Case Report

Van der Woude Syndrome: A Case Report and Review of Literature

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Abstract:

Van der Woude Syndrome (VWS) is an uncommon autosomal dominant disorder that affects embryologic facial development and is characterized by two labial pits in the lower lip and is usually associated with cleft lip and cleft palate. Congenital lip pits are frequently associated with cleft lip and/or cleft palate in VWS; nevertheless, lip pits may be the only symptom in this condition. The prevalence of VWS is about 1 in 35,000 to 100,000 births and accounting for 2% of all cases with cleft lips and palates.

A 10-year-old boy presented with bilateral pits on the lower lip, one on either side of the midpoint. There was evidence of maxillary hypoplasia and he also presented with bilateral accessory auricles. Additional deformities such as cleft lip or palate were not present. The patient's parents were eager for aesthetic correction. The lower lip pits with their tracts were excised under general anaesthesia. Wound healing and aesthetic outcome was satisfactory. Histopathological examination revealed fibrous tract, squamous epithelisation and fibres of skeletal muscle.

Keywords: Van der Woude Syndrome; genetic disorder

Introduction:

Van der Woude Syndrome also referred to in literature as autosomal dominant inherited clefting syndrome is a rare autosomal dominant condition that affects embryologic facial development and is characterized by two labial pits (fistulae) in the lower lip and is usually associated with cleft lip and cleft palate[1]. Despite the fact that Demarquay reported the fistula labia inferioris congenita in 1845[2], Van der Woude analyzed these traits and discovered a link between lower lip pits and cleft lip or palate[3]. Congenital lip pits are frequently associated with cleft lip and/or cleft palate in VWS; nevertheless, lip pits may be the only symptom in this condition[4]. The prevalence of VWS is about 1 in 35,000 to 100,000 births and accounting for 2% of all cases with cleft lips and palates[5]. VWS may be associated with other congenital features as hypodontia, maxillary hypoplasia, high arched palate, ankyloglossia, limb anomalies and congenital heart defects[6]. The VWS gene has been assigned to deletion in chromosome 1q32-q41 with mutation in the interferon regulatory factor 6 (IRF6)[7].

One of the severe manifestations of this gene mutation is popliteal pterygium syndrome, which has some features including lower lip pits or cleft lip or palate in common with VWS, with the addition of popliteal webs and genital anomalies[8].

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Case report

A 10-year-old boy with congenital deformity of the lower lips was brought to a floating hospital cleft camp by his parents. The boy did not complain of any symptoms but his parents were eager for surgical correction for aesthetic reasons. On examination, there were bilateral pits on the lower lip, one on each side of the midline (Fig. 1). There was no discharge of saliva from the pits on pressure.

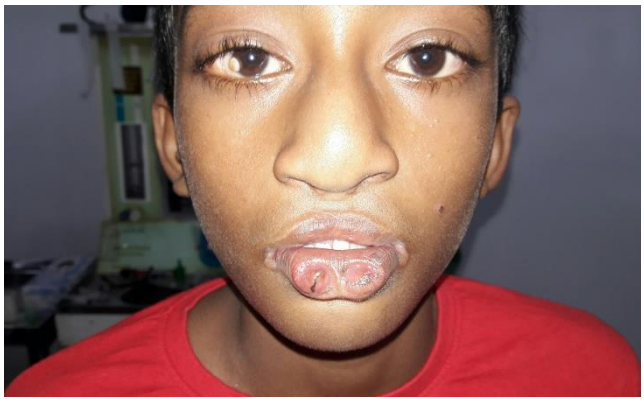

Fig 1: 12-year-old boy with Van der Woude syndrome, presenting with bilateral pits in the lower lip.

There was evidence of maxillary hypoplasia and he also presented with bilateral accessory auricles. (Fig. 2) Additional deformities such as cleft lip or palate were not present. Frank dental anomalies and malocclusions were also not evident.

Fig 2: Lateral view showing, prominent lower lip and hypoplastic maxillae. Accessory auricle was also present.

A general medical check was conducted to rule out the possibility of systemic issues. Detailed investigations such as cephalometric examinations or genetic sequencing was not possible due to the remote location of the hospital, lack of facilities and financial constraints.

Procedure

Under general anaesthesia, excision of the pits along with their tracts was done. Haemostasis was ensured and closure attained by absorbable sutures. Postoperatively the patient recovered well and wound healing was satisfactory. The patient's parents were happy with the aesthetic outcome (Fig. 3).

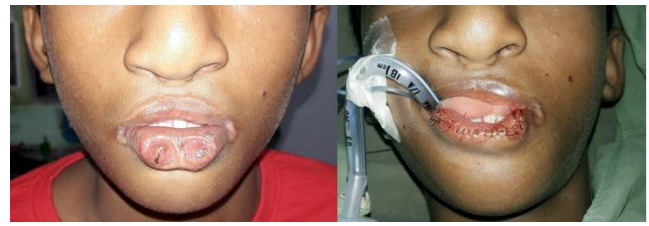

Fig 3: Before and after excision of the lower lip pits.

