Verrucous Carcinoma in a Female Patient: A Rare Case Report

Vineet Garg, Madhusudan Astekar, Gaurav Sapra, Ashutosh Agarwal, Aditi Agarwal

ABSTRACT

Verrucous papillary lesions of the oral cavity are diagnostically challenging as they include a spectrum of benign, potentially malignant, and frankly malignant lesions. Verrucous carcinoma (VC) is a distinct variety of epidermoid carcinoma with pathognomonic clinical appearance, behavior and microscopic features. These slow-growing lesions are markedly exophytic and endophytic that enlarges with direct extension rather than frank invasion, with a tendency to erode the underlying tissues including bone. The treatment of oral VC remains controversial, based on effectiveness of control and not on the potential risk of transforming VC, which can sometimes contain elements of squamous cell carcinoma.

Keywords: Endophytic, Epidermoid, Exophytic, Frankly malignant, Potential malignant, Verrucous papillary lesion.


Source of support: Nil
Conflict of interest: None

INTRODUCTION

Verrucous carcinoma (VC) was first described by Ackerman in 1948, and therefore, also known as Ackerman tumor. Other names for this tumor include Buschke Lowenstein tumor, florid oral papillomatosis, epithelioma cuniculatum and carcinoma cuniculatum. Oral VC is a well-defined type of well-differentiated squamous cell carcinoma, characterized by silent clinical and pathological features comprising approximately 3% of all primary invasive carcinomas of the oral mucosa. Though the exact etiology of VC is not well defined, chewing of tobacco and smoking are found to be the causative factors. Poor oral hygiene, oral lichenoid reaction, and oral leukoplakia may act as predisposing factors.

It is seen more commonly in males than in females in 6th or 7th decade. It occurs most commonly in the oral cavity, but can be found in the larynx, perineum and nasal fossa. The mandibular posterior alveolar crest and retromolar trigone are the most common sites of involvement, followed by buccal mucosa, palate and floor of the mouth. Verrucous carcinoma presents as slow-growing lesions that enlarge with direct extension rather than frank invasion. It is important to recognize it clinically and histopathologically, for it has a characteristic development and an exceptional prognosis if treated correctly.

Lymph node and distant metastasis are rare during all stages of this tumor. These lesions are markedly exophytic and endophytic with a tendency to erode the underlying tissues including bone.

CASE REPORT

A 50 years old female patient reported with an ulcerative growth over in the right lower buccal vestibule region since 2 months. History of present illness revealed an ulcerative growth with gradual onset and with increased progression associated with difficulty in mastication. The patient had tobacco chewing habit since 5 years, but she had quit this habit since last 4 months. Dental history revealed extraction in the same affected area 1 month back. On intraoral examination, an ulcerative growth of 3 × 4 cm was noted over right lower buccal vestibule, involving the alveolar region. The lesion extended from the distal aspect of right mandibular canine region till the right mandibular first molar. The lesion is roughly oval in shape and with overlying mucosa whitish in color. The border of the lesion was well defined. On palpation, the lesion was soft in consistency, with indurated base, tenderness with no association of pus discharge. Lymph nodes involvement was absent. On the basis of patient’s history and clinical examination, a provisional diagnosis of ulceroproliferative lesion in the right buccal vestibule was made. The differential diagnosis was comprised of squamous cell carcinoma and granulomatous lesion.

The orthopantomography revealed no evidence of any invasion in the underlying bone. The routine blood examination carried out discovered all the values lying within the normal limits. Excisional biopsy of the lesion was planned with normal surrounding margins around, followed by buccal fat pad grafting of the raw surface to prevent scarring and contractures. The
histopathological examination under low power view demonstrated hyperparakeratinized irregular, verrucous, exophytic epithelium with endophytic component having broad pushing type of rete pegs (Fig. 1). Under higher magnification, the epithelium showed minimal dysplastic features like mild alteration in nucleo cytoplasmic ratio, pleomorphism, prominent nucleoli, and few mitotic figures without any obvious invasion into the stroma. The connective tissue comprises of loose to dense bundles of collagen fibers with plump to spindle-shaped fibroblasts. Endothelial lined blood vessels with red blood cells are evident. Inflammatory infiltrate predominantly comprise of lymphocytes is also seen in juxta-epithelial region (Fig. 2). On the basis of histopathological report, a final diagnosis of VC was made. On postoperative recall, the site healed uneventfully. The patient was free from any obvious clinical recurrence during a follow-up period of 1 year.

**DISCUSSION**

Clinically and histologically oral verrucous hyperplasia, a potentially malignant disorder, resembles oral VC and may be indistinguishable from one another. The most reliable way to separate these entities on routine hematoxylin-eosin stained tissue sections is to recognize the exophytic growth patterns of oral verrucous hyperplasia from the combined exophytic and endophytic growth patterns associated with VC.4

Verrucous carcinoma are rare tumors of the oral cavity, representing anywhere from 1 to 10% of all oral squamous malignancies.5 The tumor clearly differs from squamous cell carcinoma because it is slow growing, locally destructive and rarely metastatic.6

The National Cancer Data Base had 2,350 cases of VC of the head and neck diagnosed between 1985 and 1996. Although most patients were male, oral cavity tumors were more common among older females.6 The present case report also highlights the female predominance in its occurrence.

