

# Verrucous carcinoma and squamous cell papilloma of the oral cavity: Report of two cases and review of literature

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## ABSTRACT

Verrucous carcinoma (VC) of oral cavity is a rare variant of well-differentiated squamous cell carcinoma and squamous papilloma is a benign proliferation of the stratified squamous epithelium, which results in a papillary or verrucous exophytic mass. There is a certain clinical similarity between squamous cell papilloma and VC. We presented a report of two cases which are VC and squamous cell papilloma that are showed the same clinical appearance but different pathological appearance, with a review of the literature.

**Key words:** Oral cavity, squamous cell papilloma, verrucous carcinoma

## INTRODUCTION

Oral verrucous carcinoma (VC), as defined by Ackerman, is a rare, nonmetastasizing, well-differentiated variant of oral squamous cell carcinoma (SCC).<sup>[1]</sup> Although VC has a slow and continuous local growth pattern; patients with VC have an excellent prognosis.<sup>[2]</sup> VC is occasionally developed in the oral cavity,<sup>[2,3]</sup> though it may be found on other anatomic sites including the sinus, larynx, paranasal sinuses, pyriform esophagus, nasal cavity, lacrimal duct, external auditory meatus, vagina, rectum, penis, soles of the feet and bladder.<sup>[4]</sup> In current literature, the most common sites of oral mucosal involvement are the buccal mucosa, followed by the mandibular alveolar crest, gingiva, and tongue. These VC lesions in the oral cavity typically appear as a painless, broad-based, well-circumscribed, thick white plaque resembling a cauliflower. The lesions may be white, pink or erythematous. Lymph node involvement and distant metastasis are rare in VC.<sup>[3,5,6]</sup> VC occurs more frequently in males over the sixth decade.<sup>[5,6]</sup> Histopathologic and clinical diagnosis of oral VC may be difficult, so close cooperation between pathologist and surgeon is required in order to identify the nature of the lesion.<sup>[7]</sup> The etiology of oral VC is unclear; risk factors include smoking, chewing tobacco, alcohol use, and poor oral hygiene,<sup>[8-10]</sup> but it is reported

that 15–51% of oral VCs are found in individuals without these habits.<sup>[11]</sup> Other etiologic factors include immunosuppression, human papillomavirus (HPV), and other viruses. The treatment of oral VC remains controversial. Surgery, chemotherapy, radiotherapy, or a combination of procedures has been used in the treatment of VC.<sup>[12-14]</sup> The rate of local recurrences ranges from 30% to 50%.<sup>[15]</sup>

Oral squamous papillomas are papillary or verrucous exophytic lesions of the oral cavity<sup>[16]</sup> caused by HPV, usually HPV-6 or HPV-11.<sup>[17]</sup> They involve a benign proliferation of the stratified squamous epithelium and occur most frequently on the hard and soft palate, uvula, tonsil, or epiglottis, but any surface of the oral cavity can be affected.<sup>[16,18]</sup> These lesions are often asymptomatic and tend to progress slowly. Oral squamous papillomas could mimic condyloma acuminatum, VC, or exophytic

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carcinoma because their clinical appearance is similar. Surgical removal with laser ablation, electrocautery, intralesional injections of interferon, cold-steel excision, and cryosurgery have been used in the treatment of oral squamous papillomas.<sup>[16,19-21]</sup>

There is a certain clinical resemblance between squamous cell papilloma and VC. We present two cases, one of a squamous papilloma, and the other of a VC in the form of oral lesions, both treated with a surgical excision.

## CASE REPORTS

### Case 1

A 65-year-old male was admitted to the Department of Oral and Maxillofacial Surgery, Dicle University, Diyarbakir, Turkey for an evaluation of a verrucous white lesion in the oral cavity. The patient's medical history revealed no systemic diseases. The patient had been smoking for many years. Intraoral examination showed the presence of a wide, white, verrucous lesion on the left buccal mucosa. The lesion was a cauliflower-shaped exophytic lesion with a dimension of 2.5 cm × 1 cm [Figure 1a]. According to the patient, the lesion had been present for approximately 5 years and had been slowly growing over the previous 2 months. The patient had experienced no pain or other symptoms. An extraoral examination revealed that the lymph nodes in the head and neck region were clinically normal. Local anesthesia was given around the lesion, and the exophytic portion of the lesion was completely excised for biopsy and sent for histopathological examination with a prediagnosis of papilloma. After histopathological examination of the excisional biopsy specimen, a diagnosis of VC was made [Figure 2a and b]. The clinical follow-up showed complete tissue healing, and no recurrence had been seen at the 1-year follow-up [Figure 1b].

