A Patient with Recurrent Severe Hypoglycemic Attacks: Mitochondrial Complex III Deficiency, Nuclear Type III; A Novel UQCRB Variant

Merve Koç Yekedüz1, Ümmühan Öncü1, Engin Köse1, Fatih Ezgü2 and Fatma Tuba Eminoğlu1
1 Ankara University Faculty of Medicine, Department of Pediatric Metabolism
2 Gazi University Faculty of Medicine, Department of Pediatric Metabolism

Background
✓ Mitochondrial complex III deficiency shows an autosomal recessive or a mitochondrial inheritance pattern. To date, mitochondrial complex III deficiency, nuclear type 3 attributable to a pathogenic variant of the UQCRB gene, has been identified in only two pediatric patients; both presented with hypoglycemia and lactic acidosis.

Case
✓ The male patient was admitted on the first day of life to the neonatal service and hospitalized 20 days due to tachypnea, metabolic acidosis, and severe hypoglycemia. He was admitted to the hospital seven times with abdominal pain, vomiting, and fever up to ten years of age.
✓ On his physical examination, he was at the 50th percentile and 75th percentile for weight and height, respectively. There was no dysmorphic facial feature. He had normal psychomotor development and neurocognitive functions.
✓ At all admissions, blood tests revealed hypoglycemia, metabolic acidosis, and hyperlactatemia. Blood levels of growth hormone, adrenocorticotrophic hormone, cortisol, C-peptide, and insulin were normal. Metabolic tests were repeated several times, and the analyses of blood amino acids, urine organic acid, and carnitine/acylcarnitine did not reveal any significant results. Neuroimaging test showed nonspecific cerebral white matter lesions in the posterior periventricular area.
✓ A whole-exome sequencing (WES) analysis was performed at ten years of age, identifying a novel homozygous c.309_313delAGAAA (p.glu104ArgfsTer10) pathogenic variant of the UQCRB gene. The patient’s parents were also heterozygous carriers for the same variant of the UQCRB gene.

Conclusion
Once the common causes of recurrent hypoglycemia are excluded, it is essential to perform a whole exome sequencing analysis for other rare reasons. Thus, rare disorders like mitochondrial complex III deficiency can be diagnosed. To the best of our knowledge, this is the third patient with a UQCRB pathogenic variant reported in the literature to date.