

# NAM IN A VANDER WOUDE SYNDROME

Dr Rozina Nazir <sup>a</sup>, Dr Imtiaz Ahmed <sup>b</sup>, Dr Tabassum Ahsan <sup>c</sup>

<sup>a</sup> BDS, FCPS, Assistant Professor & Head Department of Orthodontic ,Bahria University Medical and Dental College Karachi

<sup>b</sup> BDS, FCPS Assistant Professor & Head Department of Orthodontic ,DIIKIOHS, Karachi

<sup>c</sup> BDS Lecturer Orthodontic department, Dr Ishrat ul Ebad Khan Institute of Oral Health Sciences DUHS Karachi

## ABSTRACT

**Introduction:** The Vander Woude syndrome is an autosomal-dominant condition typically comprising cleft lip or cleft palate or both and distinctive pits of the lower lips. The degree to which individuals carrying the gene are affected varies widely, even within families. The variable manifestations include lip pits alone, hypodontia (absent teeth), and isolated cleft lip and palate of varying degrees of severity. **Case History.** A case of Van Der Woude Syndrome 24 days old, characterized by pits on the lower lip and bilateral cleft of the lip and palate with similarly affected mother is presented. **Progress:** Presurgical infant orthopedics was done to reduce the severity of the initial cleft alveolar and nasal deformity. NAM therapy resulted in better lip and nasal form, reduced oronasal fistula and labial deformities and it also causes 60 % reduction in the need for secondary alveolar bone grafting. After NAM primary lip repair was carried out. **Conclusion:** VDW is under reported & frequently not diagnosed. The phenomena that CLP & CP are regularly combined in the same pedigree makes it unique. A multidisciplinary approach to treatment produced an aesthetically pleasing and functional outcome.

## Key words:

Vander Woude, Cleft lip, Cleft palate, Lip pits

**Correspondence :** Dr Rozina Nazir , Assistant Professor & Head, Department of Orthodontics ,Bahria University Medical & Dental College Karachi-75260, Pakistan ,Email: [dr\\_rozina@hotmail.com](mailto:dr_rozina@hotmail.com) ,Phone: Off: +92 219 9240002-11 (Ext: 364)

## INTRODUCTION

Van der Woude syndrome (VWS) is a rare craniofacial disorder characterized by lower lip pits, cleft lip and/or palate (CL/P) and, occasionally, hypodontia.<sup>1,2</sup> This syndrome occurs in approximately 2% of CL/P patients, and is distinguished from non-syndromic CL/P by the presence of lip pits. First description of this familial disease, which is characterized by cleft lip and salivary fistula, was presented by Demarquay in 1845.<sup>1</sup> Vander woude was the first to combine lower lip with cleft lip and cleft palate, introducing a new clinical entity, while she also described its mode of heredity In 1954 van der Woude is characterized by the

coexistence of cleft lip and/or palate with salivary fistulae of the lower lip and denominated it as a separate nomological entity.<sup>2</sup>

Lip pits may be divided into three types relative to their location commissural, midline, upper lip and lower lip.<sup>3</sup> Lower lip pits are most frequently occurring congenital malformations.<sup>4</sup> Vander woude is the most frequent form of clefting, accounting for 2 percent of all cleft lip and palate cases.<sup>5</sup> Furthermore it is remarkable that both CLP and CP can be combined with lower lip pits in the same pedigree. The prevalence of the condition among patients with

clefts ranges from 0.43% to 2.5% according to different authors.<sup>6</sup>

The fistulae occur most commonly in patients with complete clefts of the lip, alveolar process and palate (in about 66%), in over 16% of patients with cleft lip alone and in 17% of patients with isolated palate clefts. The fistulae are up to 2 cm long, sometimes longer, and are situated bilaterally, with symmetrical location in 50%, asymmetrical in 32% and central in 4% of cases. About 14% of patients develop residual forms in the shape of a pit in the mucous membrane.<sup>7</sup> The walls of the fistulae are covered with nonkeratinizing epithelium which is situated above underlying compact basement membrane composed of connective tissue with stroma rich in lymphohistiocytosis cells. Neighbouring salivary glands discharge saliva to the fistula lumen.<sup>8</sup>

