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CASE STUDY

HYBRID VERRUCOUS CARCINOMA: A CASE REPORT AND ITS REVIEW

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ABSTRACT

Hybrid Verrucous Carcinoma is an uncommon tumour wherein Verrucous Carcinoma (VC) is coexisting with conventional Squamous Cell Carcinoma (SCC) within same maternal field. The differential diagnosis of verrucous carcinoma remains difficult and many a time pathological evaluation contradicts the clinical manifestation of the disease. The heterogeneous nature, infrequency of occurrence and the difficulties associated with diagnosis are discussed here. As the malignant behaviour of hybrid verrucous carcinoma is confined, careful examination of these tumor.

Key words: Verrucous Carcinoma, Hybrid Verrucous Carcinoma, Oral Cavity.

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INTRODUCTION

Verrucous carcinoma is a low grade variant of oral squamous cell carcinoma which was described by Ackerman in the year of 1948. It is typically non metastasizing but locally aggressive in nature but sometimes we surgical pathologist may come across situations where a subtle intermixing of conventional squamous cell carcinoma with this variant of SCC is seen which may exhibit different prognostic behaviour. Thus the need of different nomenclature of this collision tumour was felt and accordingly the term hybrid verrucous carcinoma was coined. First report of oral HVC was described by Jesus *et al.* (1950) a lesion which is clinically less innocuous in the form of VC may carry the risk of greater danger when it is evaluated histopathologically. As the pathogenesis of VC is still not properly elucidated a same is true for hybrid VC. The published literature suggests that 20 percent of initially diagnosed cases of verrucous carcinoma were proved to be a hybrid variant. HVC has 20 percent H/P features of conventional S.C.C and rest is VC (Woolgar, 2009)

Report of a case:

A 39 year old man was referred to our department with an exophytic ulcer proliferative mass in the left mandibular alveolar ridge and vestibule.

His history included a 20 year period of chewing tobacco around 6-8 times day and occasional alcohol consumption. The patient's medical history was insignificant. No facial asymmetries, cervical lymphadenopathy or other extra oral findings were detected. Upon intra oral examination an exophytic papillary whitish reddish mass was found to occupy mandibular alveolobuccal complex extending from canine to second molar extending both buccally and lingually. The mass was fixed to underlying bone.

Verrucous carcinoma and hybrid verrucous carcinoma

Discussion and literature review

A literature review search undertaken using the Ovid, PubMed databases from 1996 to 2016. The search criteria were limited to English language Verrucous Carcinoma Verrucous squamous cell carcinoma oral cavity and hybrid verrucous carcinoma. Articles with full text available were reviewed. Verrucous carcinoma is a slow growing tumour that presents an exophytic growth with a pebbly micro nodular surface and tends to spread locally with no evidence of metastasis even in advanced cases. The most common site of occurrence includes buccal mucosa, mandibular alveolar crest, gingiva, tongue and glottis (Depprich *et al.*, 2006) It usually occurs in the males in the fifth and sixth decades of life (Ray *et al.*, 2011). Use of smokeless forms of tobacco hence also called as Snuff dippers cancer followed by betel nut chewing and alcohol has been reported in the affected patients (Alkan *et al.*, 2010).

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Recently an association of HPV types 6, 11, 16 and 18 has been confirmed by detection of viral DNA PCR and DNA slot blot hybridization (Noble-Topham *et al.*, 1993; Lubbe *et al.*, 1996; Shroyer *et al.*, 1993). Microscopically VC usually presents with the hyperplastic epithelium with abundant keratin superficially projecting as exophytic church spire keratosis. Para keratin plugging and broad bulbous rete pegs which shows endophytic growth pattern with pushing borders (Wenig, 2002). The epithelium is well differentiated in all rete pegs and shows minimal or no pleomorphism of cells and no mitotic activity is seen. Lymphoplasmacytic inflammatory host reaction is seen in connective tissue stroma subjacent to the epithelium in varying degrees



