P-143 - GLUTARIC ACIDEMIA TYPE 1. WIDE PHENOTYPIC EXPRESSION

Spécola N\textsuperscript{1}, Núñez-Miñana M\textsuperscript{1}, Salerno M\textsuperscript{1}, Bonvin J\textsuperscript{1}, Procopio D\textsuperscript{1}, Collini M\textsuperscript{1}, Borrajo GJC\textsuperscript{2}, Raskovsky V\textsuperscript{3}, Schenone AB\textsuperscript{4}

\textsuperscript{(1)} Hospital De Niños Sor María Ludovica. \textsuperscript{(2)} Fundación Bioquímica Argentina. \textsuperscript{(3)} Hospital Nacional A. Posadas. \textsuperscript{(4)} FESEN. normaspecola@gmail.com. La Plata - Argentina

\textbf{INTRODUCTION:} Glutaric aciduria type-1 (GA1) is an autosomal recessive disorder caused by a glutaryl-CoA dehydrogenase deficiency due to GCDH gene mutations. This enzyme participates in the catabolism of lysine, hydroxylysine and tryptophan. Glutaric (in high excretory forms) and 3-hydroxyglutaric acid in urine and glutarylcarnitine in blood are increased, leading to a secondary carnitine deficiency. Acute-onset forms present during the first years of life with acute encephalopathy with extrapyramidal signs. Further subtypes are insidious movement disorder and late-onset with non-specific symptoms. Macrocephaly is usually presented from early life. \textbf{OBJECTIVE:} Describe clinical, biochemical and molecular aspects of GA1-patients assisted at present in our service. Emphasize the variable clinical presentations with at least two forms: acute and late-onset.

\textbf{MATERIALS AND METHODS:} 7 patients whose diagnosis was biochemically established through the measurement of urinary organic acid by GCMS, acylcarnitine profile, and serum carnitine (free and total) after clinical and neuroimaging (MRI) suspicion, are presented. Mutation analysis was confirmed by Sanger sequencing of gDNA. Treatment was started at diagnosis in all patients and continued until the age of 6 years. It consisted on a protein-restricted diet, supplemented with a special amino acid mixture and L-carnitine. \textbf{RESULTS:} All patients were symptomatic during the first 2 years (4 to 22 months). 5 patients presented with severe early-onset encephalopathy during a febrile illness, and developed a dystonic dyskinetic tetraplegia. Two of them substantially improved on follow-up. MRI showed striatal changes, variable cortical atrophy and enlarged sylvian fissures. The other 2 patients presented with non-specific symptoms (focal seizures) without neurological signs, and diagnosis was suspected after brain MRI showing enlarged sylvian fissures without striatal lesions, one of whom developed extensive white matter changes. Only 2 patients presented with non-excretory biochemical phenotype. Two patients were homozygous for the more frequent R402W mutation but presented with different phenotype. \textbf{DISCUSSION:} Even though the small number of patients, they represent the wide clinical phenotype of GA1. The presence of macrocephaly and a correct MRI interpretation allowed the diagnosis in the oligosymptomatic forms. Non-excretory patients need molecular diagnosis and demand an exhaustive acylcarnitines examination when low free-carnitine is present. No phenotype/genotype correlations were detected.