CASE REPORT

Case Report: Congenital absence of uvula and trismus - a rare presentation of Van der Woude syndrome [version 1; peer review: awaiting peer review]

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Abstract

Van der Woude syndrome (VWS) is the most common single gene mutation causing cleft lip/palate, responsible for approximately 2% of all cases. Inherited in an autosomal dominant pattern, VWS occurs at an incidence of 1 in 35,000 to 100,000. The most commonly reported manifestations of VWS is lip pits, cleft lip or palate. We present a case of a 34-week infant with unique and rarely reported symptoms of VWS, such as trismus and absent uvula.

Keywords

Van der Woude syndrome, autosomal dominant, gene, genetics, family history, congenital, lip pits, VWS, trismus, infant

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Introduction
Van der Woude syndrome (VWS) is the most common single gene cause of cleft lip/palate that has been reported. First described by French Surgeon Jean Nicolas Demarquay in 1845, VWS is a rare autosomal dominant condition with a frequency of 1 in 35,000 to 100,000\(^1\)--\(^3\). The clinical presentation of VWS has been well described in the literature via large multigenerational kindred studies. The most common manifestation and the cardinal feature of VWS is lip pits. This feature is present in approximately 88% affected individuals, and is the only clinical manifestation in 64% of reported cases\(^4\). Cleft lip or palate are the only other major hallmark with an estimated occurrence of 20%\(^4\). Additional reported signs of VWS are hypodontia, mucous secretion of pits, syngnathia and abnormal brain structure development\(^5\)--\(^7\).

We present a case of VWS with historically undescribed findings of absent uvula and trismus. We also elaborate on recommendations for managing a newborn that presents with respiratory distress secondary to these pathological findings.

Case presentation
A female infant, born at 34-weeks gestation, was delivered via normal spontaneous vaginal delivery to a 20-year-old G3P1011 mother that presented to the Neonatal Intensive Care Unit with worsening respiratory distress. The mother received standard prenatal care and had an unremarkable gestational course. Family history revealed submucosal cleft palate and lip pits in the patient’s mother. Maternal family history was significant for increased incidence of cleft lip/palate, as well as lip pits in multiple relatives (Figure 1). Paternal history/family history were insignificant.

General examination revealed the newborn patient in obvious physical and respiratory distress with copious mucous secretions near the oral orifice (Figure 2). Directed HEENT examination exposed two paramedian indentations with surrounding mound-like elevations exuding mucus located on the lower lip (Figure 3).

Visualization of the oropharynx was limited due to trismus; however, it revealed high arching sub-mucosal cleft palate and absence of a uvula (Figure 4). Directed pulmonary examination revealed substernal as well as intercostal retractions with shallow breathing and sounds indicating upper airway obstruction upon auscultation. The remainder of the physical examination was unremarkable.

Head ultrasound revealed no paramedial structural abnormalities from the high arching and submucosal cleft palate. Chest x-ray revealed mild granularity of lung fields bilaterally slightly more prominent in the right medial lung. Possibility of respiratory distress syndrome or neonatal pneumonia were not excluded.

Hospital course was complicated by apneic and desaturation episodes resulting in SpO2 of <88%, requiring intubation and high flow nasal cannula at 4L. Initially thought to be related to prematurity, the poor response and declining respiratory status raised concern and prompted us to investigate further. Aspiration of mucus that was produced within the pitting of the lips seemed to be the culprit to this patient’s respiratory distress. This was further supported by the fact that the patient had an improvement in respiratory status within the decubitus and prone positions versus when the patient was supine.

Figure 1. Patient’s family tree, showing multiple relatives with similar findings.
mucus secretions and aid in respiratory status, resolution of trismus to aid with initiation of oral feeds and removal of nasogastric tube, and evaluation and repair of submucosal cleft palate.

**Discussion**

In an infant presenting with absent uvula or trismus it is important to keep VWS on the differential. It is the largest syndromic cause, making up almost 2% of all cases of orofacial clefts. Furthermore, when evaluating VWS it is vital to take anticipatory steps in terms of treatment and patient guidance to avoid complications or unwanted outcomes.

In terms of anticipatory guidance, physicians should emphasize the importance of seeking early orthodontic care and speech therapy to the patient or their caregiver. Seeking orthodontic care and beginning treatment as early as 3 years old has been shown to vastly improve aesthetic outcomes compared to initiating treatment at a later age. Early speech therapy is a necessary intervention in those with VWS. It has been reported that those with VWS have higher rates of need for speech therapy by age ten than those with non-syndromic cleft lip/palate. It has also been found that those with VWS are twice as likely to undergo procedures to correct their speech problems caused by velopharyngeal dysfunction than those with non-syndromic cleft lip/palate. With our patient, we initiated inpatient speech therapy consultations to aid with oral feeding, which was imperative in establishing a basis toward patient well-being.

In terms of treatment, physicians should take early intervention with a multidisciplinary approach. Consultations with appropriate surgical specialties regarding excisions and specifically vertical wedge excisions of lip pits can lead to a good aesthetic outcome as well as avoid complications such as mucocele and pit recurrence. In our case the team felt surgical intervention was necessary to treat and prevent future aspiration-induced respiratory compromise, as seen in the patient.

The course was further complicated by limitation of oral feeds due to the infant’s inability to adequately open mouth from underlying trismus. This complication was addressed with nasogastric tube placement to aid in food delivery and frequent speech therapy consultations.

The patient was sent for evaluation by ENT to an outside hospital with three main treatment goals: excision of lip pits to stop mucus secretions and aid in respiratory status, resolution of trismus to aid with initiation of oral feeds and removal of nasogastric tube, and evaluation and repair of submucosal cleft palate.

**Figure 2.** Copious salivary mucus production near oral orifice.

**Figure 3.** Indurated lip pits found on physical exam.

**Figure 4.** High arching and submucosal cleft palate, showing absent uvula.
Conclusion
VWS can present with an absent uvula and trismus, features that can potentially complicate the hospital course of an infant and impair speech development as the infant ages. Accurate diagnosis of syndromic vs non-syndromic cleft lip and palate can guide treatment. Anticipatory treatment and patient guidance can affect patient outcomes for those with VWS.

Consent
Written informed consent for the publication of the case report including any associated images was obtained from the parents of the patient.

References
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