were significantly higher. A bilateral adrenal mass was detected and bilateral surrenalectomy was performed. Plasma calcitonin level was high. A hypoechoic, coarse calcific thyroid nodule was detected. The patient underwent total thyroidectomy and neck dissection. The parathormone (PTH) level was normal. The RET mutation was positive in the patient. It was decided to screen the family. Second case: A 50-year-old male patient was called for MEN 2A family screening. Bilateral adrenal mass was detected. Bilateral surrenalectomy was performed. Calcitonin level of 267 pg/mL was detected. Hypoactive thyroid nodule aspiration was reported as AUS. Total thyroidectomy and central neck dissection were applied to the patient. Cranial involvement was also observed in the PET/CT scan for metastasis. A mass in the left cerebellum (hemangioblastoma?) was detected in brain MR. Third case: A forty-six-year-old female patient was evaluated; a mass with size of 56x64x50 mm in the left adrenal and normal right adrenal were detected. Metanephrine and normetanephrine were significantly high in the urine. Calcitonin level was significantly high. Firm thyroid nodule was detected. PTH was normal. Left adrenalectomy and total thyroidectomy were planned. The patient refused to be treated.

MEN 2A syndrome is the most common medullary thyroid cancer. Bilateral pheochromocytoma is common. Hyperparathyroidism is observed in 20-30 % of patients.

(P-58)

Investigation of Androgen Receptor Gen Mutation Spectrum in the Turkish Patients with Disorder of Sex Development

Hüseyin Onay[1], Samim Özen[2], Tuba Sözen Türk[1], Şükran Darcan[2], Tahir Atik[3], Ahmet Anık[4], Oya Ercan[5], Olcay Evliyaoğlu[5], Gönül Çatlı, Filiz Hazan[6], Ayhan Abacı[7]

[1]Ege University Faculty of Medicine, Department of Medical Genetics, İzmir, Turkey

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

[3]Ege University Faculty of Medicine, Department of Pediatric Genetics, İzmir, Turkey

[4]Adnan Menderes University Faculty of Medicine, Division of Pediatric Endocrinology, Aydın, Turkey

[5]İstanbul University Cerrahpaşa Faculty of Medicine, Division of Pediatric Endocrinology, İstanbul, Turkey

[6]İzmir Dr. Behçet Uz Children's Hospital, Clinic of Medical Genetics, İzmir, Turkey

[7]Dokuz Eylül University Faculty of Medicine, Division of Pediatric Endocrinology, İzmir, Turkey

Androgen insensitivity syndrome (AIS) is an X-linked recessive condition resulting in a failure of normal masculinization of the external genitalia in chromosomally 46,XY individuals. This failure of virilization can be either complete androgen insensitivity syndrome (CAIS) or partial androgen insensitivity syndrome (PAIS), depending on the amount of residual receptor function. Mutations in the AR gene on chromosome Xq12 cause AIS. In this study, we aimed to investigate the mutation spectrum in Turkish patients who had AR mutation analysis with suspected gender development disorder and AR insensitivity syndrome.

The *AR* gene from the DNA material isolated from the peripheral blood of patients was amplified using appropriate primers and sequenced using the new-generation sequence analysis technique on the Mi-Seq device.

In this study, molecular analysis results of 383 individuals who underwent AR genetic analysis in Ege University Medical Genetics Department between 2011 and 2016 were evaluated retrospectively. There were 44 mutations in these cases. Of the 44 cases detected in the mutation, 16 were affected and the karyotype was 46,XY. 28 of them are the 46,XX carrier mothers, carrier relatives, or siblings of the affected cases.

New mutations were detected in our studies between 2011 and 2016-L57Q, T576I, D691Y, P672R, Q739E, p.R544KfsX8, c.1745_1747delTCT, F726S, L881V, R102G, and L863F. Different mutations can be detected in AR gene in Turkish society. In cases with disorder of sex development, *AR* should be examined.

(P-59)

A Novel *HESX1* Mutation in a Case with Panhypopituitarism

Aslı Ece Solmaz, Ayça Aykut, Asude Durmaz

Ege University Faculty of Medicine, Department of Medical Genetics, İzmir, Turkey

Pituitary gland insufficiency (hypopituitarism) is a clinical condition that results in inadequate production and release of pituitary hormones. The deficiency of one or more pituitary hormones is named partial hypopituitarism and the deficiency of all pituitary hormones is named panhypopituitarism. Hypopituitarism can be attributed to inherited or acquired causes. Our aim was to determine the molecular diagnosis in our panhypopituitarism patient with *HESX1* gene sequence analysis.

A 21-year-old woman was referred to our clinic with primary amenorrhea. Her medical history included use of growth hormone, thyroid hormone, and estrogen. Cranial MRI findings were consistent with empty sella syndrome. In the family history of the case, there was no consanguinity between the parents and no similar patient in the family. Based on findings and laboratory results, the diagnosis of panhypopituitarism was considered; *HESX1* gene sequence analysis from patient's peripheral blood revealed a heterozygous p.R128K mutation.