Surgery had been the treatment of choice for these lesions. Radiotherapy is controversial. Surgery combined with radiotherapy is most effective treatment. Recurrence rate is high in cases in which either irradiation or surgery alone is performed.2,7 In a series of 104 patients treated from 1946 to 1980 with a minimum follow-up of 2 years, a higher tendency for local recurrence was noted. Surgical excision and primary grafting with regular long-term follow-up for recurrence can be considered as a feasible option for treatment of oral VC.5 The present case report showed no such tendency of recurrence on a follow-up period of 1 year after being grafting with buccal fat pad.

Pathologists not familiar with the lesion may diagnose it as a benign lesion, such as hyperplasia, and surgeons can easily mistake it for a more aggressive form of squamous carcinoma.8 It has been suggested that this tumor is not as rare as was generally thought, because some cases are probably reported as squamous cell carcinoma.1 Oral VC is considered a low-grade and uncommon variant of oral squamous cell carcinoma. Some studies have been performed attempting the various expression profile in these lesions despite the knowledge of the cytoskeleton disturbances associated with the neoplastic development (Table 1). Immunohistochemical analysis of basement proteins like type IV collagen, laminins and fibronectin can be useful for evaluation of tumor invasion and metastasis. This will contribute to a better understanding of some mechanisms implicated with the behavior of diverse neoplasms.9,15
Table 1: Various immunohistochemical expression of verrucous carcinoma of oral cavity

<table>
<thead>
<tr>
<th>Sl. no.</th>
<th>Authors (reference)</th>
<th>Years</th>
<th>Tumor profile</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Storthz KA, et al\textsuperscript{10}</td>
<td>1986</td>
<td>IHC-HPV, ISH-HPV DNA 2, 6 and 16</td>
<td>Using immunohistochemistry and \textit{in situ} hybridization corroborates the presence of HPV DNA 2 in an oral cancer and indicates the need to investigate the oncogenic potential</td>
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<td>2</td>
<td>Oliveira MC et al\textsuperscript{9}</td>
<td>2005</td>
<td>IHC-cytokeratins</td>
<td>Using immunohistochemistry confirms the use of CK 10, 13, 14, and 16 in emphasizing the biological behavior of the VC lesions as markers of differentiation</td>
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<td>3</td>
<td>Fujita S et al\textsuperscript{11}</td>
<td>2008</td>
<td>PCR-HPV DNA, ISH-HPV IHC-p53</td>
<td>Using PCR, immunohistochemistry and \textit{in situ} hybridization demonstrated the oral VC tumorigenesis may involve the inactivation of p53, which is associated with HPV infection. Thus, multiple infections with low and high-risk HPVs and their rapid replication during hyperkeratinization may participate in the histogenesis of oral VC</td>
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<td>4</td>
<td>Gao HW et al\textsuperscript{12}</td>
<td>2009</td>
<td>IHC-CK20 + (Merkel cell), CD10 and CD34</td>
<td>CD34+ stromal cells and to a lesser extent Merkel cells but not CD10+ stromal cells reveal statistically different density during the transition from benign squamous lesion to malignant lesions, like VC and OSCC</td>
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<td>5</td>
<td>Arduino PG et al\textsuperscript{13}</td>
<td>2010</td>
<td>IHC-laminin, laminin-5, collagen IV and fibronectin</td>
<td>Verrucous carcinoma has a biological behavior different from severe epithelial dysplasia or OSCC due to its discontinuous immunohistochemical expression</td>
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<td>6</td>
<td>Rouby DHE et al\textsuperscript{14}</td>
<td>2010</td>
<td>IHC-CD68 and CD31</td>
<td>The area percentage of CD68 (tumor-associated macrophages) and mean vessel density were significantly lower in VC than different grades of OSCC. Thus increase TAMs are associated with angiogenesis and higher histopathological grades of oral cancer</td>
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<td>7</td>
<td>Zargaran M et al\textsuperscript{15}</td>
<td>2011</td>
<td>IHC-collagen IV, laminin 332;2</td>
<td>Isolated expression of type IV collagen does not clearly define that a lesion is invasive or noninvasive and evaluation of Ln-332y2 chain expression (cut-off 5%) may be useful as a marker for description of biological differences and diagnosis of oral VC from well differentiated OSCC, especially in doubtful cases</td>
</tr>
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IHC: Immunohistochemistry; HPV: Human papilloma virus; ISH: \textit{In situ} hybridization; DNA: Deoxyribonucleic acid; PCR: Polymerase chain reaction; CK: Cytokeratin; CD: Cluster of differentiation; OSCC: Oral squamous cell carcinoma; Ln: Laminin

REFERENCES