P-131 - LATE ONSET GLUTARIC ACIDURIA TYPE 1 PRESENTING AS LEUKODYSTROPHY

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INTRODUCTION: glutaric aciduria type 1 (GA1) is an autosomal recessive disorder caused by mutations in the GCDH gene, resulting in deficiency of enzyme glutaryl-CoA dehydrogenase. This leads to accumulation of metabolites, mainly glutaric acid and 3-hydroxyglutaric acid, which result toxic for the CNS. GA1 patients present with an acute onset in 80–90% of cases, developing an acute onset type with striatal injury following catabolic stress during the first 6 years of life, and consequently a predominantly dystonic movement disorder. The term late-onset has been used for patients diagnosed after the age of six years, who presented with non-specific symptoms and predominantly white matter changes on MRI.

METHODS: Revision of clinical record of a patient diagnosed with GA1

AIM: To describe a late onset case of GA1

CASE: A 22-year-old female patient complained of headache. Her physical examination was normal. MRI of the brain revealed confluent bilateral symmetric white matter lesions on T2 and FLAIR, with widening of Sylvian fissures and frontotemporal hypoplasia. A molecular leukodystrophy panel showed negative results. Exome testing identified a pathogenic variant in homozygosis (p.ArgG409Trp) in the GCDH gene, mutation that has been associated with late onset GA1. Laboratory tests revealed a high level of urinary glutaric acid and 3-hydroxyglutaric acid, very low plasmatic carnitine and elevated glutaryl carnitine, confirming GA1 diagnosis. She started treatment with L-carnitine and restriction of natural protein.

DISCUSSION: Here we present clinical, biochemical, neuroradiological and genetic data of a late onset GA1 patient. The clinical presentation was non-specific, frontotemporal hypoplasia and white matter abnormalities were seen on MRI. Diagnosis was achieved through exome sequencing and subsequent biochemical analysis. Expanded NBS would have detected this case at birth, but it wasn’t requested because it is not mandatory. Many doctors are not educated about the importance of this test. Regarding molecular panels, as late onset GA1 can present with white matter abnormalities we recommend to include GCDH in the leukodystrophy genetic panels.

CONCLUSIONS: it is important to perform metabolic tests in adult patients with white matter lesions in MRI since some treatable metabolic diseases (such as GA1) can present images of leukodystrophy.