The disease is transmitted by a gene localized between D1S245 and D1S414. High level of mutations  $1.8 \times 10^{-5}$ , contributes to the fact that loci responsible for the disease follows autosomal dominant inheritance with penetration index exceeding 80%. Due to the genetic expression, more severe forms of the disease are transmitted to the offspring.<sup>1</sup> Its incidence is estimated at 1-2.5 cases per 100,000 live births.<sup>9</sup> VWS is transmitted in an autosomal dominant mode with high penetrance and varied clinical expression however, 30-50% of VWS cases represent de novo mutations.<sup>10</sup> Mutations in the

interferon regulatory factor 6 (IRF6) gene have been found in patients with VWS.<sup>11</sup>

### CASE REPORT

A 24 days old male was referred from the Jinnah postgraduate Medical Institute to the Department of Orthodontics DUHS. Extraoral examination revealed bilateral cleft lip and palate with lower lip pits as shown in fig.1. It was diagnosed as a case of vander woude syndrome. Family history revealed that his mother is also suffering from same syndrome (fig.2).



Fig 2 Mother of baby also suffering from Vander Woude syndrome

Intraoral examination shows bilateral cleft lip and palate (fig 3).



Fig 3- Intraoral view showing bilateral cleft lip & palate & premaxilla shifted to right

Cleft was more wider on the left side than right, and premaxilla was shifted towards right. There was severe deficiency of the columella tissue. His lower lip had bilateral lip pits at the base of

two nipple-like elevations, the pit on left side was larger in size than right (fig 4)



Fig 4 Bilateral lower lip pits

Initial impression of the cleft lip and palate infant is obtained. A heavy-bodied silicone impression material is used to take the initial impression as shown in fig 5.



Fig 5 Initial impression in rubber base impression material

The impression was then poured with dental stone to obtain an accurate cast. Moulding plate was constructed for NAM, by self cure acrylic it was relined by soft denture liner and this plate was also used as feeding plate

Presurgical infant orthopedics was done to reduce the severity of the initial cleft alveolar and nasal deformity (fig 6). This enables the surgeon and the patient to enjoy the benefits associated with repair of a cleft deformity that is minimal in severity which will result in better repair of the alveolus, lip and nose. NAM therapy indicates better lip and nasal form, reduced oronasal fistula and labial deformities, 60 % reduction in the need for secondary alveolar bone grafting. The NAM appliance (NAM) consisted of an intraoral moulding plate

with nasal stents to mould the alveolar ridge and nasal cartilage concurrently. Use of the NAM technique also eliminated surgical columella reconstruction by lengthening the columella nonsurgically.

The baby was seen weekly to make adjustments to the moulding plate to bring the alveolar segments together. The nasal stent component of the NAM appliance was incorporated when the width of the alveolar gap was reduced to about 5 mm (fig 7). The rationale for delaying the addition of the nasal stent was that as the alveolar gap is reduced, the base of the nose and the lip segment alignment is also improved. This stent will serve the purpose of Non-surgical columella lengthening in bilateral cleft lip and palate.

The NAM technique has been shown to significantly improve the surgical outcome of the primary repair in cleft lip and palate patients compared to other techniques of presurgical orthopedics. Reshaping of the deformed alar cartilage and stretching of the nasal mucosa enhances the surgeon's ability to achieve a good surgical repair. Surgical closure of the lip and nose was performed at 4 months of age. Surgeon has delayed the excision of lip pits that will be performed later. After nasolabial moulding and primary lip repair esthetic results were achieved (fig 10).

