Case Report

Verrucous Carcinoma - A Diagnositic Dilemma: Case series, Differential Diagnosis, Therapy and Literature Review

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Abstract

Verrucous carcinoma (Ackerman's tumor) is a low grade variant of oral squamous cell carcinoma (OSCC). The commonest sites of involvement in the head and neck regions have been oral cavity (2-9%) and Larynx (2)% . In India, approximately 7% of oral cancers are VC. VC of the oral cavity is a different clinicopathologic tumor distinguished from the usual squamous cell carcinoma because of its local invasiveness, non metastasizing behavior, and special clinical appearance . An accurate pathological diagnosis is challenging and is facilitated by an adequate tumor sample for study and more importantly, a close collaboration between the clinician and the pathologist. Here, we present a case series of 40 cases of VC of the buccal mucosa treated by complete exision of tumor and reconstruction done by resorbable collagen membrane and showed no recurrence for the follow up of 12 months.

Key words: Verrucous carcinoma (VC), Ackerman's tumor, human papillomavirus (HPV), Darier's disease, Supra Omohoid neck dissection (SOHND) , polymerase chain reaction (PCR)

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Introduction

Oral verrucous carcinoma is a rare tumor first described by Ackerman.[1] It is a special form of well-differentiated squamous cell carcinoma with specific clinical and histological features. Various names are used in the literature to describe this entity, including Ackerman's tumor, Buschke-Loewenstein tumor, florid oral papillomatosis, epithelioma cuniculatum, and carcinoma cuniculatum.[2] The tumor grows slowly and locally, invasive in nature and unlikely to metastasize. It appears as a painless, thick white plaque resembling a cauliflower. The most common sites of oral mucosal involvement include the buccal mucosa, followed by the mandibular alveolar crest, gingiva, and tongue. Shear and Pindborg[3] described a condition termed verrucous hyperplasia in 1980. Both lesions closely resemble each

other clinically and pathologically. Verrucous hyperplasia has been considered an antecedent stage or early form of verrucous carcinoma and is believed to have the same biological potential.[4,5] Surgery has been the first choice of treatment for these lesions, and radiotherapy is controversial.[6] However, surgery combined with radiotherapy is the next most preferable treatment and may have benefits, particularly in cases of extensive lesions.[7] Recurrence rate is high in cases in which either irradiation or surgery alone is performed.

Case Series:

Study consist of 40 patients of biopsy proven verrucous carcinoma visited to department of oral & maxillofacial surgery , King George's Medical University, lucknow, India . Of the 40 patients identified with VCs, 36 (90%) were male and only four (10%) were female. The age distribution ranged from 30 years to 65 years with a mean age of 47.5 years at diagnosis. The most common site of VC within the oral cavity was the buccal mucosa (90%), alveolar ridge (8%) followed by the tongue (2%). In our series, 96% patients had the habit of chewing betel nuts, 92% both chewed betel nuts, tobacco and smoked cigarettes, and 57.7% consumed alcohol.

All the cases were evaluated clinically and radiologically with computed tomography of head and neck area, chest X-ray , blood chemistry, and complete blood cell count . Among the cases only 2 cases were T3 lesion and 38 cases were of T2 and T1 stages tumor (American Joint Committee on Cancer staging system, 1997). All of the patients were treated with surgery alone. Only two patients presented with clinically palpable nodes before surgery and underwent elective neck dissections (supraomohyoid dissections). Surgical exicision with 0.5-1 cmm normal healthy margin was done and reconstruction was done with bioresorbable collagen membrane in all the cases. Two cases underwent reconstruction with split thickness skin graft and SOHND. All the exicisied were sent for histopatological examination and confirmed the primary diagnosis of Verrucous carcinoma.

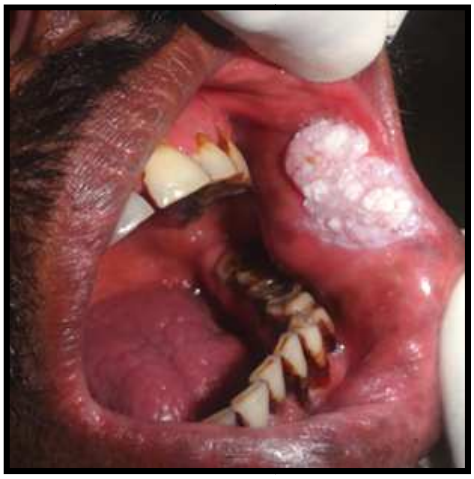

Figure 1: Preoperative intraoral view

Figure 2: Surgical exicision with normal healthy tissue margin.

