(P-08)

A Case of Congenital Generalized Lipodystrophy Type 2 with Novel *BSCL2* Gene Mutation

Fatih Gürbüz, İhsan Turan, Mehmet Taştan, Ali Kemal Topaloğlu, Bilgin Yüksel

Çukurova University Faculty of Medicine, Department of Pediatric Endocrinology, Adana, Turkey

Congenital generalized lipodystrophy (CGL) is a rare autosomal recessive disorder characterized by generalized absence of adipose tissue, extreme insulin resistance, hypertriglyceridemia, hepatomegaly, hepatic steatosis, and early onset of diabetes. Herein, we described a case with CGL2 due to novel homozygous *BSCL2* gene mutation.

Three years-seven months old girl presented with a general lack of subcutaneous fat, prominent muscular hypertrophy, hollow cheeks, triangular face, acanthosis nigricans in fold areas, especially in the neck-bilateral axilla, hypertrichosis in arms-legs, abdominal swelling due to hepatomegaly, which are characteristic physical findings of CGL. Her parents were first-degree cousins. In laboratory: Glucose 75 mg/dL (70-105), C-peptide 6.8 ng/mL (0.9-4.3), insulin 47.4 µIU/mL (1.9-23), HbA1c 5.2% (4.8-6.0), total cholesterol 132 mg/dL (< 200), and triglyceride 134 mg/dL (< 200). Hyper triglyceridemia was firstly detected at 5 years of age with metformin therapy. Despite taking metformin treatment, the patient's insulin levels increased steadily, and serum AST levels were also elevated. At the age of nine, grade 2 hepatic steatosis with hepatomegaly was detected in ultrasonography.

During follow-up, her HbA1c level has increased to 6.5% at the age of eleven years and three months. The fasting and 2-hour post-OGTT glucose-insulin levels of the patient were 152 mg/dL-158.3 µIU/mL and 209 mg/dL-95.8 µIU/mL, respectively. Insulin detemir was started in addition to metformin treatment because of diagnosis diabetes.

A clinical diagnosis of CGL was corrected by the identification of a novel homozygous mutation (IVS2 + 2 T > C) in the *BSCL2* gene. Analyzes with GenSplicer and Human Splicing Finder modeling programs show that this mutation can cause the disease.

(P-09)

Gene Conversion and Congenital Adrenal Hyperplasia: Two Case Reports

Mine Balasar[1], Beray Selver Eklioğlu[2], Pelin Taşdemir[1], Mehmet Emre Atabek[2]

[1]Necmettin Erbakan University Meram Faculty of Medicine, Department of Medical Genetics, Konya, Turkey

[2]Necmettin Erbakan University Meram Faculty of Medicine, Department of Pediatric Endocrinology, Konya, Turkey

Congenital adrenal hyperplasia (CAH) is one of the inborn metabolic disorders inherited in an autosomal recessive manner. 95% of CAH cases are due to 21-hydroxylase deficiency. 21-hydroxylase enzyme have an active gene and a pseudogene. The rearrangements between these two genes play an important role in the pathogenesis of CAH. Herein, we present the cases of two siblings with different phenotypes and different chromosomal sex who both have a large gene conversion and a point mutation.

21-hydroxylase gene strip assay and MLPA analysis were performed in the two sibling cases.

The case with male phenotype has been diagnosed with CAH due to salt-wasting crises, macrogenitalia, and hyperpigmentation when he was 1 month old. Karyotype analysis results were 46,XY and SRY(+). The female case with 46,XX has been diagnosed with CAH due to salt-wasting crises and ambiguous genitalia in the newborn period. Results of CAH strip assays were c.89C > T(P30L) (N/M), c.329-336del(Del 8bp E3) (N/M), c.290-13A/C > G (I2 Splice) (M/M) in both cases. In MLPA analysis, heterozygous increase in CYP21A1P-1 (-113 SNP) and CYP21A1-P-3 (del8nt) mutation regions, heterozygous loss in *CYP21A2*-1wt (-113 SNP) and *CYP21A2*-3 wt (del8nt) regions, and homozygous mutations in *CYP21A2*-3 wt (I2 G-C), *CYP21A2*-3 wt (I2G-A) regions were detected. It was thought that the cases have received an allele with heterozygous mutation in c.290-13A/C > G (I2 Splice) region from one parent and a gene converted allele from the other. Mutation analysis was planned for parents.

The cases were presented here in order to emphasize the importance of MLPA analysis when diagnosing CAH.

(P-11)

Heterozygous p.D61G Mutation in a Patient with Noonan Syndrome

Hüseyin Anıl Korkmaz

Balıkesir Atatürk State Hospital, Clinic of Pediatric Endocrinology, Balıkesir, Turkey

Noonan syndrome is an autosomal dominant disease resulting from mutations in the ras-associated mitogen activating protein kinase pathway involved in signal transduction associated with cell proliferation, differentiation, life, and metabolism.

