Novel PNPLA2 gene mutation in a Turkish patient causing neutral lipid storage disease with myopathy

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**Introduction:** Mutations in the adipose triglyceride lipase (ATGL), an enzyme that hydrolyzes fatty acids from triacylglycerol (TG) stored in multiple tissues into cytoplasmic lipid droplets (LDs), causes the autosomal recessive disorder Neutral Lipid Storage Disease with myopathy (NLSDM) (1). ATGL protein is coded by PNPLA2 gene. NLSDM patients are mainly affected by progressive myopathy, cardiomyopathy and hepatomegaly. Their clinical severity appears to be highly variable with particular reference to cardiac involvement (2,3,4,5).

**Case:** A 9-year-old female patient applied to the pediatric outpatient clinic because of pain in her legs. The patient had a complaint of fatigue after prolonged hunger. She was referred to the pediatric metabolism polyclinic because of elevated transaminase and creatine kinase levels in his examinations in the pediatric outpatient clinic. She was born at term with c/s at 4050 gr. Her other two siblings were healthy. Her parents were consanguineous. In the physical examination; development was normal, weight and height were 50p according to age. There was no hepatospleomegaly. In her neurological examination; muscle strength was normal in the lower and upper extremities, bilateral gastocnemius was hypertrophied. Cerebellar tests were normal. There were no neurocutaneous signs. In the laboratory tests of the patient; Transaminase elevation was first noticed at the age of 1 year. AST was 126 U/L (0-73 U/L), ALT was 167 U/L (0-41 U/L), creatine kinase was between 1600 and 3098 U/L (normal value < 190 U/L). Cardiological evaluation with ECG and heart echo scanning and abdominal ultrasonography at 8 and ½ years of age was normal. Metabolic studies including blood lipid profile and Urine organic acid analysis, tandem mass spectrometry, peroxisomal profile were also normal. Pompe enzyme level was normal. Electromyelography was consistent with myopathy. Cranial MR and Cranial Diffusion MR were normal. In the genetic study of the patient; muscular dystrophy panel, CPT 2 panel was normal. We found a novel homozygous mutation c.45C>A(p.CYS15) in the PNPLA2 gene. The patient was diagnosed with neutral lipid storage disease.
**Discussion:** Lipid storage myopathies (LSMs) are a group of metabolic disorders caused by different errors of fats metabolism (6). Impairment of ability to metabolize fats induces an abnormal lipid storage in muscle fiber, as well as in other tissues. Neutral lipid storage disease with myopathy (NLSD-M) is an ultra-rare mostly autosomal recessive disorder caused by mutations in the PNPLA2 gene, which encodes adipose triglyceride lipase (ATGL). The condition was first reported in 2007 (1,7). Her parents were consanguineous. This situation supported that the genetic transmission was autosomal recessive. In the genetic analysis of our patient, a new homozygous mutation was found in the PNPLA2 gene. The clinical features of NLSD-M include progressive myopathy, cardiomyopathy, hepatomegaly, diabetes, chronic pancreatitis, short stature and increased serum creatine kinase (CK) levels (8). Significant clinical involvement in our patient was myopathy and elevated transaminases. The degree of clinical manifestations appears highly variable: from minimal symptoms to a more severe condition, causing physical disability and premature death due to dilated cardiomyopathy. However, since NLSDM is a rare metabolic condition, the pathophysiology of the disease is largely unclear and phenotype-genotype correlations remain incomplete (9). Cardiac echocardiography of our patient was normal. This resulted in a better prognosis.

**Results:** Screening of the PNPLA2 gene should be considered for patients presenting with high levels of creatine kinase and transaminase, progressive muscle weakness, and systemic lipid accumulation.

**Resources:**