Figure 3: Soft tissue reconstruction done by biodegradable collagen membrane.

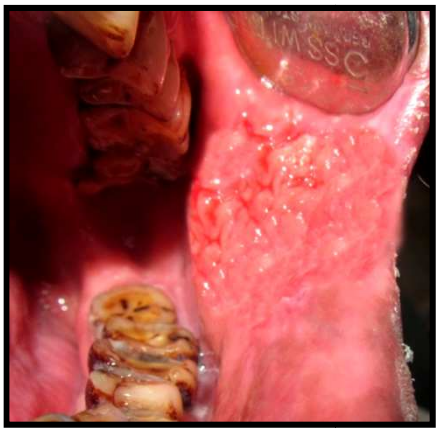

Figure 4: Healing after one week follow up

Discussion

Verrucous carcinoma, a low-grade variant of squamous cell carcinoma, is so closely aligned with the use of snuff and chewing tobacco that it has been called the "snuff dipper's cancer," even though it is not the most common form of carcinoma resulting from this habit. Million & Cassiss regarded it as a 'grade one-half' squamous cell carcinoma.[8] It is, furthermore, now known that 16-51% of oral verrucous carcinomas are found in persons without tobacco habit. VC constitutes 2 to 4.5% of all forms of squamous cell carcinoma seen mainly in males above 50 years of age and also associated with high incidence (37.7%) of second primary tumour, mainly in oral mucosa.[9] In oral cavity it occurs most commonly the buccal mucosa (61.4%), followed by the lower alveolus (11.9%). [10] V C thought to be affecting the elderly males mostly as for example in a study conducted by Walvekar RR et al. (2009), the ratio of male to female patients suffering from VC was found to be 3.6:1 with a mean age of 53.9 years.[11]

The etiopathogenesis of VC is unclear. Other etiologic agents may be involved, with immunosuppression, human papillomavirus and other viruses being most recently implicated. Nevertheless, it cannot be denied that the most common site of occurrence for this cancer remains the oral mucosa and the majority of oral cases are found in persons who habitually chew tobacco or snuff. Clinically As for oral VC, smoking, a habit of chewing betel and snuff and human papilloma virus infection (HPV), stand out as the main carcinogenic factors.[8] More recently, studies have further confirmed the association between HPV and OVC by detecting HPV– DNA types 6, 11, 16 , and 18 by polymerase chain reaction (PCR), restriction fragment analysis, and DNA slot–blot hybridization.[12]

VC in the oral cavity is characterized by a cauliflower-like exophytic growth with a cleft, pale, warty, fungating, locally aggressive, ulcerated tumor attached by a broad base, is well circumscribed and it is clearly demarcated from the adjacent mucosa. with a pebbly mamillated surface.

In the clinical differential diagnosis, the following were observed: SSC, viral verruca, amelanotic melanoma, histoplasmosis, secondary syphilis, Darrier's disease, white spongy nevus and erythematous lupus.[8] The main histopathological differential diagnosis of VC is from leukoplakia, papilloma, pseudoepitheliomatous hyperplasia, verrucous hyperplasia and highly differentiated squamous cell carcinoma.[9]

The need for neck dissection is an controversial and important consideration in planning therapy for OVC. The aggressive clinical presentation of the tumor often sways clinical judgment in favor of performing lymph node dissection, especially in the presence of clinical lymphadenopathy. This sentiment is reinforced by the fact that OVC is an extremely challenging pathological diagnosis and often even an adequate biops may miss areas of squamous differentiation. However reports suggest that lymph node dissection in OVC should be confined to immediately adjacent lymph node groups only and in cases, where any possibility of increased morbidity or mortality may arise from inclusion of neck dissection with surgical excision, it could be omitted entirely. It is

reasonable to consider a selective neck treatment such as a SOHND in situations where there is uncertainty regarding the pathological diagnosis in the face of clinically suspicious lymphadenopathy.

