

Genetic Analysis of Lipodystrophies and Recently Found Mutations

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Lipodystrophies are a group of diseases which cause selective loss of body fat tissue and tendency to insulin resistance. It may be inherited or acquired. The severity of the associated metabolic complications is proportional to the amount of fat tissue lost. The genetic forms of the disease are congenital generalized lipodystrophy (CGL) and familial partial lipodystrophy (FPL). *AGPAT2*, *BSCL2*, *CAV1*, and *PTRF* gene mutations are responsible for CGL which is autosomal recessively inherited, while *LMNA*, *PPARG*, *AKT2*, and *PLIN1* gene mutations are responsible for autosomal dominantly-inherited FPL.

In a total of 23 patients (10 families with CGL preliminary diagnosis and 4 families with FPL preliminary diagnosis) who applied to Ege University Hospital Medical Genetics Department, *AGPAT2*, *BSCL2*, *CAV1*, *PTRF*, *LMNA*, *PPARG*, *AKT2* and *PLIN1* gene mutations were investigated by sequence analysis method.

AGPAT2 gene mutation was found in 6 of CGL families, *BSCL2* in 3, and *PTRF* gene mutation in 1 of them. This group had 3 newly defined mutations. *LMNA* gene mutation was found in 3 of FPL families and one other family presented a *PPARG* gene mutation. This group had 3 newly defined mutations as well.

Finally, it is important to find out the genetic etiology in lipodystrophies in order to detect family members who are at risk and to prevent metabolic complications.

Key words: Lipodystrophy, genetics, mutation

Neonatal Diabetes Mellitus due to a Novel Mutation in the *GATA6* Gene Accompanying Renal Dysfunction: A Case Report

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Objective: Neonatal diabetes mellitus (NDM) arising from pancreatic agenesis is extremely rare. Mutations in the *PDX1*, *PTF1A*, *HNF1B*, *EIF2AK3*, *RFX6*, and *GATA6* genes have been shown to result in pancreatic agenesis or hypoplasia. We present a permanent NDM patient with pancreas agenesis and congenital cardiac defects associated with renal dysfunction which has not been previously identified.

Methods: A male infant was born at 37 weeks gestation by cesarean section because of fetal growth restriction and oligohydramnios. On the first week of life, hyperglycemia was detected. Two months later, the patient was referred to our hospital for glycemic dysregulation, renal and cardiac dysfunction.

Results: Laboratory investigations revealed a venous glucose level of 256 mg/dL with glycosuria but no ketonuria or acidosis. His serum hemoglobin A1c was 6.6% (normal range, 4.8-5.9%). The patient also had hypoalbuminemia (serum albumin: 2.9 g/dL). Total protein-to-creatinine ratio in spot urine (2.7) was elevated (normal range: <0.7) with normal serum urine and creatinine levels. Abdominal ultrasonography failed to identify any pancreatic tissue. Echocardiography revealed large secundum atrial septal defect, small muscular ventricular septal defect, valvular pulmonary stenosis, and patent ductus arteriosus. Insulin pump therapy including continuous glucose monitoring system was initiated. Analyses of exons 2-7 and exon/intron boundaries of the *GATA6* gene were performed and a novel heterozygous nonsense mutation (p.Cys414Ter; c.1242C>A) was identified in the *GATA6* gene.

Conclusion: This report describes a novel heterozygous nonsense *GATA6* mutation (p.Cys414Ter) resulting in the clinical picture of congenital heart defects, pancreas agenesis, renal dysfunction (persistent proteinuria), and NDM.

Key words: Neonatal diabetes mellitus, *GATA6* gene, renal dysfunction, pancreatic agenesis, proteinuria