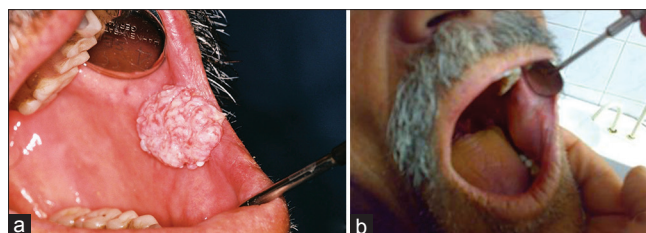
### Case 2

A 44-year-old male was admitted to the Department of Oral and Maxillofacial Surgery, Dicle University, Diyarbakir, Turkey with a painless mass on the palate. Intraoral examination revealed a pedicle exophytic lesion on the hard and soft palate border, whitish in color, with a pebbled surface, approximately 5 mm × 3 mm in size [Figure 3a]. He did not have any specific habit that could be considered a source of local irritation of the area. Local anesthesia was given around the lesion, which was then completely excised from its connection to the palate. The histopathological assessment of the lesion revealed a papillary mucosal

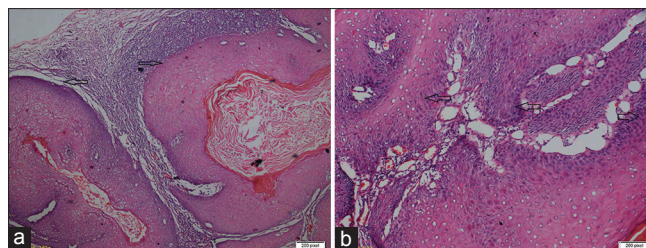
mass surrounded by parakeratinised stratified squamous epithelium of varying thickness, with a papillary surface and exocytosis [Figure 3b]. The oral pathology report confirmed our preintervention diagnosis of squamous cell papilloma. The clinical follow-up showed complete tissue healing. A 1-year follow-up was performed, and there was no evidence of recurrence of the lesion [Figure 3c].

## DISCUSSION

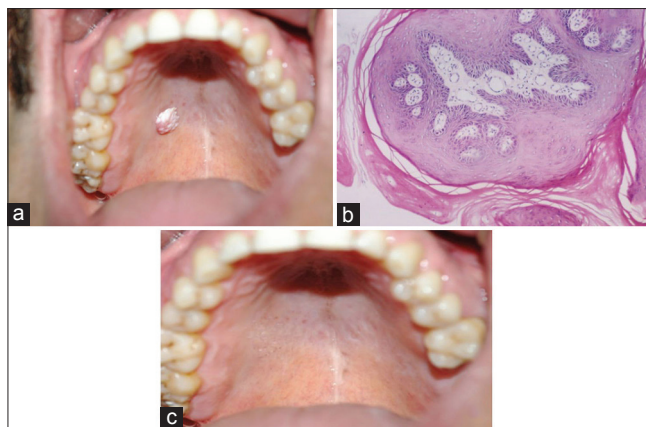
Cancer is a major problem for public health, and oral cancer is among the 10 most common cancers worldwide.<sup>[22]</sup> Among these oral cancers, SCC is the most common malignant neoplasm in the oral cavity.<sup>[23]</sup> Oral VC is a rare, well-differentiated



**Figure 1:** (a) The clinical photograph of verrucous carcinoma in the buccal mucosa (b) 1-year postoperative view of the buccal mucosa



**Figure 2:** (a) Verrucous carcinoma showing pushing border (arrows, HE, ×40) (b) minimal cytological atypia consistent with verrucous carcinoma (arrows, HE, ×100)



**Figure 3:** (a) The clinical photograph of squamous cell papilloma in the oral cavity (b) histopathological appearance of squamous cell papilloma (HE, ×41) (c) 1-year postoperative view of the hard palate

variant of SCC.<sup>[24]</sup> Oral squamous papillomas are common benign epithelial neoplastic lesions which are generally solitary and its biological potential for malignant transformation is still a matter of debate.<sup>[20]</sup>

VC has been reported in the literature under a variety of terms, including florid oral papillomatosis, Ackerman's tumor, epithelioma cuniculatum, Buschke-Loewenstein tumor, cutis papillomatosis carcinoides of Gottron, and carcinoma cuniculatum.<sup>[25]</sup> VC occurs more frequently in elderly men over 60, and the incidence of VC varies from 4.5% to 9%.<sup>[26]</sup> Oral squamous papillomas commonly occur between age 30 and 50 years, and sometimes can occur before the age of 10 years. These lesions account for 8% of all oral tumors in children.<sup>[27]</sup>

The pathogenesis of VC of the oral cavity is not clear. HPV, chewing tobacco, alcohol use, use of snuff, and poor oral hygiene are predisposing factors for the development of VC of the oral cavity.<sup>[8-10]</sup> HPV types six and 11 are the most common pathogens for oral squamous papillomas, but there is controversy regarding its viral origin.<sup>[18]</sup>

