Orofaciodigital Syndrome I

Alternative Names
OFD1
OFD Syndrome I
Oral-Facial-Digital Syndrome, Type I
Papillon-League-Psaume Syndrome

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
311200

Mode of Inheritance
X-linked dominant

Gene Map Locus
Xp22.3-p22.2

Description
Orofaciodigital syndrome type I (OFD1) is a congenital X-linked dominant disorder characterized by anomalies of the oral cavity, face and digits sometimes associated to cerebral malformations and polycystic kidney disease. Clinically, OFD1 is seen only in females since it is lethal in males. Lesions of the mouth include median pseudoclefting of the upper lip, clefts of the palate and tongue, and dental anomalies (missing or supernumerary teeth, enamel hypoplasia, and teeth malpositions). Dysmorphic features affecting the head include hypertelorism, frontal bossing, micrognathia, facial asymmetry and broadened nasal ridge. The digital abnormalities are syndactyly, clinodactyly, brachydactyly and, rarely, pre or post-axial polydactyly. Less frequently expressed phenotypic anomalies include skin milia, alopecia, deafness and trembling. Sometimes the diagnosis of OFD1 can be difficult because there is an overlap with other types of oral-facial-digital syndromes.

Molecular Genetics
Mutations in the CXORF5 gene lead to orofaciodigital syndrome type I. Human chromosomal region Xp22.3-p21.3 comprises the area between the pseudoautosomal boundary and the Duchenne muscular dystrophy gene. This region harbors several disease loci, including OFD1, CFNS, DFN6, and SEDT. It also contains a region of homology with both the short and the long arms of the Y chromosome and undergoes frequent chromosomal rearrangements.

The CXORF5 gene, originally named 71-7A, has 23 exons with two alternatively spliced transcripts: CXORF5-1 and CXORF5-2. CXORF5-2 differs from CXORF5-1 by an insertion of 663 nucleotides resulting from the use of an alternative 3-prime splice site in intron 9. CXORF5-1 encodes a deduced 1,011-amino acid protein containing a large number of predicted coiled-coil alpha-helical domains. CXORF5-2 encodes a deduced protein of 367 amino acids; the first 353 residues of CXORF5-2 and CXORF5-1 are identical. The CXORF5 gene has a CXORF5 pseudogene at Yq11.22 and another CXORF5-related locus at 5p13.2-13.1.

Epidemiology in the Arab World

Saudi Arabia
Al-Qattan and Hassanian (1997) described the case of a Saudi Arabian girl, less than two years old, with clinical features consistent with both orofaciodigital syndrome type I (Papillon Leage-Psaume syndrome) and type VI (Varadi-Papp syndrome). The girl was born to healthy non-related parents with five healthy children. The palmar/nail abnormality in the patient was associated with loss of active flexion of the interphalangeal joints. Although the patient had clinical features consistent of both OFD I (milia of face and ears, brittle and dry scalp with
alopecia) and OFD VI (cerebellar anomalies) she did not show the presence of a forked metacarpal, which is characteristic of OFD VI. It is because of a careful review of the radiological findings in the hands that the final diagnosis was placed as a new mutation of orofaciodigital syndrome type I. Two years later, al-Qattan (1999) presented a rare case of 10-year-old Saudi girl with oral-facial-digital syndrome type I. The parents were not related and were healthy, as were their other two sons and two daughters. The patient had two features that have not been previously described: cone-shaped epiphyses in the toes and trifurcation of the soft palate. No malformations of the cardiovascular, gastrointestinal or urinary systems were found. Chromosomal analysis revealed a normal female karyotype.

References

Contributors
Ghazi O. Tadmouri: 13.6.2006
Pratibha Nair: 11.6.2006
Ghazi O. Tadmouri: 1.5.2005
Ghazi O. Tadmouri: 16.4.2005