P-119 - DIAGNOSIS OF HMG-COA (3-HYDROXY-3-METHYLGLUTARYL-COA) LYASE DEFICIENCY BY UNTARGETED METABOLOMIC ANALYSIS IN PLASMA

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INTRODUCTION: HMG-CoA Lyase deficiency is a rare inborn error of leucine metabolism that causes severe episodes of hypoglycemia and metabolic acidosis. Misleading and delayed diagnoses are frequent. OBJECTIVE: The objective of this work is to describe the usefulness of metabolomic analysis in patients with hypoglycemic syndrome and suspected neurometabolic disease with nonspecific manifestations and non-conclusive biochemical findings. MATERIALS AND METHODS: We present the case of a two-and-a-half-year-old Colombian patient, who presented two episodes of severe hypoglycemia of difficult control with wide anion gap metabolic acidosis, which were preceded by frequent vomiting, stupor, and hypotonia. He was admitted twice to the intensive care unit, where hormone studies were normal. Plasma amino acids, ammonium and organic acids in urine were considered normal. The patient received symptomatic management, achieving full recovery on both occasions. Given the possibility of metabolic disease, analysis by non-targeted metabolomics in plasma was performed (Metabolon Inc.) This test identifies molecules between 50-1,500 Daltons (Da). The identification is performed using four different types of high-performance Ultra Performance Liquid Chromatography (UPLC) instruments paired with Mass Spectrometry (UPLC/MS). The identification of each molecule is confirmed against a proprietary chemical library consisting of accurate molecular weight/mass plus information on any adduction, in source fragmentation, and/or polymerization, retention time/index on the chromatography columns, and mass spectral fragmentation patterns. Overall, process variability is assessed using stable isotope standards and duplicates. RESULTS: Metabolomic analysis demonstrated elevated levels of 3-methylglutaryl carnitine, adipate, dodecanedioate, hexadecanedioate, and etradecanedioate. 3-methylcrotonylglycine was not detected, and beta-hydroxyisovalerate was normal. HMG-CoA LYASE DEFICIENCY was considered, because more than 50% (5 of 7) of the biomarkers associated with the metabolomic biochemical signature of this disorder were outside the expected range. Treatment was started with dietary restriction of leucine as a precursor of the affected metabolic pathway and L-Carnitine supplementation. CONCLUSION: Metabolomic analysis is useful for the diagnosis of HMG-CoA LYASE DEFICIENCY, and it is also a valuable tool for the study of patients with suspected metabolic disease.