

Case Report

A RARE PRESENTATION OF “VAN DER WOUDE SYNDROME” - A CASE REPORT

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ABSTRACT

Van der woude syndrome (VWS) is a condition that affects the development of face. Many people with this disorder are born with a cleft lip, cleft palate (an opening in the roof of the mouth), or both. Affected individuals usually have depressions (pits) near the center of lower lip which may appear moist due to presence of salivary and mucous glands in the pits. The frequency of this syndrome ranges from 1:1000 to 1:500 births worldwide, and there are more than 400 syndromes that involve cleft lip with or without cleft palate (Malik *et al.*, 2010). VWS is distinct from other clefting syndromes due to the combination of cleft lip and palate (clp) and cp within the same family. We are hereby reporting a variant of VWS having bilateral cleft lip and cleft palate without lower lip pits with family history of similar anomaly in father (treated).

Keywords: Van der Woude Syndrome, Cleft Lip, Cleft Palate, IRF6 Gene

INTRODUCTION

Van der woude syndrome is inherited as an autosomal dominant disease caused by a mutation in a single gene with equal distribution between the sexes. The disease has high penetrance at about 96% but the phenotypic expression varies from lower lip pits with cleft lip and cleft palate to no visible abnormalities (Malik *et al.*, 2010; Burdick and Bixler *et al.*, 1985). Van der woude observed that 27% of the offspring of affected parents had lip fistulae alone and 21% had fistulae associated with cl and/or cp (Van, 1954). Burdick *et al.*, (1985) gathered information on 864 affected individuals from 164 families. In this population, 44% had lip pits only, 37% had cleft lip (with/without lip pits and with/without cleft palate), 16% had cleft palate only (with/without lip pits), and 3% had no apparent phenotype. Overall, lip pits were observed in 86% of affected individuals. The ratio of cleft lip with or without cleft palate (cl±cp) to ‘cp only’ is about two to one in individuals with VWS (Burdick *et al.*, 1985). To make the diagnosis of van der woude syndrome, at least one of the following three findings must be present:

- Lip pits, in combination with one of the following:
 - Cleft lip with or without cleft palate (cl±p)
 - Cleft palate (cp)
 - Submucous cleft palate (smcp)
- Lip pits alone and a first-degree relative with cl±p, cp, or smcp
- Cl±p, cp, or smcp and a first-degree relative with lip pits

VWS is the most common orofacial clefting syndrome, accounting for 2% of clp cases (Rizos and Spyropoulos, 2004). The majority of VWS cases are caused by haploinsufficiency due to mutations in the interferon regulatory factor 6 genes (irf6) on chromosome 1 in the 1p32-p41 region known as VWS locus 1. A second, less common, causative locus is found at 1p34, known as VWS locus 2 (VWS2). More recent work has shown that grhl3 is the VWS2 gene. Grhl3 is downstream of irf6 in oral epithelium, suggesting a common molecular pathway leading to VWS. Prior work also suggested wdr65 as a candidate gene (Lam *et al.*, 2010; OMIM). Other irf6 related syndrome includes popliteal pterygium syndrome. The pps phenotype includes cleft lip and/or palate (91%-97% of individuals); fistulae of the lower lip (45.6%) (Froster-Iskenius, 1990); webbing of the skin extending from the ischial tuberosities to the heels, bifid scrotum and cryptorchidism in males, hypoplasia of the labia majora in females, syndactyly of fingers and/or toes, and anomalies of the skin around the nails (Lewis, 1948). Presence of

Case Report

psychomotor disabilities may be seen in rare individuals with van der woude syndrome or popliteal pterygium syndrome. However, psychomotor delay (observed in multiple family members in only one of >350 reported families studied) may be the result of an unrelated cause (Sander *et al.*, 1994).

CASES

A term 2 hour old boy baby, 1st born to 2nd degree consanguineous couple delivered through normal vaginal delivery without any perinatal complications was referred to our hospital due to feeding difficulty secondary to congenital anomalies involving face. Family history of similar complaints was present in father, for which he was treated with serial corrective surgeries according to grandparents. At presentation baby vitals were stable, head to toe examination revealed bilateral cleft lip and cleft palate with no other associated gross congenital anomalies. Systemic findings were within normal limits. Investigations like infantogram, ultrasonography and echocardiography did not reveal any other associated anomalies. Keeping family history and presenting clinical features in mind, a provisional diagnosis of Van der Woude syndrome was made, feeds with long pallada was started and paediatric surgical consultation was obtained for further management of baby.



Figure 1: Bilateral cleft lip & cleft palate



Figure 2: Father & his decent

Case Report

DISCUSSION

Clinical diagnosis based on orofacial clefts and lip pits typically occur shortly after birth. Certain defects may be difficult to diagnose, particularly a submucous cleft palate. This form of CP may not be detected except through finger palpation, as the mucosa covering the palate is intact, but the muscles underneath have lost their proper attachments. Feeding problems, impaired speech, and hearing loss are symptoms of a submucous cleft palate (Lam *et al.*, 2010). Furthermore, approximately 15% of VWS cases with orofacial clefts, in the absence of prominent lip pits, cannot be easily distinguished from non-syndromic forms of orofacial clefting (Sander *et al.*, 1994). Therefore, it is very important to closely examine these patients as well as their relatives for lip pits, especially when there is a family history of mixed clefting, in order to make the VWS diagnosis (Rizos and Spyropoulos, 2004). Dentists may also play an important role in diagnosing cases not detected at birth, as they detect hypodontia commonly associated with VWS. The patients most commonly lack the upper second premolars followed by the lower second premolars and upper lateral incisors. The absence of these teeth might play a role in the constricting of the dental arches (Rizos and Spyropoulos, 2004; Lam *et al.*, 2010).

Conclusion

Even though treatment is available for all anomalies in VWS, prevention is always choice of treatment. Unavailability of genetic studies (viz... PCR, DNA analysis) in limited resource settings like in our rural hospitals high degree of suspicion and good clinical expertise is required for diagnosis. Never the last, genetic counselling plays a very important role in preventing morbidity and financial burden to families as there is 50% chance of penetrance and expression in offspring.

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