## DISCUSSION

Because of variability of vander woude syndrome, obtaining a detailed family history is important

in diagnosing vander Woude syndrome. However, approximately 30-50% of all cases of



Fig 1 Pretreatment Picture

van der Woude syndrome arise as a de novo mutation. The pedigree should suggest an autosomal dominant inheritance pattern, unless the phenotype is the result of a de novo mutation in the affected individual. Expressivity also widely varies, and careful clinical examination of parents and relatives may be necessary. Physical examination of relatives, close examination of family photos, or interviews of older relatives may be necessary to identify minimally affected family members. Examination and genetic counseling is suggested for families that may be affected by vander Woude syndrome.

The cleft lip and cleft palate may be isolated. The severity of these symptoms widely varies and may be unilateral or bilateral. Submucous cleft palate is common and may be easily missed during physical examination. Hypernasal voice and cleft or bifid uvula may be present. A bifid uvula is also a possible isolated finding in certain individuals with vander Woude syndrome. Congenital lip pits are developmental

defects that occur on the paramedial portion of the vermilion border of the lower lip. They may be unilateral or bilateral and may occur as an isolated condition or in association with cleft lip and or cleft palate.<sup>12</sup> The majority of the labial and commissural pits occur without mucus exudation.<sup>13</sup> Although the lip pits are inherited as an autosomal dominant trait, their pathogenesis is not well understood.<sup>14</sup> They are thought to develop from notching of the lip at an early stage of the labial development with fixation of the tissue at the base of the notch or from failure of a complete union of the embryonic lateral sulci of the lip, which persist and ultimately develop into the typical pits.<sup>13</sup>

The surface opening of the lip pit may present as a circular or transverse slit or be located at the apex of nipple-like elevations. Minor salivary gland orifices open into the pits hence the salivary exudate. Although the cleft lip and palate are the major esthetic problems for these patients, exudation of mucous from the lip pits onto the lower labial skin are a source of embarrassment to the patient.<sup>15</sup> Visible or expressible saliva may be present in the lip pits because of an association with the accessory salivary glands. Pits may lead to tracts that are surprisingly long, making surgical removal challenging.

Hypodontia may be observed and most commonly presents as missing maxillary or mandibular second premolars or maxillary lateral incisors. This may be the only symptom. An association of vander Woude syndrome and

taurodontism (teeth with greatly enlarged pulp chambers) has been reported.<sup>16</sup>

The presence of salivary fistulae on the lower lip is not a significant clinical problem, but rather an aesthetic defect. The defect can be treated relatively simply, usually after basic repair procedures and the outcome of the operation is usually good and permanent. Residual slight bulging visible on the vermilion, which are the signs of scar hypertrophy, can be corrected by excision of the scar. As shown above, the presence of salivary fistulae diagnostic for Van der Woude syndrome is not the important medical problem. Much more significant is the probability of developing cleft defects by the offspring of the patients, which reaches 67%,<sup>17</sup> hence this finding is of a great significance for genetic counseling.

Surgical excision of the labial and commissural pits is indicated if the aesthetics of the individual is appreciably affected and exudation of mucous secretions can not be controlled.<sup>18</sup> Surgical excision should include the total removal of the minor salivary glands that exude secretions at the base of the pits to prevent the formation of mucoceles or cysts.

There are several benefits of the NAM technique in the treatment of cleft lip and palate deformity. A proper alignment of the alveolus, lip and the nose helps the surgeon to achieve a better and more predictable surgical result. The cleft deformity is significantly reduced in size with the NAM therapy before surgery, making

primary repair of the lip, alveolus and the nose an effortless procedure. The approximation of the alveolar processes before surgery also enables the surgeon to perform gingivoperiosteoplasty successfully. Long-term studies of NAM therapy indicate that the change in the nasal shape is stable with less scar tissue and better lip and nasal form.<sup>19</sup> This improvement reduces the number of surgical revisions for excessive scar tissue, oronasal fistulas, and nasal and labial deformities.<sup>20</sup> With the alveolar segments in a better position and increased bony bridges across the cleft, the permanent teeth have a better chance of eruption in a good position with adequate periodontal support.<sup>21</sup>