Histopathological examination of the specimen (Fig. 4) revealed fibrous tract, squamous epithelialization and fibres of skeletal muscle.

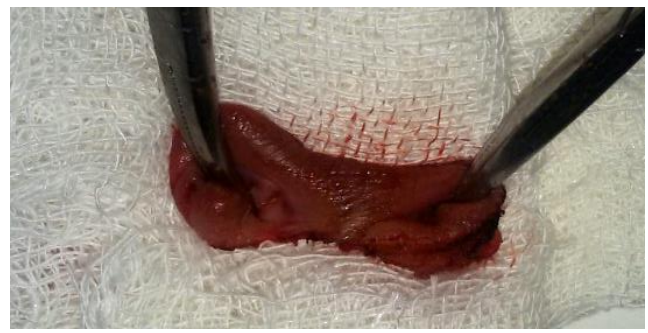

Fig 3: Specimen of excised lower lip pits along with their tracts.

Discussion

Lip pits are very uncommon congenital condition anomalies, clinically presented as bilateral or unilateral depressions in the upper lip, lower lip, or the oral commisure with or without saliva secretion from their fistula[4]. The degree of clinical symptoms of VWS varies greatly even within family members, however lower lip pits, the main feature of VWS, may be the only symptom in this illness[4].

The prevalence of VWS is about 1 in 35,000 to 100,000 births and accounting for 2% of all cases with cleft lips and palates[5]. The syndrome is an autosomal-dominant developmental malformation with variable expressivity and penetrance rate close to 80% to 100%[5]. The VWS gene has been linked to a loss on chromosome 1q32-q41, as well as a mutation in the interferon regulatory factor 6 (IRF6), however a second chromosomal location at 1p34 has also been discovered[9]. Lip pits can range in clinical appearance from asymptomatic minor depression to obvious discharging sinuses. These congenital malformations are of 3 types depending on their location: commissural, midline upper lip, and the most common kind is lower lip pits. They may be usually bilateral symmetric, but are occasionally bilateral asymmetric, microform, median, or unilateral[10]. They are likely to extend into the orbicularis oris muscle and sometimes communicated with the ducts of the underlying minor salivary glands, which may either continuously or intermittently drain small amounts of saliva[11].

There are other related traits that may or may not be present in a patient with the syndrome's cardinal indications. Cleft lip, cleft palate, hypodontia, ankyloglossia, high arched palate, limb deformities such as popliteal pterygium, and congenital heart conditions[6].

Many studies have shown links between maxillary hypoplasia and VWD, as seen in our case[12].

Other associated features which can be seen are malocclusion, long face, narrow maxilla, protrusion of maxilla, high arched palate, crossbite, bifid uvula, and syngnathia[13].

The following are considered in the differential diagnosis of Van der Woude Syndrome[14]:

1. Popliteal pterygium syndrome (PPS) that includes popliteal web, cleft lip and/or palate, lower lip pits in 60% cases, and anomalies of genitourinary system, such as cryptorchidism and bifid scrotum in males and hypoplastic labia majora and uterus in females. People with VWS have a risk of giving birth to offspring with PPS[15].
2. Hirschsprung's disease (aganglionic megacolon combined with cleft palate and lip pits)[16].
3. Orofacial digital syndrome type 1, with prominent orodental, facial, digital, renal, and central nervous system abnormalities. Orodental signs include cleft palate, bifid tongue, hypodontia, and median cleft of the upper lip and/or lip pits[17].
4. Ankyloblepharon Filiforme Adnatum—partial or complete full thickness fusion of the lid margins, cleft lip and palate, hydrocephalus, meningocele, imperforate anus, bilateral syndactyly, infantile glaucoma, and cardiac problems such as patent ductus arteriosus and ventricular septal defects[18].

As the disorder shows a high affinity with clefts and a familial type of occurrence, close examination of relatives to recognize lip pits and clefts is critical for genetic counseling[4]. Although it is accepted in the literature that many individuals do not require or want surgery, the major rationale for excision of congenital lip sinus is correction of the aesthetic abnormality[19]. Recurrent inflammation will justify removal of the lip sinus tracts in a small minority of individuals[5]. The sinus tract should be completely excised, 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[20].

Limitation

As the patient presented to us in a remote floating hospital, several necessary investigations such as cephalometric radiological examinations, detailed cardiac examinations and genetic sequencing could not be performed.

Conclusion

In conclusion, physicians should be aware of variable congenital disorders associated with lip pits. Among them, VWS has a variable clinical expression, and recognition of its lesser expression is difficult. Lip pits can be the only clinical finding which is suggestive of VWS, as in our case[4].