Table1: Clinico pathologic characteristics as suggested by Ferlito A and Recher G (1980)[13]

1.	Sites of predilection	Oral cavity, Larynx
2.	Age/Sex	Men over 50 years
3.	Habits	Tobacco user, poor oral hygiene
4.	Grade of malignancy	Low grade
5.	Metastatic	Absent
6.	Gross appearance	Exophytic, fungating, usually keratinizing
7.	Associated mucosal Changes	Leukoplakia, metachronous or synchronous squamous cell neoplasm
8.	Differentiation of cells	High grade, uniform
9.	Cytologic features of malignancy	Rare to absent
10.	Depth of lesion	Pushing to blunt invasion
11.	Cellular response	Usually predominant
12.	Hybrid malignancy	20% of cases approximately

Alternatively, a staged neck procedure is also a reasonable option if final tumor histology mandates it.[11] Operative treatment of VC may not include neck dissection, even though enlarged lymph nodes may be palpated.[12]

Microscopically, the uniform cells show none of the mitoses or dysplastic features expected with squamous carcinoma. The surface shows characteristic "church-spire" formations due to extensive keratinization. The rete pegs are rounded and bulbous and "push" into the stroma on a broad front. Again, there is no cellular atypia. Keratohyalin granules in the stratum granulosum are few or missing (in contrast to verrucal keratosis). A mixed chronic inflammatory reaction surrounds the rete pegs and may be marked.

Treatment modalities for verrucous lesions have included surgery, radiation therapy, chemotherapy, cryotherapy, laser therapy, photodynamic therapy, and treatment with recombinant alpha–interferon .Although adequate surgical excision remains the treatment of choice for the oral VC ,chemotherapy, alone or in combination with radiotherapy, has also been employed as initial treatment.[14,15] Chemotherapeutic agent alone used is intraarterial methotrexate infusion.[16] Radiation therapy alone has been contraindicated due to the possibility of anaplastic transformation from oral VC to more aggressive SCC.[17,18] Proffitt et al. suggested that anaplastic transformation may be caused by irradiation due to disregulation of a cell clone in a slow-growing tumour. Perhaps another possibility is that a hidden undifferentiated part of a verrucous carcinoma can start to proliferate later on . Studies on kinetics of verrucous carcinoma have shown a very low proportion of S-phase cells, which might explain the relatively slow response of the tumour to radiotherapy.[19,20] OVC tends to destroy bony structures such as the mandible, on a broad front, eroding with a sharp margin rather infiltrating the marrow spaces.[21] Squamous cell carcinoma (SCC) can arise in VC itself during its course.[22] The local recurrence of oral VC has been reported Frequently 38.5%.[23] The five years disease-free survival with surgical therapy was found to be 77.6% which correlates

well with control rates reported in the literature.[24]

The problems in diagnosing VC are discussed in many reports in the literature. .Verrucous hyperplasia/leukoplakia is the initial pathologic diagnosis in 60% of cases. The diagnoses of VC is proved by pathologic report of a further deep incisional biopsy or wide excision. VC exists within the histologic continuum ranging from benign squamous hyperplastic lesions to invasive squamous cell carcinoma.[17] Small superficial biopsies usually result in the diagnosis of benign hyperplasia or hyperkeratosis by the pathologist. The surgeon must take a specimen with full thickness of the tumor or deepest margin of the tumor and adjacent uninvolved mucosa to make a correct diagnosis. However, it is still difficult to provide adequate specimens from regular biopsies of large verrucous tumors in the clinic, thus, VC is often under diagnosed.[17,25] When VC was highly suggested by clinical appearance, patients should undergo deep incisional biopsies under general anesthesia.

Conclusion: VC of the oral cavity is a different clinicopathologic tumor distinguished from the usual squamous cell carcinoma because of its local invasiveness, non metastasizing behavior, and special clinical appearance. Treatment by surgery is curative if the entire lesion is excised. VC has an intrinsic potential for local recurrence that should be considered when planning surgery.

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