In the oral cavity, VC occurs on buccal mucosa, gingival and alveolar ridge. Predominantly being a squamous mucosal lesion, VC may also be found on cutaneous surfaces. Macroscopically, these VC lesions in the oral cavity appear to show a broadly implanted, exophytic cauliflower growth, well-circumscribed and with a locally invasive character.<sup>[4]</sup> Intraorally, oral squamous papillomas are found most commonly on the palate (which was observed in the case reported here), lips, buccal mucosa, gingiva, and tongue but any region of the oral cavity could be impressed, such as the uvula, epiglottis, or tonsil.<sup>[16,18]</sup> These lesions generally measure less than 1 cm in the largest dimension and appear as pink to white exophytic granular or cauliflower-like surface alterations and may be pedunculated or sessile in the configuration. The lesions are generally asymptomatic, as in the present case, although Devi *et al.*<sup>[18]</sup> and Goodstein *et al.*<sup>[21]</sup> reported two cases of a squamous papilloma of the uvula that atypically produced symptoms. Squamous papillomas are divided into two forms: Isolated-solitary and multiple-recurring. The isolated-solitary type generally appears in adults, as in the present case. Patients who are infected with the human immunodeficiency virus (HIV) frequently have multiple oral lesions. Malignant transformation of a papilloma is more common in the multiple-recurring type.<sup>[20]</sup>

Microscopically, VC has epithelial proliferation with downgrowth of epithelium into connective tissue but usually without the pattern of true invasion. The

epithelium is well differentiated and shows little mitotic activity, pleomorphism or hyperchromatism. Cleft like spaces lined by a thick layer of parakeratin extend from the surface deep into the lesion. Parakeratin plugging also occurs in the epithelium. Parakeratin lining of clefts with parakeratin plugging is the hallmark of VC. Chronic inflammatory cell infiltration in the underlying connective tissue may or may not be present.<sup>[4,5,28]</sup> In addition, all rete pegs of the epithelium tend to project into the underlying connective tissue, at more or less the same level and this is called as "pushing border."<sup>[4,28]</sup> Squamous papilloma presents as many long, thin and finger-like projections extending above the mucosal surface. Each finger-like projection is lined by stratified squamous epithelium and contains a central connective tissue. The spinous cells proliferate in a papillary pattern. Koilocytes-HPV altered cells may be observed. The upper epithelial cells show pyknotic and crenated nuclei, often surrounded by edematous or optically clear zone, the so-called "koilocytic" cell. Chronic inflammatory cells are also observed.<sup>[20]</sup>

An accurate diagnosis of oral VC could be challenging and requires an adequate biopsy specimen.<sup>[7]</sup> Diagnosis also requires experience and close collaboration between surgeon and pathologist. These lesions have a tendency to mimic benign tumors of the oral cavity.<sup>[29]</sup> For this reason, the differential diagnosis should include lesions of similar appearance such as verrucous hyperplasia, papilloma, proliferative verrucous leukoplakia, pseudoepitheliomatous hyperplasia, SCC, chronic candidiasis, and condyloma accuminatum.<sup>[29,30]</sup> In Case 1, reported above, the initial diagnosis was squamous papilloma, and after histopathological examination it was identified as a VC. The differential diagnosis of oral squamous papilloma, when solitary, includes verruciform xanthoma, papillary hyperplasia, and condyloma acuminatum. In addition, multiple squamous papillomas would consider focal epithelial hyperplasia (Heck disease).<sup>[20]</sup>

Wide surgical excision is considered the primary choice of treatment for VC. Some studies recommend that the anaplastic transformation of the VC can occur after radiotherapy, and hence radiotherapy in combination with surgery is rarely performed.<sup>[31]</sup> Radiotherapy might be the second treatment choice for VC when surgery is not correctly possible. Regarding chemotherapy, Tanaka *et al.*<sup>[32]</sup> have reported the effectiveness of preoperative chemotherapy for advanced VC of the tongue. Recently, treatment of a VC with an intra-arterial infusion of methotrexate<sup>[12,13,33]</sup> and topical 5-aminolevulinic acid-mediated photodynamic therapy

was reported.<sup>[34]</sup> Although the lesion has an excellent prognosis, local recurrences may develop. Furthermore, neck dissection is not necessary because lymph node metastases are extremely rare.<sup>[4,35]</sup> The procedure for oral papilloma diagnosis is mainly clinical, followed by cytology and then proceed by biopsy.<sup>[36]</sup> Surgical removal is the preferred treatment, and laser ablation, electrocautery, intralesional injections of interferon, cold-steel excision, and cryosurgery have all been used in the treatment of oral squamous papillomas.<sup>[16,19,20,21]</sup> Recurrence of squamous papilloma is rare except for lesions in patients infected with HIV.<sup>[16]</sup>

## CONCLUSIONS

The clinical diagnosis of VC and squamous cell papilloma is obviously important, but these two lesions can be difficult to distinguish from other lesions of similar appearance. Precise diagnosis, therefore, depends on careful collaboration between the surgeon and the pathologist.

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### Conflicts of interest

There are no conflicts of interest.

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