ABCC8 Frameshift Mutation in Exon 28 (c.3512delT) is a Founder Mutation for Autosomal Recessive Hyperinsulinemic Hypoglycemia in Eastern Anatolia

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A 12-day-old male patient was referred to our hospital due to macrosomia, tachypnea and hypoglycemia since the first day of his postnatal life. He was born at term, via C/S with a birth weight of 4500 g, as the first child of a 21-year-old healthy mother and a 26-year-old healthy father. His mother had mild gestational diabetes after 6 months of pregnancy which was regulated by a dietary regimen. Prenatal history was otherwise unremarkable. The parents and both of the grandparents were first cousins of their partners and also both of the grandmothers and grandfathers were first cousins of each other. There was no family history of similar diseases, neonatal diabetes or any inherited disease reported.

After the initial evaluation, insulin level was determined as 105 µIU/mL (C-peptide: 15.7 ng/mL) at critical sample. Metabolic screening and biochemical values were normal and the keton bodies were negative. Hypoglycemia was resistant despite high-glucose infusion rate, hydrocortisone, diazoxide, somatostatin and nifedipine. After the confirmation of hyperinsulinism, the genetic testing was performed. The patient was homozygous for ABCC8 frameshift mutation, c.3512delT in exon 28. The parents were both heterozygous for the same mutation and this result confirmed the diagnosis of autosomal recessive congenital hyperinsulinism.

After the patient underwent near total pancreatectomy, pathological evaluation confirmed the diffuse disease. Exocrine insufficiency was excluded and the patient was discharged with octreotide 45 µg/kg/d, qid, after the full enteral feeding was achieved. Although this mutation was reported by Calton et al in 2013, the clinical presentation and type of inheritance was completely different. The case which was presented in 2013 was diagnosed with focal congenital hyperinsulinism resulting from a paternally-inherited recessively-acting mutation of ABCC8 and pancreatic paternal uniparental disomy (UPD) for chromosome 11p15.

This patient was admitted from the middle-south part of Anatolia. After conducting a search of the medical literature using the terms "ABCC8 frameshift mutation c3512delT in exon 28" and "autosomal recessive hyperinsulinemic hypoglycemia", we did not identify any previously published reports of this type of inheritance. However, 4 similar cases were reported from 3 neighbor cities from the east part of Anatolia in the following months. These results were interpreted as "possibly suggesting a founder effect" by the authors. After we noticed this report, we investigated the details of family history once more. Interestingly, we learned that the great ancestors of our patient were also inhabitants of the above-mentioned region in the east. Therefore, the results of this patient confirmed that ABCC8 frameshift mutation, c.3512delT in exon 28 is a founder mutation in Eastern Anatolia.