Figure 1. Clinical Image shows an exophytic mass in the left mandibular alveolobuccal complex. (Original)

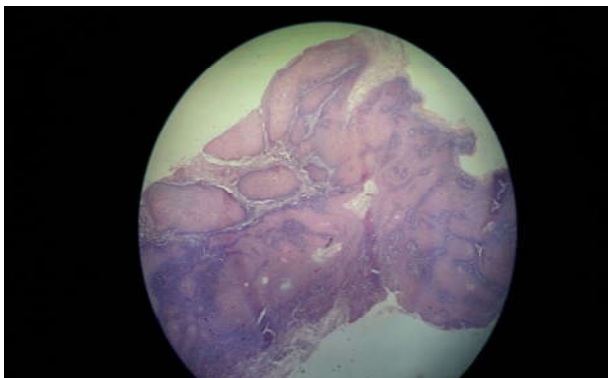


Figure 2. Histopathological Image shows H&E Stain-4X: Few neoplastic islands infiltrating into the connective tissue stroma. (Original)

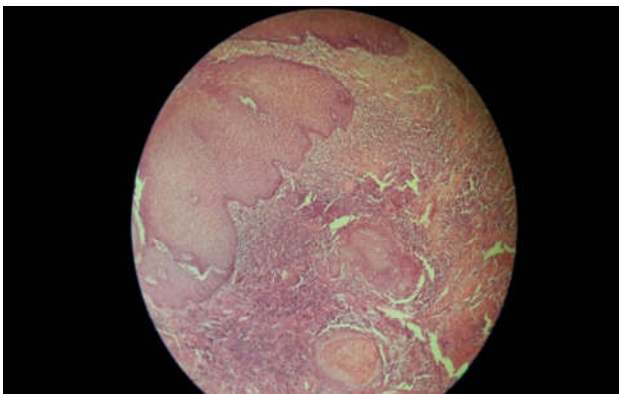


Figure 3: Histopathological Image shows PAS Stain-10X: PAS stain shows thickening of basement membrane (Original)

Unlike usual variant of SCC it does not metastasize to the lymph node but like the other variant it invades the underlying structures.

If lymph nodes are palpable they usually present as an inflammatory reaction in large secondarily infected cases. When confronted with bony structures such as the mandible the tumour tends to destroy the bony tissue on a broad front and erodes with a sharp margin rather than infiltrating into the marrow spaces (Saharia *et al.*, 1972). While surgery forms the widely accepted mode of treatment for VC, radiation is only employed in advanced cases due to reports of radiation induced anaplastic transformation in literature (Perez *et al.*, 1966).

Basement Membrane Characteristics

Recently a striking histopathological characteristic has been reported showing that verrucous carcinoma is known to be benign histologically with a locally invasive clinical course. The endophytic growth pattern that is a hall mark of this tumour is due to its resilient basement membrane that probably acts as an effective barrier to prevent the carcinomatous growth. Jiang *et al* (2001) detected that oral verrucous carcinoma cases showed a thicker basement membrane with reduplication at abundant places and a noticeably greater inflammatory cell infiltration equated to the oral SCC and dysplasia cases (Prioleau *et al.*, 1980). HVC is a non-verrucous SCC that arises synchronously with the verrucous carcinoma from the same maternal field. HVC has a strong male predilection, male to female ratio 3.6: 1 and a mean age at presentation is fifth decade of life.).

Apart from oral cavity it is also seen in oesophagus, laryngeal, vulvovaginal, penile, anorectal, Sino nasal as well as the skin of the breast, axilla, ear canal and soles of the feet. Incidentally prevalence of this hybrid variety is very high in oral cavity in comparison to other body parts. Tobacco chewing is considered the most aetiological factor. This foci of less differentiated carcinoma were attributed to so called anaplastic transformation of VC treated by radiotherapy. Perez *et al* discussed the anaplastic transformation of VC after radiation therapy and speculated that ionizing radiation may have been the aetiology of this transformation. Currently there is no sufficient evidence to attribute anaplastic transformation of hybrid VC to radiotherapy. Though we are considering HVC as a non- verrucous one but still the pathogenesis of this disease is under review whether it is a true collision tumour or a tumour with multi-phenotypic differentiation it cannot be unequivocally proved. So clonal selection and monoclonality of the tumour must be proved to establish it as a tumour with multi-phenotypic differentiation.

