Varied Presentation of Oral Verrucous Carcinoma in a Tertiary Hospital of Dhaka City

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Abstract

Introduction: Ackerman's tumor or Verrucous carcinoma is a distinguished clinic-pathological variant of squamous cell carcinoma, presenting with multiple clinical presentations. This study provides a contemporary survey of morphological presentation of oral verrucous carcinoma (OVC) in the oral cavity with site of predilection and possible etiological factors.

Method: An observational studywas conducted from January 2014 to June 2016.A suspected patient diagnosed clinically and histologically as OVC at the Dhaka Dental College Hospital (DDCH) was enrolled in this study.

Results: In this study total 15 number of patients male were 53.3% and female were 47%.

The morphological presentation of the study was proliferative and verrucous, each of which comprises 40.0% of cases. The tumor's primary site was the buccal mucosa 46.67% and history ofbetel quid chewing was 46.9%.

Conclusion: The study concluded that it is very difficult to distinguishing clinically between verrucous carcinoma and other exophytic lesions of the oral cavity. OVC presents with different morphological presentation such as proliferative and verrucous types. Buccal mucosa is the site of predilection.

Keywords: Oral verrucous hyperplasia, Proliferative verrucous leukoplakia,Verrucous carcinoma.

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Introduction:

Head and neck malignant carcinoma is the world's fifth most common cancer with incidence exceeding half a million annually.[1,2] Oral squamous cell carcinoma (OSCC) represents 95% of head and neck malignant carcinoma.[3]Oral verrucous carcinoma (OVC) accounts for 2-12% of all oral carcinomas.[4]Verrucous carcinoma is a distinct clinico-pathological entity of oral squamous cell carcinoma.

In 1948 Lauren V Ackerman was first described, which is also known as Ackerman's tumor.[5]

Various synonyms used to describe this tumor, such as Loewenstein tumor, florid oral papillomatosis, epitheliomacuniculatum and carcinoma cuniculatum.[6] The mucous membrane of the head and neck are sites of predilection, with the oral cavity and larynx is the most common site of presentation. It also occurs in esophagus, para nasal sinus, nasal cavity, genitalia, skin & sole of foot. This lesion appears as pain less, white warty, ulcerated or proliferative, soft fungating with mamillated surface and attached by a broad base resembling a cauliflower.

The tumor is predominantly common in male over the fifth to sixth decade. The clinical behavior of lesion is very destructive; it may grow very large in size and can also extensively infiltrate to destroy the adjacent tissues, including bones and cartilage. The etiopathology of the OVC is unknown, but strongly related with betel quid, tobacco use, also associated

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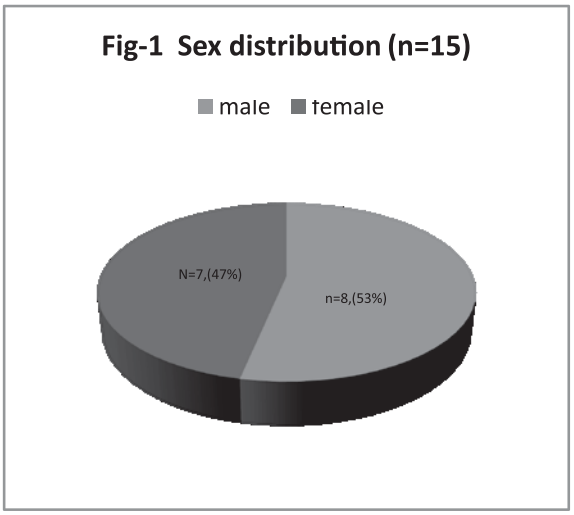
with oral precancerous lesion, alcohol & human papilloma virus. The histological appearance of OVC is a well differentiated hyperplastic epithelial lesion. With heaving a densely keratinized surface and sharply defined deep margin.Aim of the study was to identify the OVC present with different morphological presentation and also different from other similar warty and exophytic oral lesion.

Methods:

Anobservational study was conducted atthe tertiary label oral and maxillofacial surgery departmentof Dhaka Dental College and Hospital (DDCH) between Jan 2014 to Jun 2016. It waspurposive sampling method study. Total fifteen patients enrolled who were clinically and pathologically proven OVC and fulfilled inclusion criteria. All patients was treated primarily by surgery and followed-up to two years. Ethical clearance was taken from the ethical committee DDCH prior to the study. Written consent was taken from all participating patients and kept their name and other information confidential throughout the study.

Results:

This study was carried out among 15 patients who are clinically and histopathologically diagnosed oral verrucous carcinoma in different sites of oral cavity. There were male8 (53%) and 7 (47%) were female patient (ratio of M: F, 1.2:1). (Figure-1)



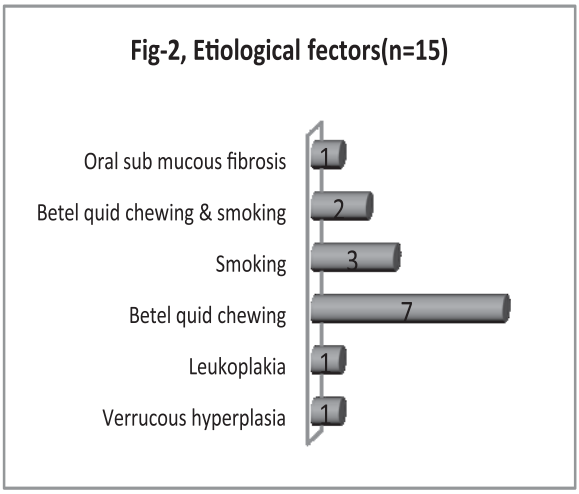
The age group (60-69) years was mostly affected (46.7%) followed by age group (50-59) years was at (40.0%) in the study population. (Table-I)

