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Case Report

# Van Der Woude Syndrome with Ectodermal Dysplasia- Case Report

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## Abstract

Congenital lip pits of the lower lip are rare developmental malformation with high penetrance, variable expressivity, and autosomal dominance. The cardinal signs in Van der Woude syndrome are congenital lower lip pits, cleft lip with or without cleft palate, and isolated cleft palate. Hypodontia is a cardinal feature that is associated with this syndrome. Ectodermal Dysplasia (ED) is a rare group of inherited disorders manifested with a defect in hair, skin, teeth, and eccrine glands. In ED there are defects in the development of tissues derived from primary embryonic ectodermal derivatives. Dry skin and sparse hair are common features seen in these patients. Partial or complete absence of teeth is reported in ectodermal dysplasia. This is a case report of an 18-year-old male with combined features of Van der Woude Syndrome (VWS) and Hypohidrotic Ectodermal Dysplasia (HED). The patient was surgically managed for the cleft lip at an early age.

**Keywords: Abnormalities; Anodontia; Cleft lip pathologies; Humans lip/abnormalities**

## Introduction

Lip pits are classified into three types based on location: commissural, midline upper lip, and lower lip (Nagore et al. 1998) [1]. Lower lip pits are congenital malformation that was originally described by Demarquay, 1845 (cited by Van der Woude). Van der Woude was the first person to introduce a new entity by combining lower lip pits with cleft lip and/or palate. According to Kitamara (Table 1), mutations in IRF6 in humans cause Van der Woude syndrome the most common syndromic form of orofacial clefting and have been identified in 70% of families with VWS [2]. Individuals with VWS have Cleft Palate (CP), Cleft Lip (CL), or Cleft Lip and Palate (CLP). 85% of those affected individuals have lower lip pits.

Ectodermal Dysplasia is a heterogenous group of disorder affecting ectodermal developmental derivatives of skin, hair, nail and teeth. Hypohidrotic Ectodermal dysplasia was first described by Thurman in 1848 and the term was coined by Weech in 1929 (Table 2).

## Case Presentation

An 18-year-old male patient had come to the Department of Oral Medicine and Radiology with a chief complaint of a decayed tooth in the right lower back tooth region. The patient had a history of palatoplasty done at 10 months age and palatal fistula closure at one year. He was born prematurely at 7 months underweight with history of speech impairment from childhood and delayed milestone. Their parents gave a history of consanguineous marriage with two children and no history of similar condition in their family. On extraoral examination, the patient was thin built had sparse hair, deviated nasal bridge, prominent ear fold, sunken cheeks, scanty eyebrows, watery eyes, bilateral symmetrical lip pits in the lower lip (Figure 1c) with a surgical scar in the upper lip (Figure 1a) and everted lips. He also had fingernail (Figure 1b) and toenail dystrophy (Figure 1d). He had alopecia, dry skin, and history of decreased sweating.

On intraoral examination high arched palate, altered crown morphology with missing permanent teeth in the maxillary and mandibular arch, and retained primary teeth 63 (Figure 2a-c). Maxillary hypoplasia with deep bite on occlusion was present. Altered crown morphology was seen in 36 and 26. Teeth congenitally missing were 17, 15, 22, 25, 27, 35, 37, 45 and 47. He had partially erupted 21 (Figure 2a) and rudimentary teeth present distal to 16.46.

**Table 1:** Time line of events.

| | |
|---|---|
| 32 day embryo | Lower lip has four growth centers divided by one median and two lateral grooves |
| 38 day embryo | Lateral groove disappears except in case of delay in the mandibular growth centers that result in lip pits. |
| Day 36 | Lip pits develop |
| Day 40 | Cleft lip |
| Day 50 | Cleft palate |

**Table 2:** Two types of ectodermal dysplasia.

| **Hypohidrotic Ectodermal Dysplasia/ Christ-Siemens-Touraine Syndrome** | **Hidrotic Ectodermal Dysplasia/Clouston Syndrome** |
|---|---|
| X Linked recessive | Autosomal dominant disorder |
| Caused by maturation in EDA, which encodes for ectodysplasin protein [3]. | Caused by a mutation in GJB6, which encodes for connexin 30 [4]. |
| They phenotypically present with sparse hair on the scalp and body, deficient eccrine sweat glands, and oligodontia or anodontia with malformed or conical teeth. There is often forehead prominence, a depressed nasal bridge, protuberant lips, and periorbital wrinkling and perioral pigmentation [5]. Subcutaneous fat is often diminished or absent. Impaired thermoregulation. | Characterized by a triad of major features that includes nail dystrophy, partial to complete alopecia and palmoplantar hyperkeratosis. Associated features include: cutaneous hyperpigmentation and finger clubbing. Sweating is preserved and there are no dental anomalies. |

