Case Report

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Van Der Woude Syndrome: A Case Report

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ABSTRACT

Background: Van der Woude syndrome is a rare autosomal dominant developmental disorder, occurring in about 1 in 1, 00,000 to 2, 00,000 individuals, caused by deletions in the chromosome band 1q32-q41. It is characterized by congenital lower lip pits, cleft lip and/or cleft palate. Other features associated with this syndrome are congenitally missing teeth, hypodontia, bifid uvula, narrow high arched palate, ankyloglossia, syngnathia, hypernasal voice, congenital heart defects and limb anomalies. The orofacial abnormalities are caused due to mutations in a gene called Interferon Regulatory Factor 6 (IRF6). Literature states that the condition is associated both with consanguineous and non-consanguineous marriages. The diagnosis has to be confirmed with gene mapping. The treatment involves professionals from both the medical and dental fields. This case report describes a rare presentation of van der Woude syndrome in a 33-year-old female patient.

Keywords: Van der Woude syndrome, Cleft lip, Cleft palate, Lip pits, hypodontia.

INTRODUCTION

Van der Woude syndrome is a form of orofacial clefting, with autosomal dominant inheritance pattern and variable expressivity[1,2,]. It is also known as Cleft lip syndrome, lip pit syndrome or dimpled papillae of the lip. Anne Van der Woude, in 1954 extensively reviewed the syndrome that later received her name[3,4]. The presence of labial pits was first observed by Demarquay in 1845 and was first reported by Epstein in 1900. The orofacial manifestations of the syndrome include lower lip pits, cleft lip and/ or cleft palate, narrow high arched palate, hypodontia, ankyloglossia, hypernasal voice[5,6]. The extraoral manifestations of the syndrome are popliteal webs, limb anomalies, accessory nipples, congenital heart abnormalities and Hirschsprung's disease[5].

CASE REPORT

A 33-year-old female patient reported to the Department of Oral Medicine and Radiology, with a complaint of decayed teeth in the lower jaw left side back teeth region for two months, with occasional sensitivity on taking hot and cold food items, and history of food lodgment on taking sticky food since three weeks. The patient has difficulty in speech due to a birth defect in the mouth since childhood, for which she consulted a doctor, and no treatment was given. Medical history was noncontributory. The patient underwent removal of the tooth in the lower jaw left side back teeth region four months back with no post-operative complications. Family history reveals the presence of lip pits in maternal family member. On extraoral examination, the face was grossly symmetrical bilaterally(Fig 1), the profile was concave, lips were potentially

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competent with bilateral depressions on either side of midline of lower lip (Fig 2).

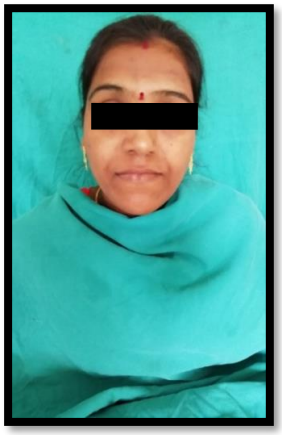

Fig 1: Front profile.

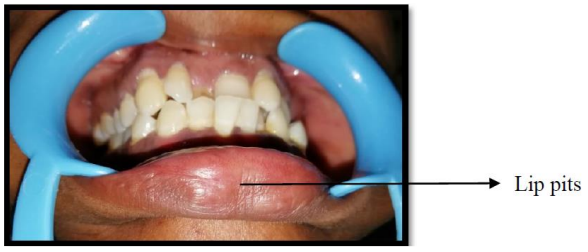

Fig 2: Lower lip pits.

Intraoral soft tissue examination revealed a midline cleft of palate extending 0.5cm away from the incisive papilla up to posteriorly. The cleft extends up to the uvula leading to the bifid uvula (Fig 3). It measured about 4x2cm; the entire nasal cavity is visible from the cleft. Dental examination revealed decayed 17, 26, 37; missing 22, 47; anterior crossbite 11, 21, 31, 32, 41; root stump 38. (Fig 4, 5) Based on the above findings, the case can be provisionally diagnosed as Van Der Woude syndrome. Differential diagnosis of Popliteal Pterygium syndrome and Orofaciodigital syndrome can be considerable.

