P-167 - LYSINURIC PROTEIN INTOLERANCE: INVESTIGATIVE PROCESS AND DESCRIPTION OF A NOVEL VARIANT IN SLC7A7 GENE

Oliveira BM¹, Menezes TV¹,², Coelho DM¹, Sitta A¹, Refosco LF¹, Schwartz IVD¹,², De Souza CFM¹

(1) Hospital de Clínicas de Porto Alegre. (2) Universidade Federal do Rio Grande do Sul.

INTRODUCTION: Lysinuric protein intolerance (LPI) or hyperdibasic aminoaciduria type 2 is an ultra rare inborn error of metabolism with autosomal recessive inheritance characterized by deficiency in the dibasic amino acid transporter (SLC7A7). The most prevalent symptoms are intestinal malabsorption, hyperammonemia, vomiting and hepatosplenomegaly. The diagnosis is made by detecting increased urinary excretion of lysine, arginine and ornithine, reduced plasma lysine, postprandial hyperammonemia, hyperferritinemia and dyslipidemia. Maintenance treatment involves protein restriction and citrulline administration.

OBJECTIVE: To describe clinical and molecularly the investigation steps of a complex clinical case that led to diagnosis of LPI. Informed consent was obtained.

CASE REPORT: A 11-year-old female patient born to consanguineous parents was referred for genetic evaluation due to suspicion of glycogen storage disease (GSD). At 6 months, she started investigation due to progressive hepatosplenomegaly, growth restriction, chronic diarrhea, protein aversion, vomiting and recurrent otitis. At age 5, liver biopsy was compatible GSD and, even without hypoglycemia, GSD treatment had been instituted. She performed molecular and radiological investigation for hemochromatosis, with no evidence of iron deposition. At age 9, she presented muscular fatigability and reduced muscle trophism, and had a pathological tibial fracture secondary to osteoporosis. Laboratory tests revealed hyperferritinemia (levels greater than 1000ng/mL), dyslipidemia and mild hyperlactacidemia; investigation for lysosomal diseases was normal; amino acid dosage showed increase of alanine and glutamine and reduction of lysine. Urinary dosing was performed, with a significant increase of lysine, alanine and glutamine, associated with increased postprandial ammonia, confirming LPI. Complete sequencing of SLC7A7 gene identified the biallelic novel variant c.1109_1133del (p.Leu370Serfs*141).

DISCUSSION AND CONCLUSION: In the presence of complex clinical phenotypes that involve short stature, specific food aversion and somatic signs, it is important to establish the hypothesis of a hereditary metabolic disease, even considering its rarity. The definitive clinical and biochemical diagnosis is fundamental to terminate a prolonged diagnostic search and to allow adequate management and genetic counseling. LPI is an ultra rare inborn error of metabolism, but with possibilities of treatment and excellent clinical response, preventing consequences of the disease. Molecular investigation also led to description of a novel variant in SLC7A7 gene.