A girl from non-consanguineous family was referred to pediatric endocrine department because of short stature. The 15-year-old girl was born with weight 2300 g by caesarean section and was followed due to pulmonary valve stenosis and mitral insufficiency in the pediatric cardiology department; she underwent cardiac surgery during the infant period. On physical examination height was 131.6 cm (< 3 p), height SDS -4.73, weight 28.7 kg (< 3 p), weight SDS -5.31, target height 150.65, and target height SDS was 1.95. Physical examination also revealed dysmorphic facial appearance with webbed neck, hypertelorism, epicanthus,

downward palpebral fissures, low-set ears rotated backward, triangular face, micrognathia, high-arched palate, widely spaced nipples, cardiac operation scar, and pectus excavatum. Full blood count, biochemical analysis, and thyroid function tests were found to be normal in terms of short stature.

Since the dysmorphic features were consistent with Noonan syndrome, p.D61G heterozygote mutation in *PTPN11* gene was found. The patient with Noonan syndrome was started treatment with 45 micrograms/kg/dose of growth hormone because of short stature and insufficient height velocity.

In this report, Noonan syndrome patient associated with heterozygous P.D61G mutation was presented. Early diagnosis and appropriate treatment will prevent the development of complications.

(P-12)

A New Mutation in an Infant with Hypercalcemia

Sevinç Odabaşı Güneş, Ayça Törel Ergür

Kırıkkale University Faculty of Medicine, Department of Pediatric Endocrinology, Kırıkkale, Turkey

Hypercalcemia is a serious condition, which may threaten life. Familial benign hypocalciuric hypercalcemia (FBHH) is a benign situation which develops due to inactivating mutation of calcium sensing receptor (CaSR). Differential diagnosis of FBHH is important in order to prevent unnecessary laboratory tests and treatments.

A three-month-old infant, who was born 2950 g on 38th gestational week to healthy unrelated parents, was admitted to pediatric endocrinology department due to high TSH levels. Her anthropometric evaluation was appropriate for her age and she did not have any dysmorphic stigmata. She was diagnosed with hypothyroidism and put on LT4 treatment. When she was 5 months old, her serum calcium was 11.34 mg/dL (8.8-10.6).

The patient did not have any clinical symptoms of hypercalcemia. Serum phosphorus, parathormone, vitamin levels, urine calcium/creatinine, urine analysis, and renal ultrasonography were normal. Oral hydration was started and her calcium level decreased to 10.8 mg/dL on follow-up. Biochemical and hormonal parameters of father and mother of the patient were evaluated to determine the etiology of hypercalcemia. Whole exome sequencing was performed to the patient and homozygote mutation on exon 7 (p.Glu1011Gln/c.3031G>C) was detected. In order to determine if the parents of the patient had heterozygote mutation or if this is a *de novo* mutation, genetic analysis was also performed to the parents.

To the best of our knowledge, the mutation found in our patient was not mentioned in the literature before. We think that this mutation may cause FBHH in our case. Functional evaluation should be performed for definitive diagnosis.

(P-13)

An Infant with Leydig Cell Hypoplasia Presenting with Bilateral Inguinal Masses

Fatma Ö. Çömlek[1], Fatma Seyrek[2], Raif Yıldız[2], Serdar Ceylaner[3], Filiz Tütüncüler[1]

[1]Trakya University Faculty of Medicine, Department of Pediatrics and Pediatric Endocrinology Unit, Edirne, Turkey

[2]Trakya University Faculty of Medicine, Department of Pediatrics, Edirne, Turkey

[3]Intergen Genetic Diagnosis Center, Ankara, Turkey

Luteinizing hormone/chorionic gonadotropin receptor *(LHCGR)* is essential for normal male sex differentiation. Inactivating mutations of *LHCGR* gene result in varying degree of Leydig cell hypoplasia (LCH) that causes 46,XY DSD.

A 2-year and 1-month-old female infant was referred to us for further evaluation of DSD. She was the fourth child of healthy consanguineous Turkish parents and was born at 38 weeks. The patient was raised as female. Her mother noticed bilateral masses on her inguinal areas and brought her to the local hospital. The abdomen USG revealed bilateral masses (possibly testicular structures) on both inguinal region. On admission, her weight was 0.95 SDS, height was 3.4 SDS, and physical examination was normal except for the palpable gonads in both inguinal regions. Her external genitalia was completely female in appearance.

Hormonal investigations showed low testosterone (13.6 ng/mL) with high gonadotropin (follicle-stimulating hormone = 6.1 IU/L and LH = 12.53 IU/L) and AMH (>23 ng/mL) levels. Serum levels of 17-OHP, DHEAS, and AS were within normal ranges. Testosterone response to 3-day HCG stimulation test was absent (sT = 14.47 ng/dL). The karyotype was 46,XY. Pelvic ultrasound revealed absent uterus and ovaries but presence of testicular structures in the superior inguinal canal bilaterally. Bone age was 2 years. The diagnosis of LCH was considered in the patient. *LHCGR* gene sequencing demonstrated a homozygous c.1435C>T (p.R479*) mutation that confirmed the diagnosis. In the parents genetic analysis is being done.

Although LHC is usually diagnosed at pubertal or postpubertal period, this case demonstrates that LCH can be seen in infancy period presenting with inguinal masses.