If patients present with associated congenital abnormalities as mentioned above, a multidisciplinary approach for treatment should be undertaken, involving plastic surgeon, ENT surgeon, and dental and/or maxillo-facial surgeon, as required.

Since there is a probability of developing cleft defects by the offspring of the patients, genetic counselling is of great significance in these patients[21].

References:

1. J. H. Hersh and G. D. Verdi, "Natal teeth in monozygotic twins with Van der Woude syndrome," The Cleft Palate-Craniofacial Journal, vol. 29, pp. 279–281, 1992.
2. Demarquay JN (1845) Quélques considérations sur le bec-de-lièvre. Gaz Méd 13: 52.
3. Van der Woude A (1954) Fistula labii inferioris congenita and its association with cleft lip and palate. Am J Hum Genet 6: 244.-256.
4. Baghestani S, Sadeghi N, Yavarian M, Alghasi H. Lower lip pits in a patient with van der Woude syndrome. J Craniofac Surg. 2010 Sep;21(5):1380-1
5. Rizos M, Spyropoulos MN. van der Woude syndrome: a review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counseling and treatment. Eur J Orthod 2004; 26:17Y24
6. A. Shweta, S. Suma,H. Shivayogi, and B.Kiran, "Van der Woude syndrome: the rarest of the rare," Contemporary Clinical Dentistry, vol. 3, no. 2, 2012.
7. Shotelersuk V, Srichomthong C, Yoshiura K, et al. A novel mutation, 1234del(c), of the IRF6 in a Thai family with van der Woude syndrome. In J Mol Med 2003;11:505Y507
8. Kondo S, Schutle BC, Richardson RJ, et al. Mutation in IRF6 causes van der Woude and popliteal pterygium syndrome. Nat Genet 2002;32:285Y289
9. Onofre MA, Brosco HB, Taga R. Relationship between lower-lip fistulae and cleft lip and/or palate in van der Woude syndrome. Cleft Palate Craniofac 1997;34:261Y265
10. Koillinen H, Wong FK, Rautio J, et al. Mapping of the second locus for the van der Woude syndrome to chromosome 1p34. Eur J Hum Genet 2001;9:747Y752
11. Mallory SB, Krafchick BR. Congenital lower lip pits. Pediatr Dermatol 2002;19:363Y364
12. Oberoi S, Vargervik K. Hypoplasia and hypodontia in Van der Woude syndrome. Cleft Palate Craniofac J. 2005 Sep;42(5):459-66.
13. S. Agarwal,M. R.Dinesh, R. M. Dharma, and B. C. Amarnath, "Van der Woude syndrome: management in the mixed dentition," Contemporary Clinical Dentistry, vol. 4, no. 1, pp. 105–107, 2013.
14. Patil, Pallavi & Deshmukh, Kiran & Mangalgi, Anand & Patil, Subhash & Hugar, Deepa & Kodangal, Saraswathi. (2014). Van der Woude Syndrome with Short Review of the Literature. Case reports in dentistry. 2014. 871460.

15. M. A.Newman,N.O.Nartey, and E. A.Nyako, "Van der Woude syndrome-report of a case," Ghana Medical Journal, vol. 39, no. 2, pp. 68–70, 2005.
16. R. J. Shprintzen, R. B. Goldberg, and E. J. Sidoti, "The penetrance and variable expression of the Van der Woude syndrome: implications for genetic counseling," Cleft Palate Journal, vol. 17, no. 1, pp. 52–57, 1980.
17. P. Janku, M. Robinow, T. Kelly, R. Bralley, A. Baynes, and M. T. Edgerton, "The van der Woude syndrome in a large kindred: Variability, penetrance, genetic risks," The American Journal of Medical Genetics, vol. 5, no. 2, pp. 117–123, 1980.
18. A. M. Gruener and M. S. Mehat, "A newborn with ankyloblepharon filiforme adnatum: A case report," Cases Journal, vol. 2, no. 8, article 8146, 2009.
19. A. Souissi, D. El Euch, M. Mokni, T. Badri, and A. ben Osman Dhahri, "Congenital lower lip pits: a case report," Dermatology Online Journal, vol. 10, no. 2, p. 10, 2004.
20. Y.Watanabe,M.O. Igaku-Hakushi, and K. Tomida, "Congenital fistulas of the lower lip. Report of five cases with special reference to the etiology," Oral Surgery, Oral Medicine, Oral Pathology, vol. 4, no. 6, pp. 709–722, 1951.
21. P. W´ojcicki, K. Kobus, and K. W´ojcicka, "Van der Woude syndrome," Dental and Medical Problems, vol. 44, no. 1, pp. 18– 21, 2007.

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