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Ellis-Van Creveld syndrome with preauricular sinus: report of two Turkish female patients

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Ellis-Van Creveld(EVC) Syndrome(OMIM 225500) is a rare chondro-ectodermal dysplasia characterized by short ribs, polydactyly, growth retardation, ectodermal and heart defects. The birth prevalence in non-Amish population is estimated as 7/1,000,000. The phenotype is variable and is inherited in an autosomal recessive pattern with parental consanguinity has been reported in about 30% of cases. Mutations in EVC and EVC2 genes, located in a head-to-head configuration on chromosome 4p16, have been associated with this syndrome. We report two Turkish female patients with EVC syndrome born to consanguineous parents.

Patient 1: A 8-year-old female patient presented with short stature, short limbs, sparse hair, blue sclera, broad base to nose, simple philtrum, high palate, hypodontia, prominent and simple ears, pectus carinatum, increased lumbar lordosis, sacral dimple, lateral deviation of the toes, dysplastic nails. She has undergone surgical correction of postaxial polydactyly of all four limbs.

Patient 2: A 2-year-old female patient presented with short stature, short limbs, prominent occiput, sparse hair, epicanthus, depressed nasal bridge, high palate, short and deep philtrum, hypodontia, preauricular sinus and skin tag behind the right ear, deep plantar creases, hemangioma located on neck(2x0.5cm), dysplastic nails. She had a history of neonatal teeth and surgical correction of bilateral postaxial polydactyly of hands.

In conclusion, we present the first report, to our knowledge, of EVC syndrome with preauricular sinus in the literature and also discuss the variable expression, management and genetic counseling.

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Interstitial dup(6)(q22.3q24) characterized by cCGH resulting from familial inv ins(6)(p11.2q25.3q22.3): case report

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We report on a female child aged 2 months, referred for complex cardiac anomalies and Down-*like* facial dysmorphisms, strongly suggesting a possible chromosomal abnormality. Chromosomal studies with high-resolution GTG banding showed an abnormal chromosome 6. The parents were investigated and their karyotypes revealed a normal chromosomal constitution in the father and an inv ins(6)(p11.2q25.3q22.3) in the mother; the latter was also present in the maternal grandmother, allowing us to conclude that the child's abnormality was a recombinant of the apparently balanced familial inverted insertion. Comparative genomic hybridization (cCGH) techniques proved that the abnormal chromosome 6 found in the proband has a duplication of the segment 6q22.3→6q24, with an extension of 24 Mb, resulting in the partial trisomy of that segment. The final karyotype of the child was thus: 46,XX,rec(6)dup(6q)inv ins(6)(p11.2q25.3q22.3)mat.ish cgh dup(6)(q22.3q24).

The patient's follow-up studies were only possible until she was 5 months and her main clinical features included dysmorphic facial features with plagiocephaly, membranous auricular and ventricular septal defects and developmental delay.

This is the first presentation of a "pure" interstitial duplication of bands 6q22.3 to 6q24. The authors enhance the importance of an adequate use of molecular cytogenetic techniques such as the use of oligonucleotide-based array-CGH in a clinical diagnostic laboratory for detecting subtle chromosome imbalances and accurately define the breakpoints in patients with atypical phenotypic characteristics, while assuring a good cost-efficiency diagnostic rate. The cytogenetic and clinical findings in this newly reported duplication are also compared with previously published similar data.

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A Novel *MEK1* Mutation in a Patient with LEOPARD Syndrome

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LEOPARD syndrome (LS) is characterized by lentigines, ECG conduction abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, growth retardation, and sensorineural deafness. *PTPN11*, *RAF1,* and *BRAF* have been reported to be causal for LS [Digilio et al. 2002, Pandit et al. 2007, Sarkozy et al. 2009]. Here, we report a patient with LS who has been found to have a novel *MEK1* mutation. The patient, a Japanese 13-years-old boy, was born at 41 weeks and 4 days of gestation with the birth weight as 4350g. He showed hypotonia and sucked poorly in the neonatal period. His psychomotor development was delayed with DQ as 55 at age 19 months. Around the age 3 years, lentigines appeared on his face and limbs. He had flexion deformity of bilateral knees. His linear growth was retarded but showed spurt from age 9 years because of precocious puberty. When seen by us at age 10 years, he weighs 22.1kg (−1.5SD), height 130cm (−1.2SD), and OFC 51.8cm (−1SD). He had multiple lentigines, ocular hypertelorism, and sensorineural hearing impairment, but showed no ECG abnormalities or hypertrophic cardiomyopathy (HCM). He was clinically diagnosed as LS according to the criteria by Voron [1976]. Molecular investigation demonstrated a *de novo* heterozygous missense mutation in *MEK1* (c.305A>G; p.E103G). To date, heterozygous missense *MEK1* mutations have been reported in four patients clinically diagnosed as cardiofacialcutaneous (CFC) syndrome without HCM in all four and with nevi in one [Dentici et al. 2009]. Heterozygous missense *MEK1* mutations could cause phenotypic spectrum including CFC and LS.

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Molecular findings of three different male under- virilization cases with 47, XXY karyotype.

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Introduction: Male under virilization is a rare condition mostly due to the mutations of hormone genes that effect male reproductive tract. One of the most important gene mutations that effect that pathway is the androgen receptor gene (AR) mutations, located at Xq12 in individuals with 46, XX. In this report, we present the *AR* and *SRD5A2* gene analysis of three different under- virilized patients with 47, XXY karyotype.

Materials and Methods: Chromosome analysis of the patients were assessed by standard lymphocyte karyotype, with Giemsa staining. PCRs were carried out by amplifying all the exons of related genes, and direct sequencing protocol was applied for mutation detection.

Results: One of the patients had no mutation in *AR* and *SRD5A2* genes, but had a 23 repeat polymorphism on exon 1 of AR gene. The second had no mutation in AR gene, had a 22 and 23 repeats polymorphism, but had a homozygous p.G196S mutation in *SRD5A2* gene. The third had a heterozygous mutation in p.F891L in *AR* gene, with a 16 and 21 repeat polymorphism, and had no mutation in *SRD5A2* gene.

Discussion: 47, XXY karyotype is a very rare condition in male virilization cases. Mutations in *AR* gene, in addition with *SRD5A2* gene, are thought to be the common reasons of this condition. According to our results, we suggest that not only the *AR* gene analysis, but also *SRD5A2* gene analysis and poly-Gln polymorphism of the exon 1 of *AR* gene have important impacts for the diagnosis of male under virilization.

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Diagnostic pitfalls and mosaic unbalanced translocations: a case of 18q- deletion syndrome

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We report a male patient with intellectual disability, club feet, growth hormone deficiency and diffuse white matter hypomyelination.