

# Growing Painful Nodule on the Lower Lip

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A 56-year-old man presented with a firm growing mass on the right lower lip of 1 year's duration. He described the mass as painful, and it often bled. The patient's medical history was notable for gastroesophageal reflux disease and human immunodeficiency virus with a recent absolute CD4<sup>+</sup> lymphocyte count of 673 cells/ $\mu$ L (reference range, 800–1050 cells/ $\mu$ L) and undetectable human immunodeficiency virus viral load. Physical examination revealed a well-circumscribed, 1.5-cm, firm, exophytic nodule with an irregular, macerated, white surface. An excisional biopsy was performed.

## WHAT'S THE DIAGNOSIS?

- a. blastomycosis
- b. squamous cell carcinoma
- c. verruca vulgaris
- d. verruciform xanthoma
- e. verrucous carcinoma

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The authors report no conflict of interest.

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## THE DIAGNOSIS: Verrucous Carcinoma

An excisional biopsy revealed an endophytic and exophytic squamous proliferation with a papillomatous growth pattern, bulbous pushing border, and confluent parakeratosis (Figure). No fungal organisms were seen. Due to clinical and histological findings, a diagnosis of verrucous carcinoma (VC) was made.

Verrucous carcinoma is a rare variant of squamous cell carcinoma (SCC) with specific clinical and histological features.<sup>1</sup> These tumors have a slow and localized growth pattern but can be locally aggressive. Metastasis of VC is rare, giving VC an overall good prognosis, with a 5-year survival rate greater than 75%.<sup>2</sup> Verrucous carcinoma typically occurs in 1 of 3 locations: the oropharynx, genitals, or soles of the feet. Depending on the site of involvement, various names have been used in the literature to describe this entity, including Ackerman tumor (solitary oral mucosal lesion), Buschke-Lowenstein tumor (genital involvement), florid oral papillomatosis (multiple oral lesions), and carcinoma cuniculatum (sole of the foot).<sup>3</sup> The most common sites for VC in the oral cavity are the buccal mucosa and gingiva.<sup>4</sup>

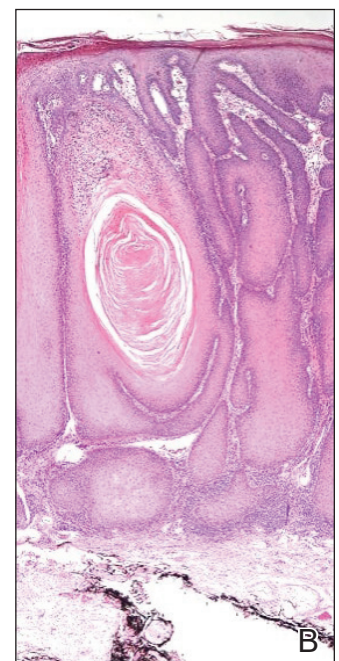
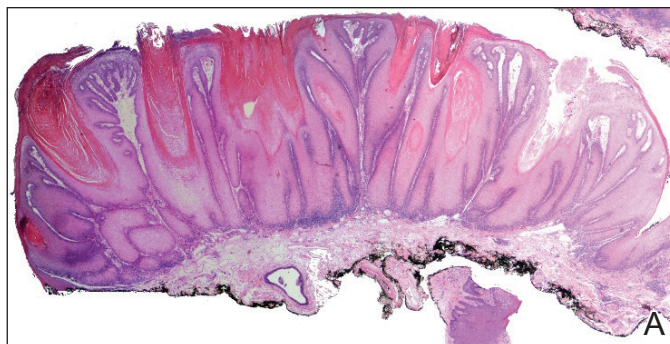
Verrucous carcinoma occurs more often among men in the sixth decade of life.<sup>3</sup> The etiology of oral VC remains unclear; however, use of chewing tobacco, chemical carcinogens, chronic irritation, human papillomavirus (HPV), and poor oral hygiene have been reported as predisposing risk factors.<sup>4,5</sup> The role of HPV in the pathogenesis of VC remains controversial, but

both low-risk types HPV-6 and HPV-11 and high-risk types HPV-16 and HPV-18 have been found in association with VC.<sup>5,6</sup>

Clinically, oral VC lesions most often present as pink-white erythematous papules or plaques with exophytic cauliflowerlike surface alterations. Although the tumors are slow growing with little risk for metastasis, they may be locally invasive with deep involvement of the surrounding structures.<sup>1</sup> Histopathologically, VC displays proliferation of the epithelium with downward growth into the connective tissue but usually without a pattern of true invasion. The epithelium is well differentiated and displays little pleomorphism or mitoses.<sup>5,7</sup> Obtaining a generous biopsy specimen is essential to view the diagnostic architecture of VC and rule out other entities, such as viral verruca, blastomycosis, SCC, and verruciform xanthoma. Squamous cell carcinoma characteristically has a more infiltrative border as opposed to the bulbous border of VC. In addition, the distribution of p53 and Ki-67 staining differs between SCC and VC. Squamous cell carcinoma shows positive p53 and Ki-67 staining for the full thickness of the epidermis, while VC has positive staining only in the lower third of the epidermis.<sup>5</sup>

Surgical resection is considered the first-line treatment of VC through excision or Mohs micrographic surgery. Radiation therapy is controversial due to the risk for anaplastic transformation. When surgery is not ideal due to the tumor size or location or the patient's

A and B, Excisional biopsy displayed an endophytic and exophytic squamous proliferation with papillomatous growth pattern and confluent parakeratosis (H&E, original magnifications  $\times 20$  and  $\times 40$ ).



preference, other treatment modalities with reported success include intralesional interferon alfa; cryosurgery; topical imiquimod; and topical or systemic cytostatic agents such as bleomycin, 5-fluorouracil, cisplatin, or methotrexate.<sup>1,2</sup>

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