Case Report

Lip Pits: An Uncommon Clinical and Histologic Finding Associated with Underlying Genodermatoses and Developmental Anomalies

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We describe the clinical and histologic features of lip pits in a patient with Van der Woude syndrome (VdWS; OMIM 119300), an autosomal dominantly inherited disorder characterized by varying combinations of paramedian lip pits, cleft lip with or without cleft palate, cleft palate alone and/or hypodontia. VdWS is the most common single-gene cause of cleft lip and cleft palate. Mutations in the interferon regulatory 6 gene (*IRF6*) are detectable in over 70% of cases. Lip pits can be seen in other disorders such as the popliteal pterygium syndrome. Pits are usually divided into three categories 1) upper lip 2) lower lip and 3) commissural. Biopsy findings can be subtle and may be overlooked without the provision of relevant historic information. No treatment is needed for mild cases, however, surgical excision is helpful in more severe cases, both to alleviate discomfort and for cosmetic reasons.
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Key Words: *lip pit, cleft palate, cleft lip, genetic*

INTRODUCTION

Dermatopathologists occasionally receive unusual specimens for examination. Without relevant clinical information, it can be difficult to make an accurate diagnosis. We recently received a specimen, without accompanying clinical history, which revealed an unusual depression with minor salivary glands situated superficially. These findings prompted us to call the referring provider to obtain clinical information. Although the clinical images and history were compelling, we found little information in the dermatology literature regarding lip pits. Review of this entity will allow dermatopathologists to recognize lip pits in their own practice.

CASE REPORT

The patient, a 7 year old African-American boy, presented for genetics evaluation of mounds on his lower lip (**Figure 1**). Family history was remarkable for lip pits/mounds in the patient's father and two paternal uncles. A paternal aunt had a history of cleft palate and a paternal first cousin had lip pits as well as a cleft of the lip and palate. The patient was born at term following an uncomplicated pregnancy to a 28-year-old P2G1 woman and her healthy 31-year-old nonconsanguineous husband. The patient was healthy and had shown normal growth and development. Multiple articulatory speech errors were noted which were related to the patient's lip mounds. Based upon the family history, a diagnosis of Van de Woude syndrome was made. Because of the unsightly appearance of the lip pits, an excision was performed. The excision revealed a depression but otherwise unremarkable epithelium (**Figure 2**).

DISCUSSION

Van der Woude syndrome is an autosomal dominantly inherited disorder with variable expressivity.[1,2] The disorder is characterized by varying combinations of lip pits/mounds, cleft of the lip with or without cleft of the palate, cleft palate alone, and/or hypodontia.[3,4,5] Growth and intelligence are usually normal for family. Paramedian lower lip pits, which most often represent fistulae, are the most common manifestation of VdWS, occurring in > 80% of patients. Most cases of VdWS are due to mutations of the *IRF6* gene, a gene which is also associated with popliteal pterygium syndrome. The clinically apparent lip mounds represent accessory salivary glands that may be associated with excessive salivary discharge. The patient of this report was very self-conscious about his lip mounds and sought medical attention to have them removed.

Van der Woude syndrome (OMIM 119300) is the most common single gene cause of facial clefts, occurring in approximately one in 35,000 to one in 100,000 Caucasians.[3] There is a high degree of penetrance, particularly for the lip

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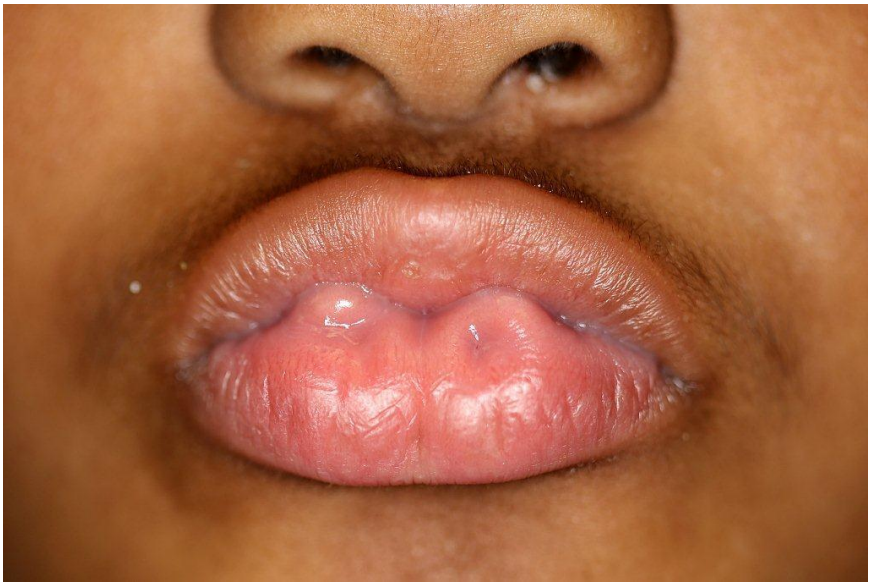

Figure 1. Striking mounds are noted on the lower lip.

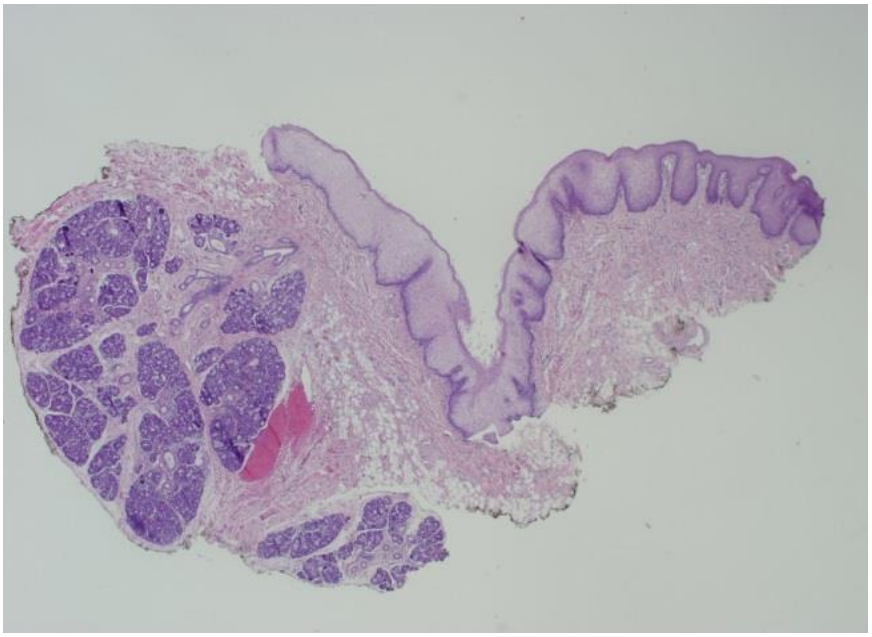

Figure 2. Histologic evaluation reveals a depression and superficially situated minor salivary glands. (Hematoxylin and eosin stained sections, original magnification 40 x).

its/mounds, but variable expressivity. The protein product of the *IRF6* gene belongs to a family of transcription factors that share a highly conserved helix-loop-helix DNA binding domain. This protein is involved in embryologic development of the head and face. Diminished *IRF6* protein would be expected to affect the development of these regions, thus causing the defects observed in VdWS. The recognition of lip pits/mounds by primary care physicians, pediatricians, dermatologists, and dermatopathologists can contribute to the detection of VdWS in patients affected by this disorder.

CONFLICT OF INTEREST
We have no conflict of interest to disclose.

ETHICAL APPROVAL
This work meets all the ethical guidelines.

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