

# Hybrid Verrucous Carcinoma: To Report or Not to Report

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**ABSTRACT:** Hybrid Verrucous Carcinoma is an uncommon tumor wherein Verrucous Carcinoma is coexisting with conventional Squamous Cell Carcinoma within same field. We report a case of hybrid verrucous carcinoma identified incidentally in a postoperative case. Hybrid lesions composed of typical Verrucous Carcinoma and invasive Squamous Cell Carcinoma accounts for about 20% of oral Verrucous Carcinoma and carries better prognosis than invasive Squamous Cell Carcinoma. This case is presented to highlight the importance of thorough microscopic examination in patients with verrucous carcinoma.

**KEYWORDS:** Hybrid verrucous carcinoma, Squamous cell carcinoma, Prognosis.

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## I. INTRODUCTION:

A Hybrid Verrucous Carcinoma (HVC) is defined as a neoplasm in which there is histological diagnostic verrucous carcinoma (VC) and a non- verrucous squamous cell carcinoma (SCC) arising synchronously from the same field.<sup>1,2</sup> Lesions with a “verrucous” surface may belong to a spectrum extending from verrucous hyperplasia (VH), pseudoepithelial hyperplasia, proliferative verrucous leukoplakia (PVL) VC to hybrid Oral Verrucous carcinoma (OVC).<sup>3,4</sup>

This rare tumor is more common in females in the seventh and eighth decades of life and the most frequent localization is buccal mucosa, followed by lip-commissure, gingiva, tongue and hard palate.<sup>5</sup> This case is reported to highlight the appearance of hybrid verrucous carcinoma and importance of diagnosing the entity.

## II. CASE REPORT:

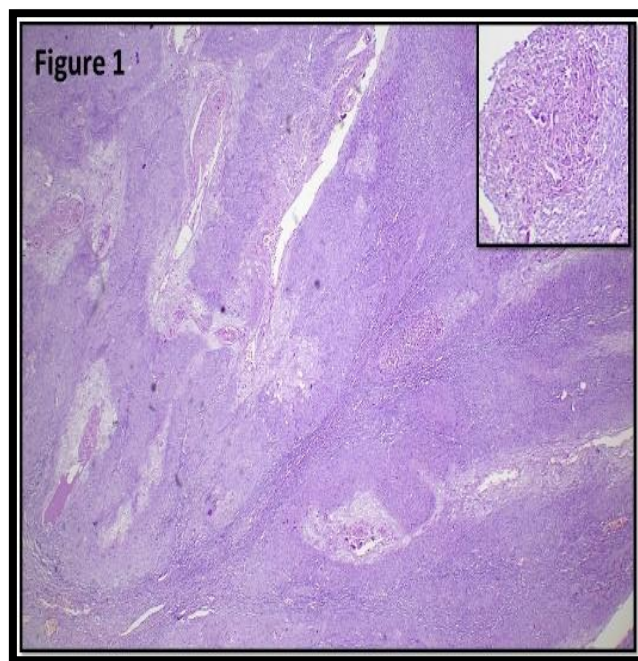
A 64-year-old male came with complaints of growth in right oral cavity for 6 months. On oral cavity examination, a verrucous growth measuring 6x5 cm in size was seen. It extended posteriorly upto anterior pillar, superiorly involved hard palate and upper gingivobuccal sulcus, inferiorly involved lower gingivobuccal sulcus and was not crossing midline. History of tobacco chewing was present for 40 years. Past history, family history, other personal history was nonsignificant. General physical examination revealed a palpable lymph node at level Ib. Systemic examination and laboratory investigations were normal.

CECT Neck showed heterogeneously enhancing soft tissue density lesion epicentered in the right superior gingivobuccal sulcus in retromolar trigone with locoregional extensions and metastatic lymphadenopathy.

Patient underwent right infrastructural maxillectomy with right infratemporal fossa clearance with right marginal mandibulectomy with tracheostomy with forehead flap reconstruction with right modified neck dissection and skin grafting.

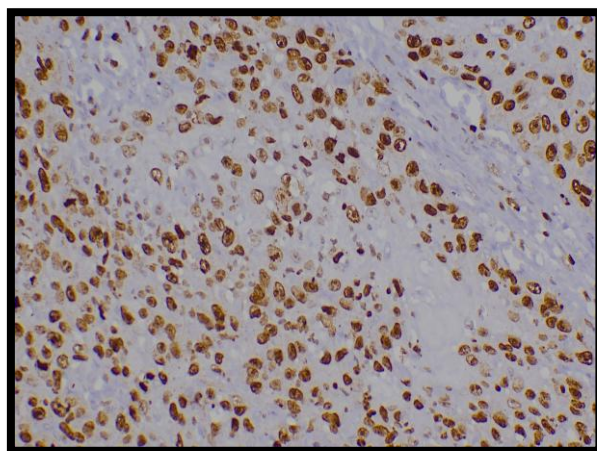
On gross received verrucous growth measuring 6x5.8x2 cm was seen at right gingivobuccal sulcus. Margins were free from tumor. Grossly, bone underlying tumor is uninvolved. On serial sectioning, 24 lymph nodes were retrieved.

