Van der Woude Syndrome

Alternative Names
VWS
VDWS
Lip-Pit Syndrome
LPS
PIT
Cleft Lip and/or Palate with Mucous Cysts of Lower Lip

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

OMIM Number
119300

Mode of Inheritance
Autosomal dominant

Gene Map Locus
1q32-q41

Description
Van der Woude syndrome is a developmental abnormality characterized by paramedian lower lip pits (fistula labii inferioris congenita) with or without cleft lip and/or cleft palate. Other less frequent features include cleft uvula and hypodontia, missing central and lateral incisors, canines, and/or bicuspids. Van der Woude syndrome is inherited as an autosomal dominant trait with high penetrance (96.7%) and variable expressivity ranging from a single barely evident depression to bilateral fistula of the lower lip and from a bifid uvula to a complete cleft palate and lip, determining various degrees of clinical relevance. It is the most common of the syndromic orofacial clefts, with prevalence in the general population estimated at 1 in 60,000. Treatment for the sequella of van der Woude syndrome includes cleft repair and ventilating tube insertion in patients with otitis media.

Molecular Genetics
Linkage and cytogenetic analysis allowed mapping of the van der Woude locus to 1q32-q41.3. Recently, it has been shown that mutations in the gene encoding the transcription factor interferon regulatory factor 6 (IRF6) cause van der Woude syndrome, and that IRF6 is highly expressed in the medial edges of the paired palatal shelves around the time of fusion. Van der Woude syndrome can be caused by loss of function mutations that result in loss of both the DNA-binding and protein-binding functions, or by IRF6 gene deletions that result in haploinsufficiency.

The IRF gene family consists of nine members encoding transcription factors that share a highly conserved helix-turn helix DNA-binding domain and a less conserved protein-binding domain. The IRFs exert diverse functions through homo- or hetero-dimer formation or interaction with other transcription factors. These functions include the regulation of host defense pathways such as the innate and adaptive immune responses, and oncogenesis.

Epidemiology in the Arab World

Kuwait
Srivastava and Bang (1989) reported 9 patients with congenital lower lip sinuses and analyzed the penetrance of the van der Woude syndrome in their families. On the basis of their observations, Srivastava and Bang (1989) concluded that van der Woude syndrome may have low penetrance among the populations studied.

Tunisia
Souissi et al. (2004) reported the case of a 15-year-old female with van der Woude syndrome with isolated lower lip pits. The presence of identical defects in the paternal grandmother, the father, and the sister was reported by the
patient and confirmed by close examination of family photos. On clinical examination, bilateral punctate depressions were located on the peak of her lower lip convexity, about one half centimeter from the median line. The lesions were surgically removed.

References

Contributors
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