(P-30)

A Case of 46,XX DSD Due to a Novel Mutation in P450 Oxidoreductase Gene

Melek Yıldız[1], Alper Gezdirici[2], Banu Aydın[1], Hasan Önal[1], Abdurrahman Akgün[1], Beyza Belde Doğan[1], Teoman Akçay[1]

[1]Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Pediatric Endocrinology and Metabolism, İstanbul, Turkey

[2]Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Medical Genetics, İstanbul, Turkey

P450 oxidoreductase *(POR)* enzyme deficiency is a rare form of congenital adrenal hyperplasia, characterized by combined and partial impairments in steroidogenic enzymes. It may be associated with Antley-Bixler syndrome.

Here we report a newborn with ambiguous genitalia, skeletal malformations, and adrenal insufficiency who was diagnosed with Antley-Bixler syndrome.

A 12-day-old newborn presented with ambiguous genitalia. She was born small for gestation age with a birth weight of 2 400 g at 38 weeks of gestation to a non-consanguineous couple. The pregnancy was uneventful except for maternal voice deepening. Her weight was 2 350 g (-1.99 SDS), her length was 49 cm (-0.12 SDS), and head circumference was 32.5 cm

(-1.47 SDS). She had prominent eyeballs, frontal bossing, dysplastic ears, bilateral upper extremity contractures, left choanal stenosis, and genital virilization (Prader stage 3) with 1 cm phallus and bilaterally non-palpable gonads.

Adrenocorticotropic hormone test showed adrenal insufficiency with a low cortisol peak (6 mcg/dL) and high 17-OH progesterone peak (50 ng/mL). Her karyotype was 46,XX. Bilateral ovarian cysts were detected on ultrasound imaging. These findings suggested *POR* deficiency and Antley-Bixler syndrome. The molecular genetic analysis of *POR* gene revealed a novel compound heterozygous mutation (IVS3-1 G > A (c.238-1 G > A)/ c.929_937delTCTCGGACT). Both parents were heterozygous for these mutations.

POR deficiency should be considered in patients with congenital adrenal hyperplasia with a history of maternal virilization during pregnancy and these patients should be evaluated for the presence of skeletal malformations.

(P-31)

New Chromosomal ins(6;7)(Q13:P22) Anomaly in Klinefelter Syndrome Detected Coincidentally in Patient with Signs of Primary Hypogonadism

Ömercan Topaloğlu[1], Bahri Evren[1], Emine Yaşar[2], İbrahim Şahin[1]

[1]İnönü University Faculty of Medicine, Department of Endocrinology, Malatya, Turkey

[2]İnönü University Faculty of Medicine, Department of Medical Biology and Genetic, Malatya, Turkey

We described our case to show that different genetic disorders can accompany Klinefelter syndrome.

An 18-year-old male patient referred to our clinic with complaints of aggressive behavior, learning difficulties, inability to gain weight, tall stature, lack of facial hair, and erectile dysfunction. He has been using valproic acid for epilepsy. On physical examination, the height was 187 cm, body weight 73.4 kg, BMI 21 kg/m^2, arm span 192 cm, upper body 91 cm, lower body 96 cm, and ratio of pubis-vertex/pubis-floor was < 1. Vital signs were normal, but he had slight mental retardation. Testes were small and in the scrotum; penis length was 2.5cm. No beard was present; axillary and pubic hairs were scarce. Gynecomastia was absent. Systemic examination was normal except for midsystolic murmur. Height of mother and father were 162 and 175 cm, respectively. With these clinical findings, pre-diagnosis of hypogonadism was established and workup was performed.

Blood count and biochemical analysis were normal; follicle-stimulating hormone was measured as 55.95 mIU/mL, luteinizing hormone 8.64 mIU/mL, total testosterone 2.42 ng/mL, and IGF-1 436 ng/mL. Scrotal sonography showed small right (15*10 mm) and left (15*15) testes. Karyotype analysis demonstrated an extra X chromosome (47,XXY) and ins(6;7)(q13:p22). By sequence analysis of exon 1 region of androgen receptor, we detected 22 CAG repeat (normally, 12-30). We diagnosed the patient as having Klinefelter syndrome. Echocardiography performed for chest pain revealed mitral valve prolapse. The patient was informed about genetic counselling and fertility. Testosterone was given for treatment of secondary sexual characteristics.

To our knowledge, our case is the first Klinefelter patient having ins(6;7)(q13:p22); however, its clinical implication is not precise yet.

(P-32)

PROP1-Related Combined Pituitary Hormone Deficiency: Case Report

Ahu Paketçi, Sezer Acar, Korcan Demir, Ayhan Abacı, Ece Böber

Dokuz Eylül University Faculty of Medicine, Department of Pediatric Endocrinology, İzmir, Turkey

Mutations of *PROP1* are the most frequent genetic defect in non-syndromic combined pituitary hormone insufficiency and are characterized by growth hormone (GH), prolactin, TSH, and gonadotropin deficiency.

A 3-year-and-3-month-old girl was referred with growth retardation and abnormal thyroid function tests. She was born

full-term weighing 3200 g and had no significant medical or family history. Body weight was 10.9 kg (-2.54 SDS), height 80.4 cm (-3.38 SDS), and head circumference was 48.3 cm (-0.57 SDS). Systemic examination was normal and her pubertal development was consistent with Tanner stage 1.

