P-072 - TARGETED NEXT-GENERATION SEQUENCING: A POWERFUL TOOL FOR TYPE 2 NEURONAL CEROID LIPOFUSCINOSIS DIAGNOSIS CONFIRMATION

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INTRODUCTION: Neuronal ceroid lipofuscinoses (NCLs), a subset of lysosomal storage disorders, are rare inherited and severe neurodegenerative conditions. CLN2, the classical late infantile type, is caused by mutations in the TPP1 gene that lead to the deficiency of the TPP1 enzyme and seems to be the most prevalent CLN type in South America. It is characterized by a clinical picture initially dominated by speech delay, seizures and ataxia, followed by progressive dementia, motor and visual deterioration, and early death. The LSD Brazil Network, which was already providing enzyme diagnosis for CLN2, more recently implemented targeted next-generation sequencing (TNGS) for the CLNs. OBJECTIVE: To evaluate TNGS as a tool to improve CLN2 diagnosis. MATERIALS AND METHODS: In the period of one year (May 2017-April 2018), 656 Latin American cases (from Argentina, Brazil, Chile, Colombia, Ecuador and Mexico) were referred to the LSD Brazil Network for CLN2 investigation. Dried blood spots (DBS) were collected for biochemical (assay of TPP1 activity) and molecular (TNGS) analyses. Enzyme assay was performed using fluorimetry, and TNGS was performed using a previously validated panel including the TPP1 gene (with 100% of coverage). RESULTS: From the 656 samples, 46 showed activity of the TPP1 enzyme below the lower reference level (4 nmol/h/mL). TGNS was performed in these samples, and in 37 of them pathogenic mutations in both alleles of the TPP1 gene were found, confirming the diagnosis. CONCLUSION: Diagnosis of CLN2 can be conveniently performed in the same DBS sample, using enzyme activity for screening and TNGS for diagnosis confirmation.