HESX1, *POU1F1*, *PROP1*, *LHX4*, *LHX3*, and *OTX2* genes have been associated with combined pituitary hormone deficiencies to date. The R128K mutation in the *HESX1* gene has not been previously reported, and *in silico* predictions for that mutation suggested that this might be the disease-causing variant. This case report provides a contribution to the literature by defining a new mutation in *HESX1* gene.

(P-60)

Homozygous *SHOX* Gene Deletion Detected by Array-CGH in a Girl with Langer Mesomelic Dysplasia

Adam Najafli, Birsen Karaman, Bilge Nihan Satkin, Umut Altunoğlu, Oya Uyguner, Seher Başaran

İstanbul University İstanbul Faculty of Medicine, Department of Medical Genetics, İstanbul, Turkey

Langer mesomelic dysplasia (LMD; MIM 249700) is characterized by hypomelia with severe hypoplasia of ulnae and fibulae, and bowed, thickened radii and tibiae, causing deformities of the hands and feet. LMD is caused by homozygous mutations in the *SHOX*/*SHOXY* (short stature homoebox) gene, of which bi-allelic mutations or gross deletions cause Leri-Weill dyschondrosteosis (LWD). The aim of our study was to determine the genetic etiology of LMD.

Our patient was a 16-year-old female with LMD, the second child of healthy first-cousin parents. She had micrognathia, disproportionate short stature with various musculoskeletal findings (absence of the distal flexion creases of the 3rd, 4th, and 5th fingers on the right hand and camptodactyly of the 3rd, 4th, and 5th fingers on the left ; tibial bowing). X-rays revealed hypoplasia of ulnae, fibulae, and the mandible.

Chromosome analysis and FISH investigation by using *SHOX* gene probe revealed normal results. The intended sequence analysis with the aim of investigating possible mutations failed due to obtaining PCR amplification with no product. Array comparative genomic hybridization (a-CGH) study showed a 174 kb homozygous deletion, encompassing the *SHOX* gene. Proband's parents were heterozygous for the same deletion by a-CGH.

The addition of the a-CGH study to the algorithm is also important in terms of diagnostic contribution in the search for mutations in the *SHOX*/*SHOXY* gene responsible for the formation of the LMD phenotype.

(P-61)

Four 46,XY DSD Cases with Novel Mutations in AR and *SRD5A2* Genes

Agharza Aghayev[1], Güven Toksoy[1], Firdevs Baş[2], Umut Altunoğlu[1], Birsen Karaman[1], Şükran Poyrazoğlu[2], Feyza Darendeliler[2], Hülya Kayserili[1], Seher Başaran[1], Z. Oya Uyguner[1]

[1]İstanbul University İstanbul Faculty of Medicine, Department of Medical Genetics, İstanbul, Turkey

[2]İstanbul University İstanbul Faculty of Medicine, Department of Pediatrics, Division of Pediatric Endocrinology, İstanbul, Turkey

Androgen receptor (AR) defects and 5α-reductase (5α-RD) deficiency in 46,XY disorders of sexual development (DSD) present with indistinguishable phenotype. Affected individuals can present with a wide spectrum, from a female genital tract to ambiguous genitalia and mild virilization. The hemizygous mutations in the AR (Xq11.2-q12) encoding AR are associated with X-linked androgen insensitivity, and bi-allelic mutations in *SRD5A2* cause enzyme deficiency, converting testosterone (T) to dihydrotestosterone (DHT). Based on genetic diagnostic algorithm, *SRD5A2* is screened when T/DHT is >10, and AR is screened when < 10, and vice versa for cases with unidentified mutations, presenting with locus and allelic heterogeneity. Identifications of mutations responsible for phenotypes is effective in genetic counseling, managements, and follow-ups.

In this study, we aimed to investigate the genotype-phenotype relationship by evaluating clinical, hormonal, and genetic findings of four cases with ADS or 5α-RD deficiency in 46,XY DSD.

Clinical manifestations and hormone levels (basal luteinizing hormone, follicle-stimulating hormone, T, DHT, T/DHT ratio with short-term stimulation of hCG test) were evaluated and chromosomal abnormalities were excluded in cases with 46,XY. AR (NM_000044.3) and *SRD5A2* (NM_000348.3) were evaluated by Sanger sequencing and variants were investigated by using molecular databases.

AR was screened in three cases whose T/DHT < 10 (Case 1-2-3) revealed three novel variants in each: synonym (c.330G > C; p.Leu110 =), frameshift (c.2585delAGCTCCTG; p.K862Rfs*16), and missense (c.2084C > T; p.Pro695Leu). *SRD5A2* was screened in one case whose ratio was >10 and revealed two different variants (one known and one novel) in compound heterozygous status, confirmed by parental testing; c.[164T > A];[269A > C] (p[Leu55Gln];[His90Pro]. The all novel mutations were analyzed by *in silico* programs and family segregation for inheritance model.