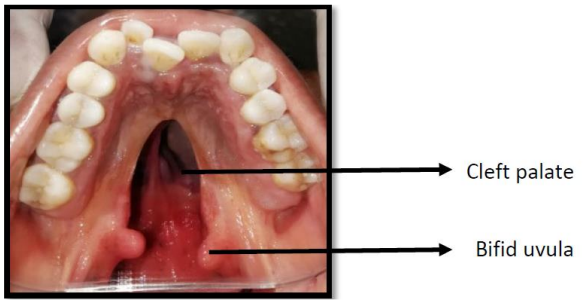

Fig 3: Maxilla showing cleft palate and bifid uvula.

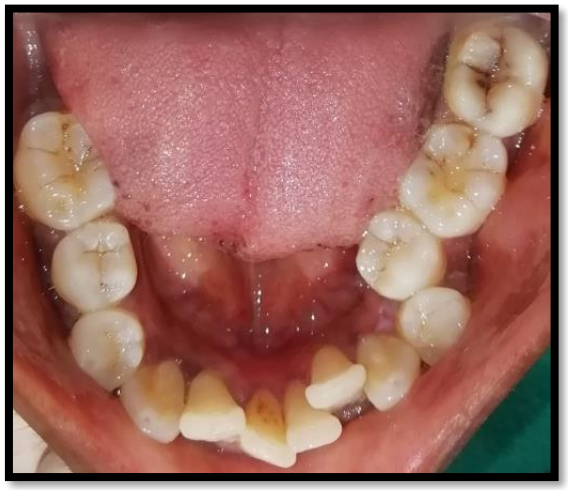

Fig 4: Mandible showing lower anterior crowding

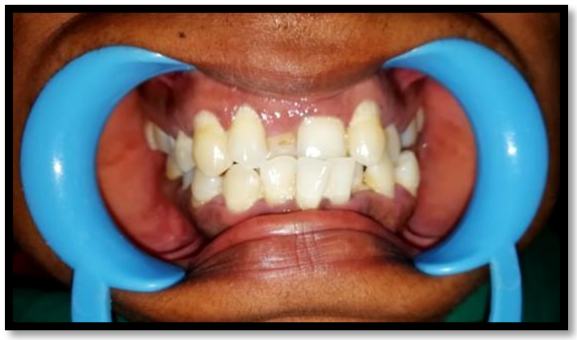

Fig 5: Anterior crossbite

Further investigations were performed- Occlusal topographic view of the maxilla, Orthopantomograph, CT head and neck, and 2D Echocardiogram. Occlusal topographic view of maxilla reveals a large defect in the midline of the hard palate and missing 22 (Fig 6). Orthopantamograph reveals discontinuity in the palate and missing 22,47(Fig 7). CT reveals a large defect along the midline of the hard palate extending up to the soft palate (Fig 8). Deviated nasal septum with bony spur noted towards right impinging middle and inferior turbinate. Visualized sections of the C-spine showed a bifid spinous process. 2D-ECHO with Doppler study revealed no abnormality. The patient has been advised restorations for needful teeth. Later, she was referred to the Department of Prosthodontics for the fabrication of an obturator. Both upper and lower alginate impressions were made, and a palatal obturator was fabricated to aid in the speech of the patient (Fig 9)

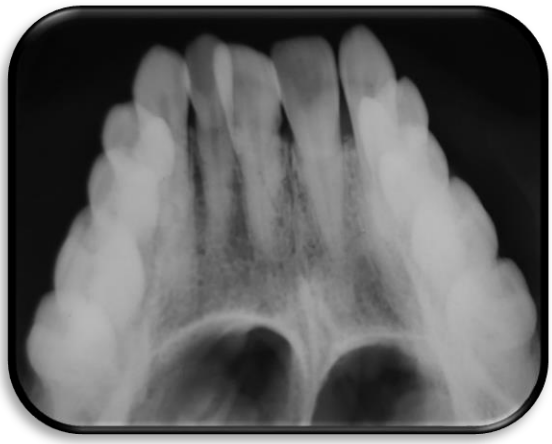

Fig 6: Occlusal topographic view of maxilla showing cleft in the palatal region.

