Original Article

Van Der Woude Syndrome: A Case Series at Chu D' Treichville, Abidjan, Cote D' Ivoire

Abstract

Background: Van der Woude syndrome (VWS), characterised mainly by lower lip pits and orofacial cleft (OFC), is the most common syndrome associated with an OFC. It is inherited as an autosomal dominant, high penetrance disorder with variable phenotypic expression and caused by the genetic mutation of the interferon regulatory factor 6 gene (IRF6). This study showcases the syndrome's variable phenotypic expressivity in six cases seen at Chu d' Treichvile, Abidjan, and Cote d'Ivoire. **Materials and Methods:** A review of six cases at the above-named hospital. Data collected include age at presentation, gender, type of cleft, presence or absence of lip pits, and family history of VWS. **Results:** Six cases of VWS were reviewed with an age range from 2 to 39 years and a male-to-female ratio of 1:2. Three of the patients had a bilateral cleft lip, one case of unilateral cleft lip and palate, another single case of cleft palate only while the sixth patient has no cleft deformity. All the patients have bilateral lower lip pits except one with a single median pit on the lower lip. There is a family history of VWS in three of the patients. **Conclusion:** Our study demonstrates the variable expressivity of VWS as different forms of lower lip pits and OFC. The presence of lower lip pits should be a signal for examination of family members to identify other cases and those likely to have cleft babies. Genetic mapping to detect mutation of IRF6 genes will be of tremendous aid in the effective diagnosis of VWS.

Keywords: *Cleft lip and palate, lip pits, Van der Woude syndrome*

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Introduction

Orofacial clefts (OFCs) remain the most common congenital abnormality in the orofacial region and next only to club foot on the list of most prevalent congenital abnormalities in the whole body.[1] They may present as cleft lip with or without a cleft palate or cleft palate only and are usually associated with a multitude of syndromes, one of which is Van der Woude syndrome (VWS).

VWS is a rare autosomal dominant developmental disorder, first described by Dr. Anne der Woude in 1954. It is the most common form of syndromic—OFC, with a prevalence of 2% and a worldwide disease incidence of 1:70,000 to 1:100,000.[2,3] The clinical manifestation of the condition is variable as they may have lower lip pits, cleft lip with or without cleft palate, or no phenotypic abnormality at all.[2] Lower lip pits have been reported in 88% of VWS patients, and they are the only visible defect in 64% of cases.[4] The presence of lower lip pits may be due to the incomplete or nonfusion of lateral lip processes. Dental hypoplasia, high-arched narrow palate, ankyloglossia, and hypodontia are some of the oral findings associated with VWS,[5] but there are also reports of limb anomalies and cognitive impairment.[3,6,7] VWS has been identified to be genetically due to the mutation of interferon regulatory factor 6 (IRF6).[8] It is, therefore, not out of place to screen all patients who appear to have nonsyndromic OFCs for this genetic mutation so that a line of management can be outlined for effective management by the relevant specialists.

This study is a review of six VWS cases seen at the Cleft clinic of Chu d' Treichville, Abidjan.

Materials and Methods

Patients with features suggestive of VWS and seen at the above-named Clinic from August 2014 to December 2022 are included in this study. Other data in the report include gender, age at presentation, type of OFC, presence or absence of lower lip

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Table 1: Summary of main features of the VWS cases

	Age at presentation (years)	Gender	Type of cleft	Presence of lower lip pits	Other abnormalities	Familial history of pits
A	39	F	BCL	Yes	Yes	Yes
B	14	M	BCL	Yes	Nil	Yes
C	9	F	CP	Yes	Yes	Yes
D	2	M	UCLP	Yes	Nil	No
E	7	F	Nil	Yes	Nil	No
F	19	F	BCL	Yes	Nil	No