Histological analysis of surgical specimen showed keratinized stratified squamous epithelium. The tumor cells arranged in exophytic papillomatous showing broad rete ridges with pushing margins. Individual cells were large polygonal with minimal nuclear atypia. Stroma shows chronic inflammatory cell infiltrates. Foci of invasion < 2mm was noted. (Figure 1)



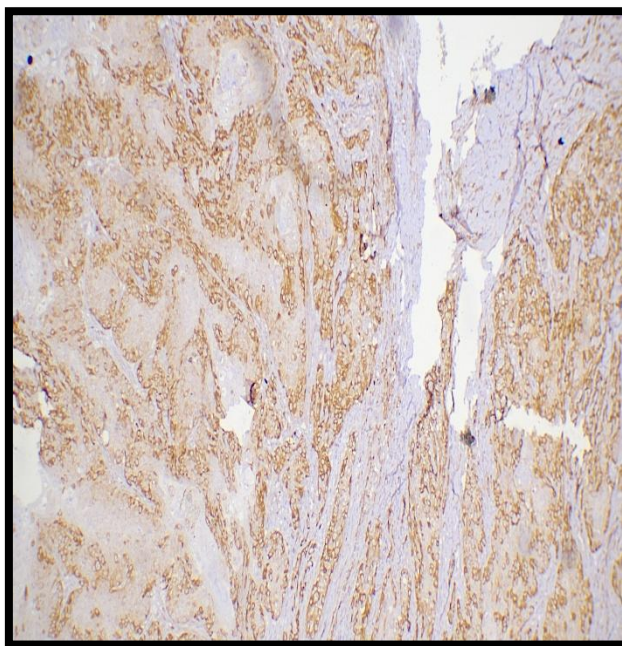
**Figure 1: H&E image of Pushing borders of Verrucous carcinoma. Image Inset – Foci of invasion.**

Out of 24 retrieved lymph nodes, 1 lymph node showed tumor deposits without extracapsular extension and 1 lymph node showed reactive changes. Rest of the 22 lymph nodes were free from tumor deposits. Immunohistochemistry was done for Ki 67 and p16. Ki67 showed 40% positivity( Figure 2)



**Figure 2 : Image of Ki67 index**

P16 showed Diffuse/ block positivity (Figure 3)



**Figure 3: Image of P16 showing block positivity.**

### **III. DISCUSSION:**

VC is described as any exophytic growth of well-differentiated squamous cell carcinoma which generally present as white, warty lesions. They are slow growing tumors known to have low metastatic potential with good prognosis.<sup>3</sup> Betel nut chewing, poor dental hygiene and Human Papilloma Virus (HPV) infection have been implicated in the development of oral VC.

Lesions with a verrucous surface may belong to a spectrum extending from verrucous hyperplasia, pseudoepithelial hyperplasia, proliferative verrucous leukoplakia, VC to hybrid OVC.<sup>4</sup>

VH is pathologically described as an overgrowth of the differentiated keratinized epithelium. PVL is similar to VH with the addition of dysplastic or atypical features. VC, on the other hand, has the above mentioned features and also the pathognomonic destructive pushing border at its interface with connective tissue and has intact basement membrane. Hybrid VC has a VC plus an element of SCC as evidenced by the destruction of the basement.<sup>4,6</sup>

The histopathological criteria given in a study for distinguishing VH from VC are: (i) long and narrow heavily keratinized verrucous processes or broad and flat verrucous processes that are less keratinized; (ii) absence of invasion of the hyperplastic epithelium into the lamina propria as compared with the adjacent normal mucosal epithelium; and (iii) presence of cytologic/architectural features of dysplasia.<sup>7</sup>

Most authors suggest that hyperplasia can be best differentiated from VC in biopsies taken from the margins of the tumor. Hybrid VC is graded and staged similar to SCC but within hybrid VC, the proportion of conventional SCC component may vary, since prognosis of VC is better than SCC it may be assumed that cases with the major proportion of VC would more likely have better prognosis.<sup>8</sup>

Locoregional recurrence in hybrid VC is associated with poor outcome as in cases of conventional SCC; this is quite in contrast to VC. VC is associated with recurrence after repeated excision but only few cases can lead to death especially when it dedifferentiates into much poor grade on recurrence.

In a study, it was stated that the depth and extent of invasion (SCC areas) within VC are critical for the establishment of tumor prognosis. The authors of this study have demonstrated that nodal metastasis and local recurrence were significantly more common in tumors presenting invasive areas over the cut off value of 2 mm than in pure VC or VC showing either epithelial dysplasia or minimal areas of conventional SCC.<sup>8</sup>

In the most definitive study on VC with a component of conventional SCC in 104 cases and noted that 20 of them (19.2 %) demonstrated foci of less-differentiated squamous carcinoma with the VC (hybrid tumors). After treatment, these latter tumors had a slightly higher rate of local recurrence, but none of the pure VC and none of the “hybrid” tumors had nodal or distant metastases.<sup>9</sup>

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Ki67 immunostaining plays a very important role in diagnosing the invasive foci as compared to the verrucous carcinoma. In our study, Ki67 showed proliferative index of 40% in invasive focus. P16 is considered as proxy marker for HPV infection. Overexpression of P16 in oral cancer is considered as a possible marker for high-risk HPV infection.<sup>10</sup>

#### **IV. CONCLUSION:**

Hybrid verrucous carcinoma have a slightly worse prognosis than conventional verrucous carcinoma but better than SCC. Hence it is important for pathologist to look for foci of invasion in all cases of VC. Ki67 and p16 though not a requisite may add to the management.

#### **Acknowledgements:**

**Ethics approval:** The study was conducted in accordance with the guidelines of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar

**Consent to Participate and Consent to Publish declaration** - Written informed consent was obtained from the patient for publication of this case report and accompanying images

#### **Competing interests**

The authors declare that they have no competing interests

#### **Funding**

No funding from an external source supported the publication of this case report.

**Data Availability Statement** - Not applicable

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