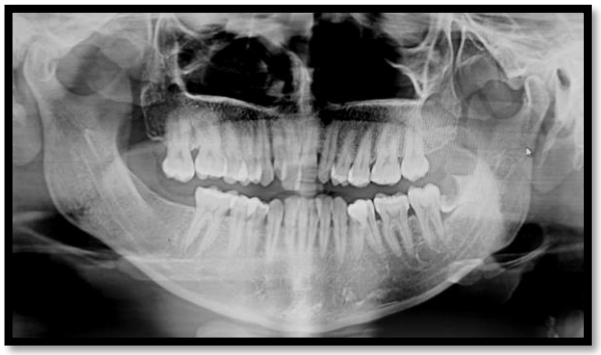

Fig 7: Orthopantomograph(OPG) showing cleft in the maxilla

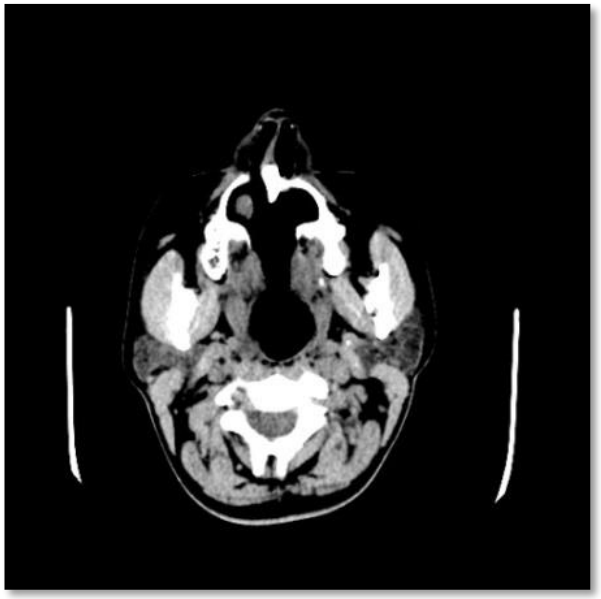

Fig 8: Axial Computed Tomography showing a large defect in palate extending up to uvula.

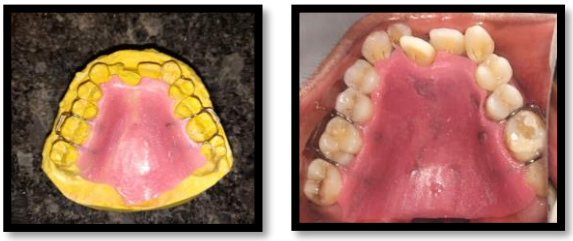

Fig 9: Palatal obturator prosthesis

DISCUSSION

Van der Woude syndrome is a rare form of orofacial clefting with a high incidence of penetrance and variable expressible nature, occurring in about 1 in 1,00,000 to 2,00,000 individuals[7]. The prevalence of Van der Woude syndrome was reported to be ranging from 0.37% to 6% among the population with orofacial clefting, with females being most prone to this syndrome[4]. Micro deletion on chromosome bands 1q 32-q41 is known to cause a genetic defect of lip pits. Recently, it was identified that mutations in gene encoding Interferon Regulatory Factor 6 (IRF6) causes this syndrome by Kondo[6]. Almost 46 mutations in IRF6 associated with this syndrome have been identified to date[4]. About 30%–50% of cases of van der Woude syndrome arise as de novo mutations and as the condition is autosomal dominant, it will be transferred to the next generation[8]. From the affected parent, the risk of inheriting cleft is 22.43%, whereas inheriting only lip pits or the individual being non-penetrant is 27.57%. The cardinal features of Van Der Woude syndrome are lower lip pits, cleft lip and/ or cleft palate and hypodontia.

LIP PITS

The lip pits are found in the lower lip, upper lip or oral commissures, with a marked predilection for the lower lip. They are located in the vermilion border of the lip and on the mucocutaneous line at a distance of 5-25mm from each other[5]. They are congenital malformations that are rare. Lower lip pits are also called fistula labiiinferioriscongenita, labial humps, labial cysts, labial fistulae, and paramedian sinuses of the lower lip[2]. The lip pits may develop from notching of the upper or lower lip during the early stages of labial development, with the tissue being fixed at the base of the notch or due to incomplete union of lateral sulci of the lip,

which persists and develops into pits. According to Rizos and Spyropoulos, incomplete expression of the trait is when there is the unilateral or median presentation of the pit. Completely expressed traits show bilateral lip pits[1].

Types of lip pits

- Unilateral or bilateral
- Circular or oval
- Transverse, slit-like or sulci[8]

Unilateral lip pits are commonly seen on the left side (Watanabe et al., 1951; Newman and Shulman, 1961) and rarely on the right side (Ruppe and Magdeleine, 1927; Kulkarni et al., 1995). Microforms of the lower lip exist like transverse mucosal ridges and nipple-like elevations, which may fuse in the midline to produce a snout like structure[8].