Studies have also demonstrated that 60% of patients who underwent NAM and gingivoperiosteoplasty did not require secondary bone grafting.<sup>22</sup> The remaining 40% who did need bone grafts showed more bone remaining in the graft site compared to patients who have had no gingivoperiosteoplasty.<sup>21</sup> Fewer surgeries also result in substantial cost savings for families and insurance companies.<sup>23</sup> Lee *et al.* demonstrated that midfacial growth in the sagittal and vertical plane was not affected by NAM and gingivoperiosteoplasty.<sup>24</sup> Since the initiation of NAM, there has been a significant difference in the outcome of the primary surgical cleft repair. With proper training and clinical skills, NAM has demonstrated tremendous benefit to the cleft patients as well as to the surgeon performing the primary repair.

Other oral manifestations: Although infrequently reported, other symptoms include syngnathia (congenital adhesion of the jaws); narrow, high, arched palate; and ankyloglossia (short glossal frenulum or tongue-tie). Ankyloglossia and cleft uvula were reported by Shawaf and Mani.<sup>25</sup>

In order to carry out the philosophy of ‘total treatment’, the collaboration of team is involved. This interdisciplinary collaboration will result in a remarkable improvement of the patient’s aesthetics (Fig 10). The quality of this patient’s life improved considerably after treatment and earlier management of this case will result in improved self-esteem at a much earlier age. It is hoped that the multidisciplinary management of patients with orofacial defects will be encouraged. Seeking treatment early in child’s life allows for timely surgery, speech therapy, and dental care.

**CONCLUSION**

VDW is under reported & frequently not diagnosed. The phenomena that CLP & CP are regularly combined in the same pedigree makes it unique. A meticulous examination of the patient with lip pits may reveal a hidden form of cleft e.g. submucous cleft. Physical examination should include as many members of VDW patient’s family as possible and genetic counseling is highly recommended. Management of this case involved the collaboration of different specialists in dentistry and because of earlier management this patient will earn years of improved self-esteem.



Fig 6 Baby with moulding plate & Taping initially



Fig 7 Baby with moulding plate, extraoral taping & nasal stents after 2 months



Fig 8 Profile view right side before & after NAM.