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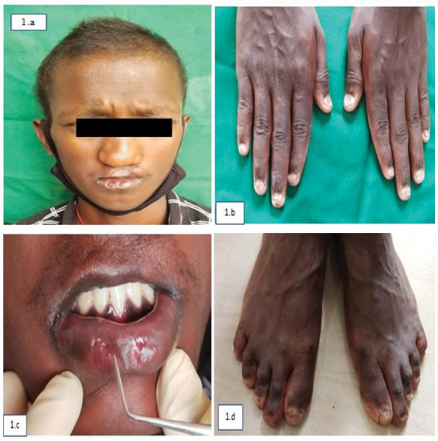

**Figure 1**: Extraoral features. A) Protuberant lips, sunken cheeks, sparse hair, maxillary deficiency & surgical scar on upper lip. B) Nail dystrophy in hands. C) Congenital lower lip pits. D) Nail dystrophy presented in toes.

The differential diagnosis includes alopecia areata, Aplasia Cutis Congenita, Rothmund-Thomson syndrome, focal dermal hypoplasia syndrome, Werner's syndrome.

Maxillary occlusal radiograph (Figure 3a) revealed crowded maxillary teeth 16,14,13,12,11, 21, 63, 23, 24, 26. Mandibular occlusal radiograph (figure 3b) revealed 36, 34, 33, 32, 31, 41, 42, 43, 44 and 46. Based on the radiological findings a provisional diagnosis of Ectodermal dysplasia was made.

Panoramic radiograph showed impacted 21. A rudimentary tooth was presented distal to 16 and 46. Impacted rudimentary tooth was seen impinging 36 distally were congenital missing 17, 15, 22, 25, 27, 35, 37, 45 and 47. Coronal radiolucency involving pulp in 16 and 46 was evident (Figure 4).

The patient's 46, was conservatively managed (Figure 5) and was advised for oral prophylaxis measures, restoration of decay tooth, and orthodontic correction later.

## Discussion

Van der Woude syndrome is a congenital malformation that presents with lower lip pits and cleft lip or cleft palate condition. Hypodontia is a cardinal feature in Van der Woude Syndrome observed in 10% to 81% [6]. Microdeletion in chromosome bands [7] 1q32-q41 and mutation in Interferon Regulatory Factor 6 gene (*IRF6*) are known to cause VWS and have a high penetrance between 0.89 and 0.99 [8]. HED is inherited as autosomal dominant, autosomal recessive, or X-linked manner. The majority of individuals with HED have the X-linked form. The mode of inheritance may be determined in some instances by family history and in others by molecular genetic testing [9]. The lateral incisors and second molars are commonly

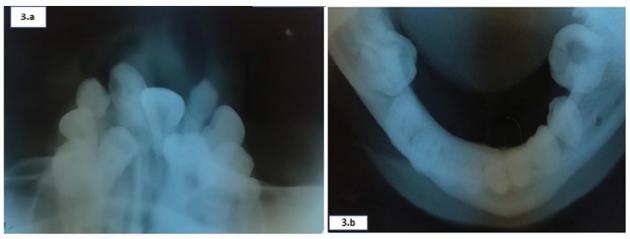

**Figure 3**: Maxillary and mandibular occlusal radiograph. a) Maxillary occlusal radiograph presented with crowded maxillary teeth, retained deciduous and missing permanent teeth. b) Maxillary occlusal radiograph presented with missing 45, 47 and altered crown morphology in 36 and 46, Coronal radiolucency in 46.

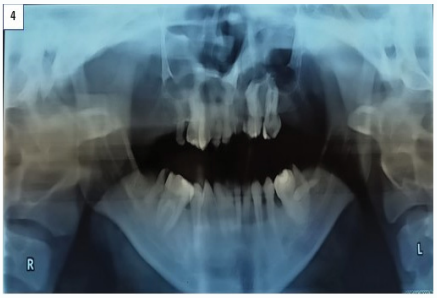

**Figure 4**: Panoramic radiograph presented with crowded maxillary teeth, altered crown morphology and retained deciduous teeth with missing 17, 27, 15, 12, 25, 27 impacted 21.