Lip pits are usually asymptomatic (Shprintzen et al., 1980), but there may be intermittent or continuous salivary or watery secretions, which may occur spontaneously or during mastication or fear or apprehension (Soricelli et al., 1966). There is the rapid accumulation of mucous during and before meals or when crying in the case of infants. The condition may worsen during winters, which results in excoriation and chaffing of the lip. There may be an occasional collection of food particles in the sinuses(Hoffman, 1971).

CLEFT LIP AND PALATE

Cleft lip and cleft palate are orofacial clefts that are major structural birth defect with an incidence of 1 in 500–1000 births. There are about 400 syndromes with cleft lip and without cleft palate. Van der Woude syndrome accounts for about 2% of cases of cleft lip and palate worldwide. Clinical features include facial deformation, feeding problems, frequent middle ear infections, which require interventions from multiple disciplines for treatment. Speech therapy is indicated to correct problems arising from muscular defects of the cleft[1].

The congenital anomalies can be divided into three types[9]

a) Disruptions: A rare anomaly that is related to the breakdown of the original normal foetal developmental process

E.g. Craniofacial cleft resulting from amniotic bands

b) Deformations: They occur secondary to mechanical forces leading to anomalies of a lesser degree when compared to the disruption

e.g. Club foot, Cleft palate, Pierre Robin sequence etc.

c) Malformations: A morphologic defect in an organ from an intrinsically abnormal developmental process

e.g. Polydactyly, Congenital heart anomalies, Cleft lip etc.

Syndromes associated with cleft lip and palate include Monogenic syndromes and Chromosomal syndrome. Monogenic syndromes are Van der Woude syndrome, with most of these cases linked to Chromosome 1q32-q41 and Treacher Collins syndrome. A review by Gorlin described 72 monogenic syndromes involving Oral clefts. A follow-up report by Cohen identified 154 monogenic syndromes, and, more recently, 487 were identified in the 2001 version of the London Dysmorphology Database. Chromosomal syndromes include Velocardiofacial syndrome, an autosomal dominant condition associated with abnormality of chromosome 22q.

HYPODONTIA

Hypodontia is defined as the developmental absence of one tooth or more. The absence of all teeth (anodontia) is rare. The term oligodontia is used to define the developmental absence of multiple teeth, usually associated with systemic manifestations. It is commonly classified according to the severity of the condition

1. Mild-to-moderate hypodontia: Absence of usually two teeth or more but fewer than six teeth, excluding third molars

2. Severe hypodontia: Absence of six teeth or more, excluding third molars. It may be associated with microdontia

3. Oligodontia; Absence of multiple teeth, usually associated with systemic manifestations.

Hypodontia is considered as a cardinal associated feature and has been observed in 10%–81% of all

van der Woude syndrome patients, with a number of teeth missing in maxilla almost double that in the control group.[10, 11]

OTHER FEATURES

Ankyloglossia, high arch palate, enamel hypoplasia, syngnathia, syndactyly, bifid uvula, hypernasal voice, congenital heart defects, accessory nipples, limb anomalies, brain abnormalities are other associated features of Van der Woude syndrome. The dimples are usually circular, but they may be transverse slits or sulci.[2, 3, 6. 7]

DIAGNOSIS

Diagnosis of van der Woude syndrome can be achieved with both family and medical history. The clinical picture gives most of the diagnosis of the condition, as there were cardinal signs. Other investigations to be carried out for confirmation are gene mapping for IRF 6 gene mutations, 2D cardiogram to check for heart defects. Since this syndrome is autosomal dominant, similar clinical presentation in any member of the family can contribute to the diagnosis.

The present case has cardinal clinical signs of lip pits, cleft palate and hypodontia. Though lip pits were not that characteristic, in this case, family history of lip pits helped us to arrive at a diagnosis of Van der Woude syndrome. To prevent any future life hazards, 2D Echocardiogram was performed to rule out any cardiac anomalies, which revealed no abnormalities. Since the patient was not esthetically concerned and considering the age and social conditions of the patient, an obturator was suggested and fabricated.