It should be clinically and histopathologically differentiated from verrucous hyperplasia and papillary squamous cell carcinoma which exhibit overlapping features. - Oral Verrucous Hyperplasia is a pre malignant lesion which usually occurs in the fourth decade of life with male predominance 2:1 and the most common site of occurrence is buccal mucosa. Clinically it presents as verrucous, exophytic with sharp or blunt projections on surface. Tobacco lime quid placement in placement in buccal vestibule is considered to be the key aetiological factor. Verrucous Hyperplasia is a histopathological entity which shows considerable clinical and histopathological resemblance to verrucous carcinoma. This was first described by Shear and Pindborg (1980) and differentiated from Verrucous Carcinoma (Shear, 1980). They separated the entity based on lack of invasive growth in the Verrucous Hyperplasia that is entirely superficial to adjacent normal epithelium.

These surface projections were classified based on morphology into sharp and blunt types, while Verrucous Carcinoma on contrary exhibited a downward growth pattern of otherwise similar rete ridges. For this distinction it is very necessary that biopsy should include adjacent normal epithelium. In Verrucous Hyperplasia the proliferation of upper and lower extent appears fixed. A line drawn across the lowest or deepest extent of the epithelial proliferation is relatively straight and parallel to a line drawn across the base of normal adjacent epithelium. PSCC is a variant of SCC which occurs predominantly in males in the sixth and seventh decade of life and the most common site is larynx followed by the oropharynx and nasopharynx. PSCC presents as a soft, friable, polypoid exophytic tumour with papillary projections. Microscopically the tumour is characterized by showing papillary growth with thin fibrovascular cores covered by immature basaloid cells or dysplastic squamous cells with minimal or no keratinisation (Cardesa *et al.*, 2005). IHC-Immunohistochemically assessment of cellular proliferation showed a significantly high mean percentage of Ki-67 expression in comparison to VC.

Prognostic significance of hybrid verrucous carcinoma

The SCC component of hybrid VC has the ability to metastasize and is expected to behave as conventional SCC. Initial reports of neck metastasis in the literature of VC were later attributed to presence of hybrid VC because classic VC did not metastasize (Oliveira, 2006) in a study it was seen that chances of occult metastasis was 13.5% in contrast to conventional SCC which shows a minimum of 30% occult metastasis even in early cases (Byers *et al.*, 1998). Since occult metastasis is often associated with decreased survival, prognosis of hybrid carcinoma appears to be better than conventional SCC. Patients with the development of another oral cancer 20mm farther from the primary cancer were considered as second primary. In a study conducted by Jones *et al* the rate of second primary was 9.1% at 372 months in their study of 104 cases. Development of second primary was associated with poorer outcome in oral hybrid VC as revealed in current series, this finding was parallel to the study by Schwartz *et al* and hordyk *et al.*, who reported poor prognosis in head and neck carcinoma associated with second primary cancer. Hybrid verrucous carcinomas are associated with increased second primary as compared to conventional SCC and even early than the later. The patients with second primary oral cancer had 19.5 fold increased risk of death when compared to patients without second primary oral cancer in oral hybrid VC. Whether second primaries in their study were radiation induced or due to wide areas of carcinogen sensitization resulting in field changes as explained by Slaughter *et al.* (1953) or extensions of a primary tumour clone, cannot be interpreted without further analysis.

Conclusion

Further studies on a large number of patients diagnosed with VC from multiple biopsy sites should be carried out to find out the prevalence rate of HVC. Further specific markers should be identified which can prospectively determine the VC cases having the propensity to undergo malignant transformation.

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