



VERRUCOUS CARCINOMA IN ASSOCIATION WITH OSMF – 2 CASE REPORTS

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ABSTRACT

Verrucous carcinoma (VC) otherwise known Ackerman's tumor is a distinct variety of epidermoid carcinoma with characteristic clinical presentation, behavior and histological features. It usually presents as a hyperplastic epithelium, abundant keratin superficially with a church-spire keratosis and also presenting parakeratin plugging which is characteristic of this VC. Oral squamous cell carcinoma (OSCC) is seen in one-third of the oral sub mucous fibrosis (OSMF) patients. Whereas the development of verrucous carcinoma is rare. We are presenting a rare report of 2 cases of verrucous carcinoma occurring in conjunction with OSMF. These patients presented to the OP with a chief complaint of restricted mouth opening and a growth which on biopsy turned out to be a Verrucous carcinoma in conjunction with OSMF.

List of abbreviations: Oral verrucous carcinoma (VC), Oral squamous cell carcinoma (OSCC), Oral submucous fibrosis (OSMF), Proliferative verrucous leukoplakia (PVL), Verrucous hyperplasia (VH).

Key words: Verrucous carcinoma, Ackerman's tumor, Oral submucous fibrosis, Epidermoid carcinoma, Oral squamous cell carcinoma, exophytic.

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INTRODUCTION

Verrucous carcinoma (VC) is a separate clinico-pathologic entity which was initially described by Ackerman in 1948. It is known by various synonyms such as Ackerman's tumor, Buschke Lowenstein tumor, florid oral papillomatosis, epithelioma cuniculatum, and carcinoma cuniculatum. [1] The tumor has slow growth characteristics, is invasive in nature and does not metastasize [2]. It is a variety of epidermoid carcinoma with a characteristic clinical appearance, behavior and histopathological features [3]. It is exophytic, papillary in nature with a rough, pebbly surface. The exact etiology of

verrucous carcinoma is not well defined. Many have suggested chewing of tobacco and smoking as the causative factors. Other predisposing factors may be poor oral hygiene, oral lichenoid reaction, and oral leukoplakia. This tumor differs from squamous cell carcinoma because it is slow growing, locally destructive and does not metastasize. It has male predilection and occurs during the 6 th or 7 th decade of life. It presents as a white, warty, exophytic growth with a broad base. Schrader *et al.* and Jordan suggested verrucous carcinoma is a slow growing exophytic lesion that spreads by lateral extension and is locally destructive. It has rugae-like folds interspersed with deep clefts. Intraorally it common occurs in the buccal mucosa, followed by the mandibular alveolar crest, gingiva, and tongue. Shear and Pindborg in 1980 described

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a condition termed verrucous hyperplasia (VH). Involvement of deeper contiguous structures happens after extensive involvement of the buccal mucosa [4]. Patients give a history of chewing tobacco, may have poorly fitting dentures, poor oral hygiene and/or, carious and jagged teeth [5]. Surgery is the first choice of treatment for these lesions, surgery combined with radiotherapy is the most preferable and may have better results in case of extensive lesions. VC may progress to invasive squamous carcinoma and release metastases. Recurrence is noticed at a higher rate in cases in which either irradiation or surgery alone is performed. [6]

Oral sub mucous fibrosis (OSMF) is a potentially malignant epithelial disorder caused due to chronic betel nut chewing habit [7]. OSCC is seen in one-third of the OSMF patients whereas the reported cases of VC are rare in. Herein, we are presenting 2 case report of verrucous carcinoma in a 57-year-old and 68-year-old male patient with OSMF.

Case Report 1:

A 57-year-old male patient reported to our outpatient department with a chief complaint of a growth in relation to the cheek adjacent to the upper and lower right back tooth region for 6 months. History revealed that the growth started small and gradually increased to the present size. He had difficulty in mastication as the growth interfere during the process of mastication. He has a habit of chewing pan masala for the past 10 years. He did not reveal any significant medical and surgical history.

Local examination revealed on inspection restricted mouth opening. Blanching and hyperpigmentation of the right and left buccal mucosa & soft palate. Erythematous appearance of the right buccal mucosa extending from retromolar region to the commissure. Mouth opening of 25mm, tongue protrusion of 20 mm (Normal). Uvula was of normal shape and was in normal position. On palpation, multiple fibrotic bands palpable in the right and left buccal mucosa. A single circumoral band also palpable. Mucosa was tough and leathery on palpation.

