LIPIN1 DEFICIENCY: A NOVEL MUTATION IN A PATIENT WITH RECURRENT RHABDOMYOLYSIS

Zeliha Haytoğlu, Deniz Kor, F. Derya Bulut, Sebile Kilavuz, Esra Kara, Burcu Köşeci, Ezgi Burgaç, İrem Kaplan, Sevcan Bozdoğan, Neslihan Özc, Özd Hergüner, H. Neslihan Önenli Mungan
Cukurova University Faculty of Medicine, Department of Pediatrics

BACKGROUND
Lipin-1 deficiency is an autosomal recessive disorder due to mutations in LIPIN1 gene. The clinical presentation is often severe, characterized with recurrent rhabdomyolysis, occurring especially in early childhood and frequently triggered by febrile illnesses and less commonly by exercise, anesthesia, and fasting. As creatine kinase (CK) levels can rise up to 10,000 IU/L, renal failure may exist. Autopsies of these patients revealed also cardiomyopathy and hepatosteatosis. Between the attacks usually clinical evaluation is normal, although chronic myolysis with proximal weakness can be observed. Lipin-1 deficiency should be considered in children with recurrent rhabdomyolysis who had normal plasma acylcarnitine profile. Diagnosis is made by molecular analysis. Symptomatic treatment of rhabdomyolysis includes aggressive intravenous fluid administration, monitoring of kidney and heart functions and electrolytes, at the end haemodialysis if renal function is felt to be at risk.

CASE PRESENTATION
A 6-year-old male presented with myalgia and recurrent rhabdomyolysis. His parents were consanguineous. One of his cousins had Duchenne Muscular Dystrophy. The first rhabdomyolysis episode occurred at the age of 18 months following an acute gastroenteritis. Second episode occurred after a prolonged hypoglycemia due to a gastroenteritis at 4 years of age and CK levels were above 200 000U/L. Between the episodes, CK levels were mildly elevated. He had no chronic diseases. Growth parameters and developmental milestones were appropriate for his age. Systemic, neurological, and cardiological evaluation revealed no abnormalities. Urine organic acid and acylcarnitine profile were both normal. Electromyography was compatible with myogenic pattern. Intramyocellular lipid deposition was observed on muscle biopsy. Molecular analyses for myophosphorylase deficiency and carnitine palmitoyltransferase-2 deficiency detected no mutations. Genetic analysis for LIPIN1 gene put forward a novel, homozygous missense p.D481H (c.1441G > C) pathogenic variant.

CONCLUSION
Loss-of-function mutations in genes encoding aldolase, phosphofructokinase, glycogen storage enzymes, CPT1, CPT2, very-long-chain acyl-CoA dehydrogenase enzymes, or subunits of cytochrome c oxidase have been reported to cause myopathy and rhabdomyolysis. Lipin1 deficiency is another relatively common genetic cause of rhabdomyolysis in children which leads to morbidity and mortality. As, the metabolic profile including fatty acid oxidation, CPT2 activity, and respiratory complex activities of lipin1-deficient patients does not reveal any clues and triglyceride, lactate, cholesterol, creatinine levels are completely normal, genetic analysis is crucial for specific diagnosis. Considering the mortality probability during the rhabdomyolysis bouts and ambiguous prognosis, its, it is necessary to draw the attention of pediatricians, pediatric neurologists, and nephrologists, who are frequently dealing with the cases. Up to 60% of patients with unexplained recurrent rhabdomyolysis in early childhood who have normal acylcarnitine profile are shown to have lipin-1 deficiency. We report this case, as a novel mutation was detected and there were two different inherited cause of rhabdomyolysis in the same family.