Congenital Lip Pits and Van der Woude Syndrome

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Van der Woude syndrome is an autosomal dominant disease characterized by lower lip pits with or without cleft lip and/or cleft palate. The lip pits commonly have salivary glands that drain into them, which leads to salivary flow from the lip pits. Lip pits may be associated with submucosal palatal cleft, velopharyngeal insufficiency, or genitourinary or cardiovascular anomalies. The pits are treated by surgical resection. The authors report a case of van der Woude syndrome with isolated lip pits and speech difficulties that had been unrecognized until the patient was 6 years old. The surgical technique is described to ensure that the often-bifurcating tracts are removed entirely.

**Key Words:** Histopathology, lip pits, surgical technique, van der Woude syndrome

Lip pits are rare anomalies that can occur in the upper lip, lower lip, or the oral commissure. Although lip pits may be seen near the oral commissure or midline upper lip, most occur on the lower lip and are associated with van der Woude syndrome. This syndrome is an autosomal dominant condition with 80% to 90% penetrance consisting of lower lip pits and cleft lip and/or cleft palate. Van der Woude (VWS) syndrome has been localized to a 500 to 800 kilobase deletion at the 1q32–41 region. Thirty percent to 50% percent of these patients represent de novo mutations.

VWS affects about 1 in 75,000 to 1 in 100,000 births, and 1% to 2% of patients with cleft lip or palate. Seventy percent of lip pits are associated with cleft lip or palate. The other 30% have minimal findings, including hypodontia or isolated lower lip pits. A comprehensive review of the literature found only 10 reports of isolated lower lip pits.

**Clinical Report**

A 6-year-old white boy presented for treatment of a deformity of his lower lip. The lower lip deformity (Fig 1) represented two paramedian, invaginated, soft, painless, nonsecreting lesions. The symptoms were unchanged throughout the child’s life, but the family was concerned about his cosmetic appearance as he prepared to begin elementary school. The rest of the patient's medical history was otherwise negative, except for “speech problems.” The patient’s family history was negative for the presence of lip pits. On examination, the patient was found to have a submucosal cleft and a hypernasal voice. The remainder of the patient’s social, birth, and medical history were unremarkable. Based on these clinical findings, the patient underwent genetic testing, which revealed a deletion in the 1q32–41 region. Results of his cardiovascular and genitourinary evaluations were normal.

The lower lip pits were removed using a wedge excision to provide a more cosmetic appearance to the child’s lip. Intraoperatively, the pits were found to be narrow. One milliliter of warm bacitracin ointment was mixed with injectable methylene blue dye and, with the use of a 20-Ga angiocatheter, injected into the tract of the pit. This allowed tracing of the tract to its depth, which was 1.5 cm in length. There was branching of the tract at its distal end. The pit tracts penetrated the orbicularis oris muscle. On histopathologic examination, the sinuses showed the pits to be lined with mucosal epithelium with normal appearing salivary glands lining the sinus tracts. There was a focus of mild mucosal hyperplasia with mild inflammation and fibrosis. Skeletal muscle was also present, indicating the orbicularis oris surrounded the tract (Fig 2).

**Discussion**

In normal development, fusion of the mandibular arch and sulcus lateralis of lower lip occurs at
5.5 weeks, whereas fusion of the maxillary and nasofrontal processes occurs at 6 weeks. It is theorized that a common event may simultaneously disrupt fusion in both locations. This accounts for the strong association between lip pits and cleft lip and/or palate.

Of all associated features seen with lip pits, hypodontia is the most common sign. Hypodontia has been found in 10% to 81% of all patients with VWS. Other associated anomalies seen in patients with lip pits include syndactyly of the hands, clubfoot, genitourinary abnormalities, and cardiovascular anomalies. Parents often mistake these pits as depressions caused by the maxillary central incisors, even though the pits are present from birth, months before maxillary incisors erupt. As often occurs, the depressions in our patient were thought to have developed because of pressure from his teeth, and our patient had not had any other evaluation of the pits. Thus, it is important to have patients evaluated for other anomalies associated with the lip pits because the pits often are not recognized by the patient’s primary care physician.

Although the penetrance of the genetic deletion associated with VWS is high, it is not 100%. For example, in a seven-generation family investigation, lip pits were found in 88% of those with the genetic mutation and were the only manifestation in 64%. Clefts occurred in 21% of the patients. For a patient with lip pits alone, the risk of cleft in an offspring is 22%, with 95% confidence. If the patient has a cleft in addition to lip pits, the risk of having a child with a cleft increases to 39%. However, if the patient has a cleft only but his/her parent has lip pits, the risk of an offspring with cleft is 30%. Genetic counseling is recommended for families with affected members after careful family history is obtained. Because minor manifestations, such as shallow pits or submucosal clefts, may not be apparent to the family members, evaluation of photographs or preferably examination of family members must be performed.

Phenotypically, VWS and popliteal pterygium syndrome (PPS) overlap. PPS consists of popliteal webs, cleft lip and/or palate, lower lip pits (present in 60%–71% of cases), and anomalies of the genitourinary system, including hypoplastic labia and uterus in females and cryptorchidism and bifid scrotum in males. All characteristics of VWS may be found in PPS, and the two disorders affect the same allele. Thus, it is important to counsel patients with VWS who have cleft lip and/or palate that their offspring may show signs of PPS, including the genitourinary abnormalities. It is imperative to obtain a comprehensive family history and examine multiple family members to distinguish VWS from PPS.

Lower lip pits are classically bilateral and paramedian, as seen in Figure 1. These pits form canals ranging in length from 1 to 25 mm, which generally extend into the orbicularis oris muscle. Previously, fistulography has shown that the sinus tracts can be long and bifurcated, with a total length of 5 to 6 cm. Accessory salivary glands frequently drain into these tracts, and because of the action of the orbicularis oris muscle, the saliva is propelled to the surface, leading to mucous secretion from the pits. This leads to an

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**Fig 1** Close-up view of the patient’s lower face in anterior view.

**Fig 2** Histopathologic section of the lip pit demonstrating minor salivary gland tissue in the upper left side of the image, normal stratified squamous epithelium of the lip on the right side, and part of the tract of the sinus going up and down in the center of the image (stain, hematoxylin and eosin; original magnification, ×100).
unappealing cosmetic problem, especially before and during mealtimes for the patient, and distresses the parents.

The treatment of the pits is surgical excision. In excising the pits, it is important to ensure proper removal of the entire tract because the presence of salivary tissue in any residual tract will lead to cyst formation. The diameter of the tracts can vary between a very small orifice or be as wide as 6 mm. Because the tracts can bifurcate, using a lacrimal probe to trace the tract may lead to leaving tract branches behind. We routinely use bacitracin ointment mixed with methylene blue dye to track preauricular pits, sinuses, and cysts during excision and used it in this case as well. The benefit of mixing bacitracin ointment with the dye is that it provides a dyed viscous coating in the entire tract, which will not readily extrude and discolor the surgical field if the tract is inadvertently entered. Histopathologic specimen sectioning of the entire specimen should preferably be performed to ensure complete removal. If there is residual sinus tract present, it likely will manifest itself as a mucosal cyst that can later be removed using a buccal incision.

In summary, the recognition of lip pits is important given the multiple other associated anomalies. Proper evaluation and treatment of these associated abnormalities and genetic counseling is of utmost importance. The treatment of this disorder is surgical excision. Genetic evaluation to detect the genetic mutation is diagnostic and will assist in counseling.

REFERENCES