On inspection, a growth was evident in relation to the right buccal mucosa near the commissure measuring

approximately 1 x 2.5 cm in size. Surface of the growth was rough and proliferative. It had well defined borders and was of an irregular shape. The mucosa surrounding the growth appeared erythematous (Figure 1). On palpation inspectory findings regarding site, size and shape is confirmed. It extended 3.5cm from the retromolar region posteriorly and 1 cm from the commissure of the lip anteriorly. It was present along the plane of occlusion. It was well defined with a rough and proliferative surface. Firm in consistency. Non-tender on palpation. The right submandibular lymph nodes were palpable, single > 1cm in size, soft, freely mobile and tender. Based on the history and clinical features a provisional diagnosis of Malignant growth suggestive of verrucous carcinoma was considered.

CT revealed an ill-defined mild asymmetrical thickening seen in right buccal mucosa abutting the retromolar trigone. No obvious lytic / sclerotic lesions seen in the adjacent bone. No significantly enlarged nodes seen in the neck

The lesion was surgically excised with wide margins and sent for histopathological investigation. It returned with a report of verrucous carcinoma (Figure 2). Patient is under followup and has been advised radiotherapy for complete resolution of the lesion.

Case report 2:

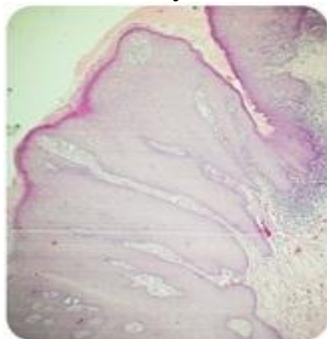
A 68-year-old male patient reported to the outpatient department with a chief complaint of growth in relation to the right buccal mucosa for the past 6 months. The growth started small and gradually attained the present size. He gives a history of pan chewing for the past 15 years.

Local examination revealed on inspection restricted mouth opening. Blanching and hyperpigmentation of the right and left buccal mucosa & soft palate. Mouth opening of 20mm, tongue protrusion of 18 mm. Uvula was of normal shape and was in normal position. On palpation, multiple fibrotic bands palpable in the right and left buccal mucosa. Mucosa was tough and leathery on palpation.

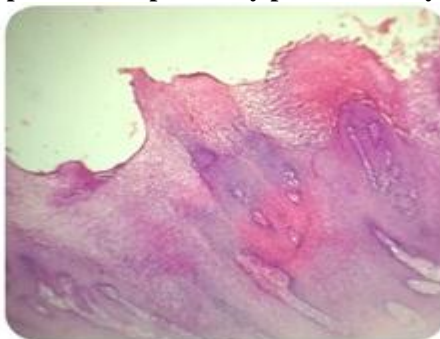
Figure 1. Exophytic lesion in relation to the right buccal mucosa



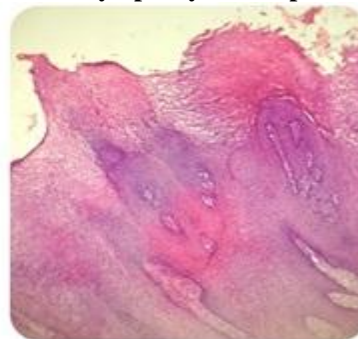
Figure 2. The H& E stained section (Figure 2) shows acanthotic epithelium with parakeratin plugging and pushing margins with long, broad and flat ended rete pegs. The epithelial cells exhibit nuclear pleomorphism and hyperchromatism, prominent nucleoli and epithelial whorls, increased mitotic activity is also evident. Focal areas of chronic inflammatory cell infiltrate is present subepithelially predominantly consists of lymphocytes and plasma cells.



