Van Der Woude Syndrome (VDWS) - An Overview

ABSTRACT

Van der Woude syndrome is a rare autosomal dominant disorder. The typical manifestations include lower lip pits, cleft lip and/or palate, hypodontia, bifid uvula and ankyloglossia. Careful diagnosis helps to differentiate this rare syndrome from other syndromes which may present similar features. A multidisciplinary approach is needed to improve the facial appearance and boost up the self esteem of the patient. This paper reviews the etiology, clinical features, diagnosis, differential diagnosis and treatment modalities of Van der Woude syndrome.

Key words: Van Der Woude Syndrome; Cleft Lip; Cleft Palate; Lip Pits.

Orofacial cleft (OFC) remains a prominent health issue in developed and developing countries alike. With a worldwide prevalence of approximately 1.2 / 1000 live births, OFCs are the commonest craniofacial birth defects in humans. Van der Woude Syndrome (VWS) is the most common form of syndromic Orofacial clefting accounting for 2% of all cases. This paper reviews the etiology, clinical features, diagnosis, differential diagnosis and treatment modalities of Van der Woude syndrome.

Van der Woude syndrome, also known as lip-pit syndrome and cleft lip/palate and paramedian sinuses of the lower lip, is a rare autosomal dominant disorder, thought to occur with an incidence of approximately 1 in 60,000 live births and without gender predilection. The distinctive feature of VWS is the presence of lower lip pits and/or sinuses, which are present in approximately 85% of cases. In some rare cases, a single barely visible pit might be the only distinguishable feature of VWS. Other anomalies that are frequently associated with VWS include hypodontia, submucous cleft palate and bifid uvula.

Van der Woude syndrome is a dominantly inherited developmental disorder characterized by pits and/or sinuses or the lower lip, cleft lip with or without cleft palate (CL/P), isolated cleft palate (CP), bifid uvula (BU), and hypodontia (H). Van der Woude syndrome has an autosomal dominant hereditary pattern with a variable expressivity, and its penetrance has been estimated at 80%, however later reports have shown that the penetrance is close to 100%. Eighty percent of gene carriers are not diagnosed because they are nonpenetrant, among the penetrant gene carriers, however, as many as 80% may not have been recognized in the past.

Familial occurrence of lower lip pits and clefts was first described by Demarquay in 1845. Watanabe et al. reviewed some 100 cases in 1951, and Van der Woude delineated the syndrome in 1954. Further important contributions came from Cervenka et al, who presented 66 personally observed cases and reviewed some 450 others, and Rintala and Ranta, who studied the incidence among cleft cases from the Finnish malformation registry. Finally, Burdick et al performed a genetic study.

Most reported cases of VWS have been linked to chromosome 1q32-q41 (VWS1), but a second VWS locus (VWS2) has been mapped to 1p34. Recently, the interferon regulatory factor-6 (IRF6) gene, localised to the VWS1 locus on chromosome band 1q32.2, was shown to harbour mutations in patients with Van der Woude and/or popliteal pterygium syndrome.

Etiology

Etiology of this syndrome is remarkably variable, it was initially mapped to human chromosome 1q 32 – q 41 and later reported result from mutation in gene encoding Interferon Regulatory Factor 6 (IRF6). Genetic counseling, a highly recommended for this abnormality includes information on the likelihood of gene transmission, and possible ways of expression and penetrance. A full family history is essential before counseling can be given to patients of isolated cases of clefts. The treatment of such cases should be excision of the labial and commissural pits if esthetics is a major concern. It should include total removal of the minor salivary glands that exude secretions at the base of pits to prevent formations of cysts and mucoceles. The treatment should be in collaboration with plastic surgery, oral and orthodontists. Other treatments like cross bite corrections, maxillary expansions, restorations, should also be carried out. A multidisciplinary approach is very necessary to carry out the treatment thus improving the self esteem at an early age.

Oral Features

Lip Pits / Fistulas - Congenital lip fistula is a very rare malformation and represent the most common clinical finding in VWS having an interruption in the development of lateral groove of lower lip which is on the fourth week intraterine life. Consequently, there is a gradual obliteration until finishes the growth, resulting in lip fistula. It may minor salivary glands in its internal portion or even invaginating to orbicular muscles of lip that communicates to ductal system of major salivary glands. Discomfort caused by spontaneous or induced drainage of saliva / mucus when pressure is applied or during a meal as well as poor aesthetics match is one of the main complaints of patients with congenital lip fistula. It is asymptomatic and there is not tendency to obstruction or infection that may be inflamed in a special situations such as individuals with suction of lip, lacerations and others.
The surface oepip may present as a circular or transverse slit or be located at the apex of nipple like elevations. Its diameter may be up to 3mm and its depth can range from 1 to 15mm. Most of the lip pits are located in the lip vermilion and on the muco-cutaneous line at a distance of about 5-25 mm from each other. Although usually bilateral and symmetrically placed, an asymmetric single pit, a central single pit, or bilateral asymmetric pits may occur.