DIFFERENTIAL DIAGNOSIS[2,5,8,11]

Disease	Features
Popliteal Pterygium Syndrome	The rare, autosomal dominant anomaly with a variety of manifestations, including lower lip sinuses, popliteal webbing, cleft lip, cleft palate, syndactyly, and genital and nail anomalies
Orofaciodigital Syndrome type 1	Disorder including lower lip sinuses, clefts of the jaw and tongue in the areas of the lateral incisors and canines, malformations of the face and skull, and mental retardation
Hirschsprung disease	Aganglionic megacolon combined with cleft palate and lip pits
Ankyloblepharon filiform adnatum	Cardiac or central nervous system anomalies, ectodermal syndromes, cleft lip and/or palate

TREATMENT

Treatment of van der Woude syndrome is a multidisciplinary approach involving speech therapy, cardiology, orthodontics, prosthodontics and surgical departments. It includes surgical correction of lip pits, cleft lip and palate, prosthodontic fabrication of obturator, orthodontic correction of malocclusions. If the lip pits are secondarily infected due to inflammation, antibiotics and analgesics can be prescribed along with meticulous oral hygiene practice[1]. Sinuses of the lip should be excised to prevent infections, but simple excision has drawbacks like lower lip muscle loosening and inability to whistle[5]. A palatal obturator can be fabricated to aid in mastication and speech.[12, 13]

Lam et al. studied 22 patients with Van der Woude syndrome, 64% of patients showed cleft lip and palate. Another study was done by James et al., in which 11 patients were studied, and 6 of them showed both cleft lip and palate[2]. According to Schinzel and Klausler, the lip pits are associated with clefts in about half the patients. Among these, two-thirds have cleft lip or cleft lip palate, and one-third have cleft palate alone[4].

CONCLUSION

Van der Woude syndrome is frequently underreported and frequently not diagnosed. With proper identification and appropriate understanding of oral manifestations and clinical features, the dentist plays an important role in the diagnosis and management of patients with rare syndromes like van der Woude syndrome. Even though treatment is available for all anomalies, prevention is always a choice. The clinical features of this syndrome vary greatly, so dentists should remember the phenotypic variations of the

condition in individuals affected. Early identification and management of the anomalies are necessary for improving the well being of the patient. Genetic counselling is also very important to prevent further transmission to the next generations.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

REFERENCES

1. Rajendran R. Shafer's textbook of oral pathology. Elsevier India; 2009.
2. Hasan S, Khan NI. Van der woude syndrome-a case report. Recent Research in Science and Technology. 2011;3(12):53-7.
3. Gorlin RJ, Cohen Jr MM, Hennekam RC. Syndromes of the head and neck. Oxford university press; 2001 Sep 27.
4. Trishala A, Kumar S. Van Der Woude Syndrome-A Review. Journal of Pharmaceutical Sciences and Research. 2016 Jun 1;8(6):495.
5. Reddy RS, Ramesh T, Vijayalaxmi N, Reddy RL, Swapna LA, Singh TR. Van der Woude syndrome-A syndromic form of orofacial clefting. Journal of clinical and experimental dentistry. 2012 Apr;4(2):e125.
6. Reddy KV, Ramesh TV, Rajasekhar G, Rao GV, Kruthi N. Van der Woude Syndrome: Case Reports and a Review. Journal of Indian Academy of Oral Medicine and Radiology. 2011 Apr 1;23(2):136.
7. More CB, Varma S, Tailor M, Bhavsar K. Van der Woude syndrome: Report of two cases with supplementary findings. Indian Journal of Dental Research. 2013 May 1;24(3):387.
8. Goswami S. Van der woude syndrome: A report of four cases. Archives of Medicine and Health Sciences. 2017 Jul 1;5(2):248.
9. Venkatesh R. Syndromes and anomalies associated with cleft. Indian journal of plastic surgery: official publication of the Association of Plastic Surgeons of India. 2009 Oct;42(Suppl):S51.
10. Dhanrajani PJ. Hypodontia: etiology, clinical features, and management. Quintessence international. 2002 Apr 1;33(4).
11. Bordin et al. Ankyloblepharon Filiforme Adnatum in a Newborn. American Journal of Perinatology 2015; 5(1). E12-13.
12. Rizos M, Spyropoulos MN. Van der Woude syndrome: a review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counselling and treatment. The European Journal of Orthodontics. 2004 Feb 1;26(1):17-24.
13. Phore S, Panchal RS. Van der Woude syndrome: A rare case report. International Journal of Oral Health Sciences. 2017 Jul 1;7(2):108.