Fig 9 Profile view left side before & after NAM



Fig 10 Baby before & after NAM & Primary lip repair

## REFERENCES

- <sup>1</sup> Burdic AB, Bixler D, Puckett CL. Genetic analysis in families with van der Woude syndrome. *J. Craniofac. Genet. Dev. Biol.* 1985, 5, 181–208.
- <sup>2</sup> Van der Woude. *Fistulae labii inferioris congenita and its association with cleft lip and palate.* *Am. J. Hum. Genet.* 1954, 6, 244–256
- <sup>3</sup> Nagore E, Sanchez-Motilla J M, Feber M I, Serrano G, Bonillo J, Aliaga A. Congenital lower lip pits (Vander Woude Syndrome): presentation of 10 cases. *Pediatric Dermatology* 1998 15:443-445
- <sup>4</sup> Watanabe Y, Otake M, Ito H, Tomida K. Congenital fistulas of the lower lip. *Oral Surgery* 1915, 4:709-722
- <sup>5</sup> Schutte B C, Sander A, Malik M, Murray J C. Refinement of the vander woude gene location and construction of a 3.5-mb YAC contig and STS map spanning the critical region in 1q32-q41. *Genomics.* 1996 36: 507-514
- <sup>6</sup> Ranta R., Rintala A.E. Correlations between microforms of the Van der Woude syndrome and cleft palate. *Cleft Palate J.* 1983, 20, 158–162.
- <sup>7</sup> Onofre M.A., Brosco H.B., Taga R. Relationship between lower lip fistulae and cleft lip and/ or palate in Van der Woude syndrome. *Cleft Palate Craniofac. J.* 1997, 34, 261–265.
- <sup>8</sup> Onofre M.A., Benedito Brosco H., Urias Brosco J., Taga R. Congenital fistulae of the lower lip in Van der Woude syndrome: a histomorphological study. *Cleft Palate Craniofac. J.* 1999, 36, 79–85.
- <sup>9</sup> Rizos M and Spyropoulos MN: Van der Woude syndrome: a review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counselling and treatment. *Eur J Orthod* 26: 17-24, 2004.
- <sup>10</sup> Item CB, Turhani D, Thurnher D, et al: Van Der Woude syndrome: variable penetrance of a novel mutation (p.Arg 84Gly) of the IRF6 gene in a Turkish family. *Int J Mol Med* 15: 247-251, 2005.
- <sup>11</sup> Kondo S, Schutte BC, Richardson RJ, et al. Mutations in IRF6 cause Van der Woude and popliteal pterygium syndromes. *Nat Genet* 32: 285-289, 2002.
- <sup>12</sup> Gorlin RJ, Pindborg JJ, Cohen MM. *Syndrome of the Head and Neck.* 2nd ed. New York: McGraw-Hill Inc. 1976.
- <sup>13</sup> Christian J, Gorlin RJ, Anderson VE. The Syndrome of pits of the lower lip and/or palate: genetic considerations: *Clin Genet* 1971; 2: 95-103.
- <sup>14</sup> Supp, JP, Eversole LR, Wysocki GP. *Contemporary Oral and Maxillofacial Pathology:* Mosby Company 1997; 22.
- <sup>15</sup> Everett FG, Wescott WB. Commissural lip pits *Oral Surg* 1961; 14: 202-209.
- <sup>16</sup> Nawa H, Oberoi S, Vargervik K. Taurodontism and Van der Woude syndrome. Is there an association?. *Angle Orthod.* Sep 2008;78(5):832-7.
- <sup>17</sup> Shprintzen R.J., Goldberg R.B., Sidoti e.J. The penetrance and variable expression of the Van der Woude syndrome: implications for genetic counseling. *Cleft Palate Craniofac. J.* 1980, 17, 52–57.
- <sup>18</sup> Ord RA, Sowray JH. Congenital lip pits and facial clefts. *Br J Oral Maxillofacial Surg* 1985; 23: 391.
- <sup>19</sup> Maull DJ, Grayson BH, Cutting CB, Brecht LL, Bookstein FL, Khorrumbadi D, et al. Long-term effects of NAM on three-dimensional nasal shape in unilateral clefts. *Cleft Palate-Craniofac J.* 1999;36:391–7
- <sup>20</sup> Sato Y, Grayson BH, Cutting CB. Unilateral cleft lip and palate patients following gingivoperiosteoplasty. San Diego: American Association of Orthodontist; 1999.
- <sup>21</sup> Lee C, Grayson BH, Cutting CB. The effect of Gingivoperiosteoplasty on the outcome of secondary alveolar bone graft. Seattle: American Cleft Palate-Craniofac Assoc; 2002.
- <sup>22</sup> Santiago PE, Grayson BH, Cutting CB, Gianoutsos MP, Brecht LE, Kwon SM. Reduced need for alveolar bone grafting by presurgical orthopedics and primary gingivoperiosteoplasty. *Cleft Palate-Craniofac J.* 1998;35:77–80.
- <sup>23</sup> Pfeifer TM, Grayson BH, Cutting CB. NAM and gingivoperiosteoplasty versus alveolar bone graft: An outcome analysis of costs in the treatment of unilateral cleft alveolus. *Cleft Palate-Craniofac J.* 2002;39:26–9.
- <sup>24</sup> Lee CT, Grayson BH, Cutting CB, Brecht LE, Lin WY. Prepubertal midface growth in unilateral cleft lip and palate following alveolar moulding and gingivoperiosteoplasty. *Cleft Palate-Craniofac J.* 2004;41:375–80.
- <sup>25</sup> Al Shawaf MD, Mani NJ. Case Report and Differential Diagnosis of Van der Woude's Syndrome and Congenital Commissural Pits. *Saudi Dent J* 1990; 2: 21-23.