The laboratory workup showed TSH 1.99 µIU/mL (0.4-5.0 µIU/mL), fT_3 2.66 pg/mL (1.57-4.71 pg/mL), fT_4 0.62 ng/dL (0.8-1.9 ng/dL), and cortisol 6.42 µg/dL (5-25 µg/dL). Celiac antibodies were negative. Pituitary MRI was reported to be normal. L-thyroxine therapy was started with the diagnosis of central hypothyroidism. While euthyroid, the stimulation tests showed insufficient GH response and normal cortisol response thus GH therapy was initiated. At the age of 12 years and 6 months (bone age 12 years), serum prolactin, follicle-stimulating hormone, and luteinizing hormone (LH) levels were found to be 2.15 ng/mL (3.8-26.7 ng/mL), 0.31 mIU/L, and 0.27 mIU/L. Results of LHRH test was consistent with hypogonadotropic hypogonadism (peak LH 0.4 mIU/L) and estrogen therapy was started. Low-dose adrenocorticotropic hormone test was performed because of low basal cortisol. Cortisol response was insufficient and hydrocortisone treatment was added with the diagnosis of central adrenal insufficiency. Repeated MRI showed a pituitary length of 4 mm. *PROP1* analysis revealed a previously reported, homozygous c.301_302delAG (p.Leu102Cysfs*8) mutation.

Mutations of the *PROP1* primarily affects thyrotroph, lactotroph, gonadotroph, and somatotroph cells. Adrenocorticotropic hormone deficiency is variable. Genetic analysis is important for identification of etiology.

(P-33)

Schmid Type of Metaphyseal Chondrodysplasia with COL10A1 Mutation

Emine Ayça Cimbek[1], Yaşar Şen[2], Aşkın Şen[3], Sevil Arı Yuca[2], Fuat Buğrul[2]

[1]Van Training and Research Hospital, Clinic of Pediatric Endocrinology, Van, Turkey

[2]Selçuk University Faculty of Medicine, Department of Pediatric Endocrinology, Konya, Turkey

[3]Fırat University Faculty of Medicine, Department of Medical Genetics, Elazığ, Turkey

The Schmid type of metaphyseal chondrodysplasia (MCDS) is characterized by short stature, widened growth plates, and bowing of the long bones, resulting from autosomal dominant mutations of COL10A1.

We report a patient with MCDS and COL10A1 mutation.

A 4-year 7-month-old boy was referred to our hospital because of bowing of the legs and short stature. His mother showed short stature and bowing of the legs, too. His height and weight were 75 cm (< 3th p) (-2 SDS) and 21.6 kg (75-90th p), respectively. Ca, P, ALP, PTH, and 25-OH D levels were normal. Radiographs showed findings compatible with MCDS. p.W651*(c.1952G > A) (heterozygote) mutation in the *COL10A1* gene was identified. The patient was diagnosed with MCDS.

We report this patient with MCDS and COL10A1 mutation as it is a rarely seen case.

(P-34)

A Case Report of Seckel Syndrome

Hatice Özışık[1], Banu Şarer Yürekli[1], Samim Özen[2], Füsun Saygılı[1]

[1]Ege University Faculty of Medicine, Department of Endocrinology and Metabolism Diseases, İzmir, Turkey

[2]Ege University Faculty of Medicine, Department of Pediatric Endocrinology, İzmir, Turkey

Seckel syndrome is an inherited autosomal recessive disorder characterized by short stature, microcephaly, prominent nose, and typical facial appearance. DNA damages can be detected in different genes, mainly in 3rd and 18th chromosomes. By means of its genetic heterogeneity and easily detectable morphological features, clinical diagnosis can usually be made.

A 19-year-old female patient was diagnosed with Seckel syndrome in pediatric clinic due to typical features of this syndrome at the age of 15. The patient, who already had type 1 DM, applied to our clinic in order to be followed.

On physical examination, prominent nose, flat forehead, micrognathia, high-arched palate, triangular narrow face, and large pinnae were present. On physical examination, height was 136 cm, weight 40 kg, and BMI was 21.63 kg/m^2. Clinodactyly, nail dystrophy, and mental retardation were detected. On cardiac examination, systolic ejection pulse on pulmonary focus was detected. There was no narrative of consanguineous marriage. Her treatment was metformin 500 mg 2x1, pioglitazone 15 mg 2x1, lispro insulin 3x9 units, and glargine insulin 16 units. Her menstrual period was regular. In laboratory examination, FBG was 101 mg/dL, HbA1c was 8.6%, B12 was 176 pg/mL (197-866), hypophyseal hormones were normal. Euthyroid Hashimoto thyroiditis was present. In echocardiography, ASD secundum 6-7 mm was detected. Vitamin B12 replacement was started; pioglitazone was stopped while the doses of insulin were increased. Last value of HbA1c was 6.6%.

Owing to its genetic heterogeneity, molecular prenatal diagnosis is difficult. Involvements may occur in endocrine, cardiac, gastrointestinal, and hematological systems.