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

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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

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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.