10 X



40 X



100 X

Figure 3. Exophytic lesion in relation to the right buccal mucosa



Intraorally on inspection a growth (Figure 3) was evident in relation to the right buccal mucosa with lobulated appearance and measuring approximately 2x2.5 cm. It had well defined borders and was of an irregular shape. Extended 2cm from the commissure of the lip anteriorly to the retromolar region posteriorly. The colour of the lesion was pink with erythematous areas. The surrounding mucosa appeared normal. On palpation, it was firm in consistency and non-tender. The right submandibular lymph nodes were palpable. 2 nodes, >1cm in size, soft, non-tender and freely mobile. Based on the

history and clinical features a provisional diagnosis of Malignant growth suggestive of verrucous carcinoma was considered.

The lesion was subjected to biopsy and the tissue was sent for histopathological investigation. It returned with a report of verrucous carcinoma.

DISCUSSION:

Oral submucous fibrosis (OSMF) is a chronic premalignant condition of the oral mucosa which was first described by Schwartz 1952 (8). Pindborg (1966) defined

OSMF as “an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat”.(2, 3) Oral sub mucous fibrosis (OSMF) is a pre-malignant condition which comes in the category of potentially malignant epithelial lesions (PMELs) characterized by fibrosis of the lining mucosa of the upper digestive tract involving the oral cavity, oro-and hypopharynx and the upper third of the oesophagus. The fibrosis involves the lamina propria and the sub mucosa of the tissues and may often extend to the underlying musculature resulting in the deposition of dense fibrous bands which gives rise to limited mouth opening, a hallmark of this disorder [9,10].

The diagnosis of oral sub mucous fibrosis is usually based on clinical signs and symptoms which include oral ulcerations, burning sensation (particularly with spicy foods), marbling appearance of the affected mucosa with restricted mouth opening [4,11].

The potentially malignant nature of this condition has been well documented. A malignant transformation rate of 7.6% over a period of 10 years was described in an Indian cohort study while the relative risk for malignant transformation was reported to be as high as 397.3 %.

OSMF may cause atrophy in the epithelium, increasing carcinogen penetration. Studies suggest that dysplasia is seen in about 25% of biopsies of OSMF cases, and the rate of transformation to malignancy varies from 3% to 19%. [7]

Oral sub mucous fibrosis may cause atrophy of the epithelium increasing carcinogen penetration. The evidence supporting the malignant potential of OSMF includes: [12]

1. higher prevalence of leukoplakia among OSMF patients;
2. high frequency of epithelial dysplasia
3. histologic diagnosis of carcinoma without clinical signs of carcinoma
4. concurrent finding of OSMF among patients with oral cancers; and
5. a higher incidence of oral cancers among patients with OSMF.

The cases reported here had history of chewing gutkha and tobacco with lime that contained areca nut along with other harmful ingredients which had led to the development of oral sub mucous fibrosis. Development of oral squamous cell carcinoma is seen in only one-third of OSMF patients, the occurrence of verrucous carcinoma is said to be extremely rare.

Chang *et al.*, [13] in their study, suggested that chewing areca quid is the major risk factor in the development of

verrucous hyperplasia and verrucous carcinoma. A distinction should be made between verrucous hyperplasia and verrucous carcinoma. Verrucous hyperplasia was described by Shear and Pindborg in 1980. [14] Bulut *et al.*, [15] in their study on 12 cases of oral verrucous carcinoma, showed that it is difficult to distinguish verrucous hyperplasia and verrucous carcinoma clinically. Most of the verrucous carcinoma that develops in smokeless tobacco users occurs in older individuals who have practiced the habit for several years. Whereas in Verrucous hyperplasia according to the study result by Vinay K Hazarey *et al.*, Prevalent habit pattern associated with verrucous hyperplasia was found to be tobacco and lime quid placement in buccal vestibule (36.84%) followed by mixed habit pattern (31.57%). Mixed habits includes simultaneous consumption of different tobacco preparation like pan with or without tobacco, bidi/cigarette smoking, areca chewing, areca and tobacco combinations include kharra, gutkha, mava chewing. The tumor occurring in younger individuals has been rarely documented. Friedell and Rosenthal [16] in 1941 reported eight cases of verrucous carcinoma; all were men over 60 years. Ackerman in 1948 reported 31 cases of verrucous carcinoma in old men with many years of duration of tobacco chewing. Sorger in 1960 [17] reported four cases of verrucous carcinoma in men above 70 years. Ours is in accordance with cases reported by other authors.

