (CLN2) is a rare, progressive disorder caused by mutations in the TPP1 gene resulting in deficiency of the enzyme tripeptidyl peptidase 1 (TPP1). The typical phenotype presents with seizures and/or ataxia in the late-infantile period (age 2-4), in combination with a history of language delay followed by progressive childhood dementia, motor and visual deterioration and early death. Atypical phenotypes are characterized by a later onset, and in some instances longer life expectancies. Typical and atypical forms of CLN2 have increasingly been recognized since enzyme replacement therapy became available.

**AIM:** to analyze the clinical, biochemical and molecular findings in six patients diagnosed with atypical CLN2.

**MATERIALS AND METHODS:** a retrospective medical record review was conducted at our centre for this case series of six CLN2 patients diagnosed between years 2016 and 2018. TPP1 enzyme activity was determined in dried blood spots (DBS) and confirmed in leukocytes. Genetic analysis was done in all 6 patients.

**RESULTS:** six patients were diagnosed of CLN2. The median age at first symptom was 7,2 years old (range 6-9) and the median age at diagnosis was 13,2 yo (range 9-17). Cerebellar atrophy and ataxia were present in all patients. The initial diagnostic method was exome sequencing in one patient and TPP1 enzyme activity in five patients. From the five patients that underwent DBS test, 4 showed absent activity. The mean activity in leukocytes of the 5 patients was 4,6 nmol/h/mg protein (range 1,7-8,8). Mutation analysis showed at least one of the following: c.887-10A>G and c.827A>T in each patient. Three patients are receiving enzyme replacement therapy and their symptoms remain stable.

**CONCLUSIONS:** this case series expands the clinical, biochemical and genetic characterization of atypical CLN2 patients. We didn’t find that residual enzyme activity underlines a late onset phenotype. As ataxia was the common symptom we suggest including TPP1 DBS enzyme activity in the workout of ataxia. It is very important to be aware of these atypical forms of the disease to ensure early diagnosis, optimal patient care, prompt treatment and family support.