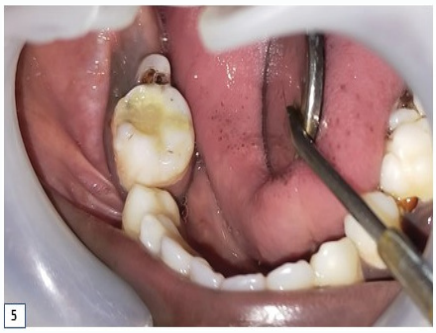

**Figure 5**: Resorted 46.

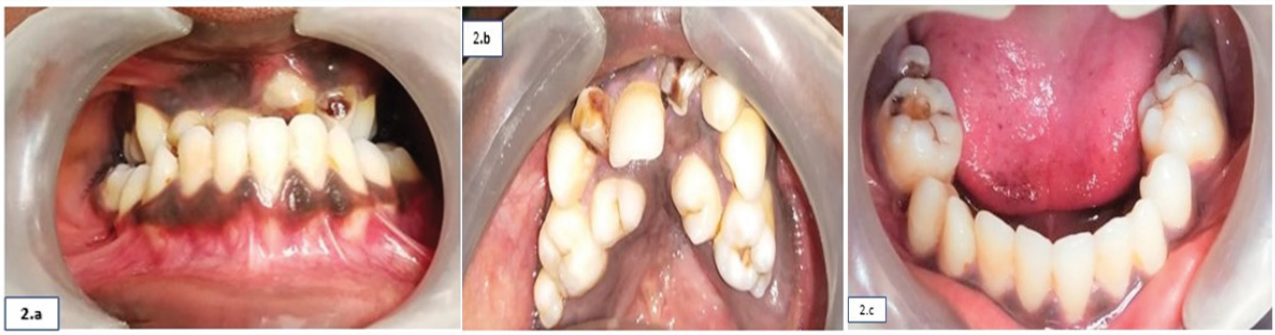

**Figure 2**: Intraoral features a, b and c a) on occlusion. b) Crowded maxillary arch with missing 17, 15, 22, 25, 27 retained 63 altered crown morphology in 26 rudimentary teeth present distal to 16. c) Mandibular arch presented with missing 45, 47, 35, 37 and altered crown morphology in 36 rudimentary teeth present distal to 46.

affected in the deciduous or permanent teeth or both [10].

Microforms are a mild expression of the gene that may be seen only on detailed examination on affected probands that includes transverse mucosal ridges and conical elevations (nipple-like) on a verrucous eminence in the lower lip either unilaterally or bilaterally [11]. Our case report presented with hypodontia which is one of the features in VWS with surgical management of cleft lip and palate and presence of lower lip pits. Extra oral features of sunken eyes, depressed nasal bridge, sparse hair and eyebrows, nail dystrophy and altered crown morphology with congenitally missing permanent teeth are features of hypohidrotic ectodermal dysplasia. No physical abnormalities were noted. The patient underwent treatment for speech therapy and patient was recommended for IQ testing. Thus, our case report presented with a final diagnosis of Van der Woude syndrome along with features of hypohidrotic ectodermal dysplasia.

The procedure for lip pits in Van der Woude syndrome may appear straightforward, there is no guarantee of esthetically desirable results even in the best of hands, and the excision can be challenging [12]. Four techniques of excision were performed *via* modified routine excision, routine excision, vertical wedge excision, and inverted-T lip reduction [13]. Prenatal diagnosis of ectodermal dysplasia been diagnosed by fetal skin biopsy through fetoscopy by 20 weeks of gestation [14]. Sweat test and skin biopsy should be suggested in case of pointed conical teeth.

In ectodermal dysplasia early dental care management, bonding of conical shaped teeth; orthodontics is necessary. Dental implants in older children, replacement of dental prosthesis as often every 2.5 years and dental implants in adults are required. Therapeutics to maintain oral lubrication and control caries [9] and dietary counseling for individuals with chewing and swallowing difficulties are needed. Skin care for eczema and exposures for dry skin is required. Saliva substitutes and optimal fluoride exposure are necessary in those individuals having a marked salivary flow reduction.

## Conclusion

Van der Woude syndrome with ectodermal dysplasia is a rare case seen in an individual population. Routine follow-up with early dental care for esthetics improves the physical and mental status of the individual.

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