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003 - A Novel CLN8 Mutation Underlies a Late Infantile Variant of Neuronal Ceroid Lipofuscinosis in Latin America

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Introduction: Neuronal ceroid lipofuscinosis (NCL), inherited neurodegenerative diseases of all ages, presents with storage of lipofuscin-like lipopigments in cerebral neurons and peripheral tissues. Mutations in CLN8 gene causing epilepsy progressive with mental retardation (EPMR) of Scandinavia and late infantile variant (vLI) phenotype in other countries had not yet been described in Latin America. The change p.Pro229Ala, found in the DNA of 2 individuals from Argentina and Mexico, was not validated as a mutation. **Aim:** To analyze and to validate changes in CLN8 gene in individuals suspected of vLI NCL. **Participants:** Fifteen individuals with normal *palmitoyl protein thioesterase 1* (*PPT1) and tripeptidyl peptidase 1* (*TPP1*) enzymes, positive electronic microscopy, and lack of mutations in other NCL genes. **Method:** Polymerase chain reaction, sequencing, and bioinformatics analyses were performed on the coding region of CLN8 gene, and validation of mutations was carried out on 200 control alleles. **Result:** The novel mutation c.1A>G, p.Met1Val, was validated for an Argentinean child with clinical suspicion of vLI who presented at the age of 3 years with onset of seizures, psychomotor retardation, myoclonus, cortical and cerebellar atrophy, and electronic microscopy with fingerprint and curvilinear profiles. Ocular disorders have not been studied. She died at 12 years of age. The changes p.Pro229Ala and p.Pro3Pro were validated as polymorphisms of the local population, which have been found, respectively, in 10 of 100 (1 in homozygous state) and 1 of 100 controls. **Conclusion:** The girl with vLI phenotype is the first confirmed CLN8 (vLI) case in Latin America. In the future, CLN8 should be considered in the search of possible mutations in individuals with vLI in the region.

004 - A Novel Familial Case of Diffuse Leukodystrophy Related to NDUFV1 Compound Heterozygous Mutations

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Introduction: Mitochondrial leukodystrophy due to complex I deficiency is an entity with high genetic heterogeneity, the mutations of the gene *NDUFV1* being one of the causes of this disease. It is an autosomal recessive entity that causes a variable phenotype, from a fatal neonatal onset to neurodegenerative disorders in adulthood. **Problem Studied:** We report 2 siblings, 5 and 2 years of age, with nystagmus, ataxia, impaired consciousness, hemiparesis, hyporeflexia, and psychomotor regression. In brain magnetic resonance imaging, signal abnormalities in large regions of the cerebral white matter were observed, suggesting a demyelinating disease. **Materials and Methods:** Genomic DNA was obtained from whole blood. The complete coding region of *NDUFV1* was amplified in patients and their parents. Each amplicon was purified. Direct sequencing was performed. Intron 6 and exon 7 amplicons from patient 1 were cloned. A skin biopsy was performed in the mother. RNA was isolated. The *NDUFV1* complementary DNA (cDNA) was amplified and directly sequenced. In silico analysis was performed. Following diagnosis, treatment with ubiquinol and riboflavin was started. **Results:** Both patients have the missense mutation c.1156C> T and the 42-base pair deletion in the gene *NDUFV1*. Bioinformatics analysis indicates that this deletion leads to messenger RNA (mRNA) synthesis with a premature stop codon. Probably, mutant mRNAs were recognized and degraded by the nonsense-mediated mRNA machinery. Analysis of the maternal *NDUFV1* cDNA supports this hypothesis. **Conclusion:** Our results add information on the molecular basis and the phenotypic features of mitochondrial disease caused by *NDUFV1* mutations. We can affirm that the mutations are causative of the phenotype. The patients are having a good therapeutic response to the treatment.

005 - Adherence to Treatment in a Group of Teenagers and Adults With Classic Phenylketonuria in Cuba

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Introduction: In Cuba, the National Program of Precocious Detection of Hyperphenylalaninemia began during the year 1983 for newly born infants in Havana and was generalized to the whole country since the year 1986. All patients who were