Microforms exist such as transverse mucosal ridges of the lower lip and bilateral somewhat conical elevations of the lower lip mucosa. The latter are associated with cleft palate but not with cleft lip. Such microforms of VWS can be detected only by careful examination of the patient and by the coexistence of a cleft and family history.

Cleft Lip / Palate: Cleft lip and/or palate is one of the ten most frequent congenital malformations and affects 2 in 1000 living newborns. It may be manifested either by cleft upper lip, cleft lip and alveolar process, isolated cleft of the hard and/or soft palate or a complete lip, cleft alveolar process, and cleft palate. The malformation occurs uni- and bilaterally. A complete unilateral cleft lip and palate and an isolated cleft palate are the predominant forms. The etiopathogenesis of the defect has not been clearly explained. Apart from genetic agents (17–20%), environmental factors are believed to play an important role. More than 400 syndromes include cleft lip (CL) with or without cleft palate (CP) in their etiology. Van der Woude syndrome (VWS) is one of the most common accounting for about 2% of all cases of CL/P worldwide. IbIRTH, individuals with CL/P have facial deformation, feeding problems, and frequent middle ear infection, the treatments of which require interventions from multiple disciplines. At the age of speech acquisition, speech therapy is often needed to correct problems resulting from muscular defects of the cleft. As the individual continues to grow, defects in tooth development and malocclusion require dental and sometimes surgical treatment.

Hypodontia: Hypodontia is considered as a cardinal associated feature and has been observed in 10-81% of all VWS patients, with the number of teeth missing in the upper jaw almost double that in corresponding control groups. The teeth missing infrequency are the upper second premolars, the lower second premolars, and the upper lateral incisors.

Submucous Cleft Palate: It is common and may be easily missed on physical examination. Hypernasal voice and cleft or bifid uvula are clues to this diagnosis. It is possible as well that a bifid uvula is an isolated finding in certain individuals with the Van der Woude syndrome. Infrequent anomalies include congenital adhesion of the jaw (syngnathia), narrow arched palate and ankyloglossia (tongue tie).

Extraoral Features: The reporteeextraoral manifestations are rare but include limb anomalies, popliteal webs, and brain abnormalities. Accessory nipples, congenital heart defects, and Hirschsprung disease have also been reported. It is uncertain whether these extraoral manifestations unassociated additional anomalies or infrequently expressed aspects of Van der Woude syndrome.

Diagnosis
The diagnosis of VWS (isolated or familial) is conclusive when a patient has, at least, one of the features: isolated lip fistula, lip fistula and cleft lip (CL) and/or cleft palate (CP), isolated and familial lip fistula having first degree with CL and/or CP, CP and CL with a close family member with a lip fistula.

More extreme phenotypes in parents tend to produce more extreme expression in their children. However, the lesser expressions of VWS are common and should be actively looked for when counseling families about cleft lip or cleft lip and palate. All affected parents should be cautioned that they carry a risk of 50% for each child with a cleft lip or palate or both. The potential of embryoscopy to detect minor malformations such as cleft lip allows for early termination pregnancy with VWS.

Differential Diagnosis
1. Popliteal pterigium syndrome-popleteal webs, cleft lip/palate, lower lip pits, anomalies of genitor-uterine tract as cryptorchidism and bifid scrotum in males, hypoplastic labia majora and uterus in females.
2. Oro-facio-digital syndrome- includes orofacial features of cleft palate, bifid tongue, hypodontia, lip pits etc. with digital, renal and central nervous system abnormality.
3. Aganglionic megacolon combined with CP and lip pits (Hirschsprung disease).
4. Ankyloblepharon filiform adnatum.

Treatment
The treatment of VWS patients includes all necessary surgical and multidisciplinary procedures for the correction of serious anamolies including clefts. Rarely spontaneous shrinkage has been observed with congenital lip pits. However, surgical excision is needed in cases of mucous secretions, cosmetic problems and chronic uncontrolled inflammation. A case of squamous cell carcinoma was reported as developing from chronically inflamed lip pits which cautions us for thorough evaluation, early intervention and treatment of this condition.

Watanabe et al reviewed and the surgical techniques available for the excision of the lip pits. In all cases, excision of the sinus tract should be complete, because if some of the mucous glands attached to the fistula are left behind, this could allow a mucoid cyst to form. Loosening of the lip muscle has also been reported as a drawback of the operation. When late post are evaluated, an aesthetically poor lip is often found, and treatment requires two or more operations, due to residual deformities. An alternative technique using a gutta percha point and blue methylene has also been reported. This is done in order to identify better fistula pathway to be excised in a congenital lip fistula in patients with VWS.
Conclusion
Craniofacial developmental deformities are of major aesthetic concern to th. These include cleft lip, cleft palate and lower lip fistulae. Many syndromes occur with the typical involvement of cleft lip and palate. One such syndrome is Van der Woude syndrome. The condition is of rare occurrence, should be carefully diagnosed and early multidisciplinary management should be instituted.

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References
11. Demarquay JN. Quelquess sur le bec-de-lievre: impr. Félix Malteste; 1845.
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How to cite this article

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Source of Support: Nil
Conflict of Interest: None Declared