Long-Term Follow-up for Patients with Mitochondrial Carbonic Anhydrase 5A Deficiency

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Introduction: Mitochondria carbonic anhydrase 5A (CA5A) deficiency (MIM # 615751) is an ultra-rare inherited metabolic disorder caused by biallelic mutations in *CA5A* gene. The combination of hyperammonemia, lactic acidosis and ketonuria with or without hypoglycemia is highly suggestive of CA5A deficiency. We report the long-term follow up of the first two reported cases of CA5A deficiency.
Case presentation: The index patient is a 13-year-old female and her sibling, an 11-year-old male, who presented with neonatal hyperammonemia associated with hypoglycemia, elevated lactate, ketonuria, and respiratory alkalosis with decreased HCO3. The diagnosis was made in the two affected siblings through the TIDEX study that identified homozygous pathogenic variant in *CA5A* gene (NM_001739.1: c.697T>C, (p.Ser233Pro)). The clinical course of the index patient revealed three additional episodes of decompensation triggered by intercurrent illnesses and presented similar to her neonatal presentation, while her sibling did not experience any further episodes of decompensation. These episodes were successfully treated with parenteral dextrose, enteral carglumic acid and occasionally parenteral lipids. Management of intercurrent illness includes sick day formula high in carbohydrates and fats. Currently, they display normal growth and development suggestive of favourable prognosis and in keeping with the previously reported cases.
Discussion: Early diagnosis of CA5A allows prompt treatment, thus prevents severe complications. With the proper management, the long-term outcome is reassuring, and does not seem to affect the psychomotor development or physical growth. Impact on life longevity needs to be assessed for longer durations. In addition, our cases suggest some intrafamilial variability, which requires further assessment.