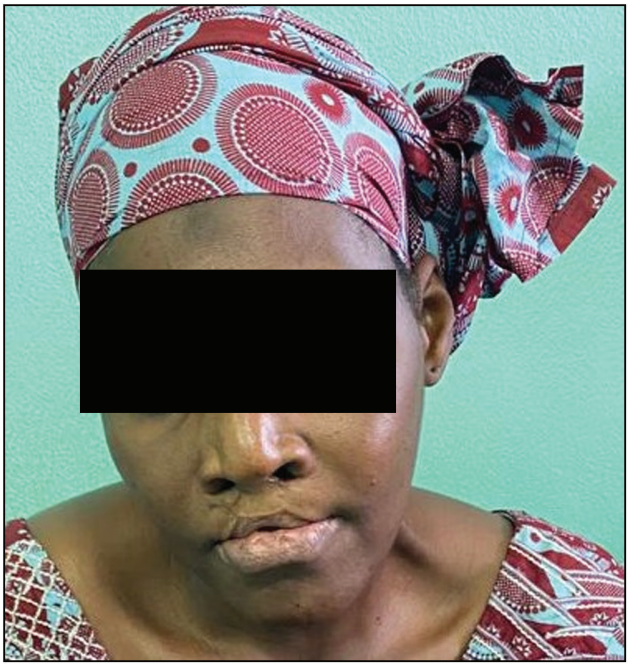

Figure 1: Patient A with repaired bilateral cleft lip and bilateral paramedian lower lip pits

Figure 2: Patient F with repaired bilateral cleft lip and a single median lower lip pit

pits, presence of other abnormalities, and familial history of the cleft. This is shown in Table 1.

Results

Six patients presented within the study period. The ages of the patients range from 2 years to 39 years, four (66.67%) being females and two males, with a female-to-male ratio of 2:1.

Bilateral cleft lip is the most common phenotypic expression of OFC in this study (60%), with 20% having cleft palate only, while one of the cases has lower lip pits without OFC.

Lower lip pits are found in all the six cases reported, with the majority (five) being bilateral paramedian lower lip pits [Figure 1], while the remaining one is a midline lower lip pit [Figure 2]. Hypodontia is the other major anomaly recorded in 33.3% of the cases seen, but its presence could not be ascertained in other patients as they do not yet have the full complement of teeth.

Discussion

The mean age of presentation in this series is 10.2 years. This is due mainly to the poor health-seeking behaviour that results from the poor awareness which is prevalent in this part of the world.[9] Also, 60% of patients in this series are females, a finding consistent with the reports by James *et al.*[10] (63.6%) and Omo-Aghoja *et al.*[11] (65.2%). However, Lam *et al.*[12] and Rizos and Spyropoulos[13] found no significant gender predominance in their studies.

The classic presentation of the condition is bilateral paramedian lower lip pits[8,12,14] as seen in the majority (83.3%) of our reported cases. There is one patient with a single median lower lip pit, similar to what was described as an incomplete expression of the VWS trait by Ziai and Benson.[15] Furthermore, the lower lip pit is the only clinical feature seen in one of the cases: a possibility similarly reported by James *et al.*[10] The presence of bilateral cleft of the lip, unilateral cleft of the lip and palate, and isolated cleft palate in this series also corroborate the variable phenotypic expression of the cleft in VWS that is well documented in the literatures.[10,12,16] The phenotypic expression of only lower lip pits and no cleft by a patient in this series is also supported by a previous study which also suggests a higher risk of having a baby with cleft lip and palate in such individuals.[17]

As reported, the familial history of VWS in 50% of patients in this series conforms with the high penetrance and autosomal dominant nature of VWS. Martelli-Junior *et al.*[18] have documented a 22% risk of having a cleft child if the parents have a lip pit only, 30% if the patient or sibling has a cleft only, but increasing to 41% chance if the patient has both lip pit and cleft.[5] In our series, a mother with having lip pit and cleft lip had three children, with two of them having both lip pits and cleft, while the third child has none of the features. Also, hypodontia has been conventionally linked with VWS, as is seen in 33.3% of patients in this series.[17]

There are previous reports of discharge from lip pits, probably due to continuity between the lining of labial mucosa extending into orbicularis muscle and minor salivary glands, which may require a surgical cosmetic repair of the lip pits.[14,19] There is, however, no history of such discharge in this series, but all patients with cleft lips with or without cleft palate have their clefts repaired satisfactorily.

Finally, although the diagnosis of VWS is mainly clinical, a pedigree charting and examination of family members of cases will assist greatly in proper counselling because of the increased risk of cleft in these families. Genetic mapping or investigation to detect mutation in the IRF6 gene will even give more credence to these counselling sessions.

Conclusion

Lower lip pits are pathognomonic in the diagnosis of VWS; their presence should therefore signal the need for further examination of family members to identify other cases and those likely to have cleft babies. Genetic mapping to detect mutation in IRF6 will go a long way to aid the effective diagnosis of VWS and similar conditions that may require the knowledge and skills of multiple disciplines in the field of medicine and dentistry in the West African country.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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