Oral verrucous carcinoma (VC) is a rare, specific variant of well-differentiated oral squamous cell carcinoma with characteristic clinical and histological features. The incidence of verrucous carcinoma varies from 4.5% to 9% or even higher as reported in some centers. In oral cavity, verrucous carcinoma constitutes 2% to 4.5 % of all forms of oral squamous cell carcinoma. The most common areas affected by oral verrucous carcinoma are the buccal mucosa and the lower alveolus with a reported incidence of 61.4% in relation to the buccal mucosa and 11.9% for the lower alveolus [18]. It occurs most commonly in males in their 5th-6th decades of life. The etiology of verrucous carcinoma is not well defined. According to Shear and Pindborg, tobacco chewing appears to be the major causative factor for verrucous carcinoma. [14]. The oral hygiene is invariably poor in all the cases. Tobacco appears to be a major risk factor in the causation of verrucous lesions [19]. In our patient, chewing gutkha and tobacco with lime seemed to be the causative factor.

VC can be described clinically as papillary, verrucoid, fungating, or cauliflower-like. VC may develop from the progression of proliferative verrucous leukoplakia (PVL) and progress to carcinoma [20]. Verrucous carcinoma is a locally invading tumor and does not go for distant metastasis. If lymph nodes are palpable, they usually present an inflammatory reaction in large secondarily infected lesions. In our case, lymph nodes were palpable. Abrupt transition from normal epithelium to endophytic growth is taken as an important parameter to

differentiate verrucous carcinoma from other benign verrucous growths. The epithelium is well-differentiated in all the rete pegs. Alternatively, VC may develop *de novo* or from an existing PVL. The tumor may also be found on different sites including skin, paranasal sinus, bladder and anorectal region, male and female genitalia, sole of the foot, and ear. [21]

Ferlito *et al.* (1980) emphasized on the following classic description for the diagnosis of VC: [22]

- Fungating warty tumor
- Thickened club-shaped, papillomatous projections which push rather than infiltrate into the underlying tissue
- Deeply projecting cleft-like spaces with degenerating keratin and later cystic degeneration of central portion of the filiform projections
- High degree of cellular differentiation with absence of features of malignancy
- Considerable inflammatory response in invaded tissues
- Rare regional lymph node and distant metastasis.

The most important differential diagnoses of verrucous carcinoma include: (i) Oral squamous cell carcinoma showing verrucoid features, (ii) Proliferative verrucous leukoplakia (PVL), (iii) epithelial hyperplasia, (iv) pseudo-epitheliomatous hyperplasia, (v) verruca vulgaris, and (vi) keratoacanthoma [23].

Grinspan has divided Verrucous Carcinoma into four types: [24]

Type I A: The type which is characterized by acanthosis, papillomatosis, leukoedema, moderate ortho- or para-keratosis, hypertrophic inter-papillary crests and stratification of the basal layer;

Type I B: which is characterized by cryptic depression of the epithelial surface, invagination of the epithelium and a fistulous tendency;

Type II: characterized by areas with the characteristics of type I A or type I B with hyperchromatic nuclei and atypical mitosis;

Type III: This is characterized by areas of type I or type II with features of oral squamous cell carcinoma with anaplastic cells and metastasis that are frequently observed in this type.

The prognosis of verrucous carcinoma is better than that of other kinds of life-threatening malignant tumors. Various treatment modalities include surgery, chemotherapy, radiation, or combination of these with photodynamic therapy which has recently been used [25]. Surgery is the primary mode of treatment of verrucous carcinoma. Combined therapy with irradiation is found to be useful when the tumor extends to the retromolar region. Cytostatic drugs like alpha interferon can be used as a supportive therapy where surgery is contraindicated. It helps in delaying the growth of the tumor. It has been stated that a combined modality involving both surgery and radiotherapy is more successful in treating the lesion.

CONCLUSION

Verrucous carcinoma may arise *de-novo* or from preexisting potentially malignant lesions. Oral sub mucous fibrosis (OSMF) is a condition associated with an increased risk of malignant transformation. Verrucous carcinoma is an indolent, low-grade, carcinoma with benign histologic appearance. There are very few cases of verrucous carcinoma (VC) in cases diagnosed with OSMF reported in literature. Surgical resection with adequate margins and postoperative radiotherapy is the treatment of choice.

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