Table-I Age distribution (n-15)

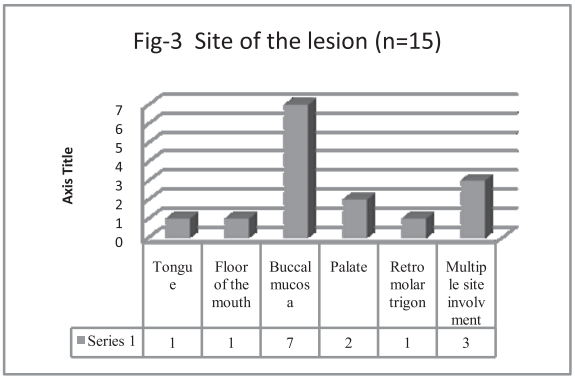
Age range	Frequency	Percent (%)	Mean	±SD
<50	2	13.3		
50-59	6	40.0	2.333	.72375
60-69	7	46.7		
Total	15	100		

SD- Std Deviation

The incidence of betel quid chewing, smoking, and both intake was 7 (46.9%), 3 (20.0%), and 2 (13.3%), respectively. Leukoplakia, Sub Mucous Fibrosis and Verrucous hyperplasia each is also represent 1 (6.7%) respectively. (Figure-2)



In study population most of the lesion involved in buccal mucosa 7 (46.67%), multiple site (lower alveolus, floor of the mouth, buccal sulcus &buccal mucosa) involved in 3 (20%) cases and palatal mucosa involved in 2 (13.30%) cases..(Figure-3)



The most common morphological presentation of lesion was both 'proliferative' and 'verrucous' each of which comprising 6 (40.0%) of the sample. followed by an ulcerative 2 (13.3%) and ulcer proliferative growth 6.7%. .(Table-II)

Table-II: Morphological presentation (n=15)

Type of presentation	Frequency	Percent (%)	±SD
Proliferative	6	40.0	
Verrucous	6	40.0	
Ulcerative	2	13.3	
			.91548
Ulcer proliferative	1	06.7	
Total=	15	100	

SD- Std Deviation

Discussion:

Verrucous carcinoma is a variant of oral squamous cell carcinoma characterized by a predominantly exophytic overgrowth of well-differentiated keratinizing epithelium having minimal atypia and with locally destructive pushing margins at its interface with underlying connective tissue. OVC present with a specific clinical and histological presentation, this distinguishable feature from squamous cell carcinoma (SSC) makes OVC pathology of interest in the field of research. As far known there are no relevant studies in our country (Bangladesh), which have evaluate the clinical presentation of OVC. An observational study was done with 15 patients, where male patients were 8 (53%) & female patient was 7 (47%). The male female ratio was 1.2:1 mean age was 58.3 years. The common affected group was 60-69(46.7%) years. The second most affected group 50-59 years was 40.0% and lowest group was below 50 years.Ray *et al.*seen most common in over sixth decade males.[7]OVC traditionally occurs more commonly in older males, above the sixth decade.[8] In Brenton et al. review sixty percent of the patients were male and the median age was 67 years at diagnosis.[9] Fonts et al. showed as equal sex distribution in their studies.[10] Tadashi found female predominance (F-6 & M-4) in his histological study of OVC in 10 Japanese patients.[11] Hansenshows in his long term study over the thirty patients of OVC found (M: F is 1: 4).[12] This dissimilarity may be due to their different habit, culture & exposure of carcinogen.

The aetiology of OVC is not well known[7] and the incidence of betel quid chewer was 46.9%, smoker 20.0% and both user were 13.3% in our observation. Chung *et al* reported that 55.6% (five out of 9 patients) of the patients with verrucous lesions were areca quid chewers, and they suggested that areca quid chewing could be a major causative factor for these lesions in Taiwan.[13] 50% of the patients smoked tobacco (six out of 12 patients), and they also suggested that cigarette smoking is the major risk factor for their OVC patients.[14,15,16]Brenton et al. described the sources of the carcinogens include tobacco, alcohol, marijuana or cigarette smoking, and betel nut act as a predisposing factors.[9]Spiro proposed tobacco & betel quid chewing is a significant etiologic factor for the development of OVC.[17]Jacobson and Shear surveyed 198 cases of OVC and described 15 personally-observed cases, where incidence of smoking was found to be 77% (7 out of 9 patients).[18]

Sundstrom et al & Oliveira et al., also found the strong association of OVC with smoking, alcohol, and HPV infections.[19,8]Verrucous carcinoma is suggestive association between HPV.[20] HPV subtypes 6 and 11 were the most predominant identified HPV infections.[21]

Coexisting lesion leukoplakia was 6.7%, oral SMF 6.7% and verrucous hyperplasia was 6.7% present in ourstudy population. Rajendran et al., recorded leukoplakia in association with OVC in 48% cases of their 426 patient observations.[22]Brenton et al., suggested VC exists within the histological continuum ranging from benign squamous hyper plastic lesions to invasive squamous cell carcinoma.[9]OVC develop from premalignant lesion.[23,24]

Figure 1: Proliferative type

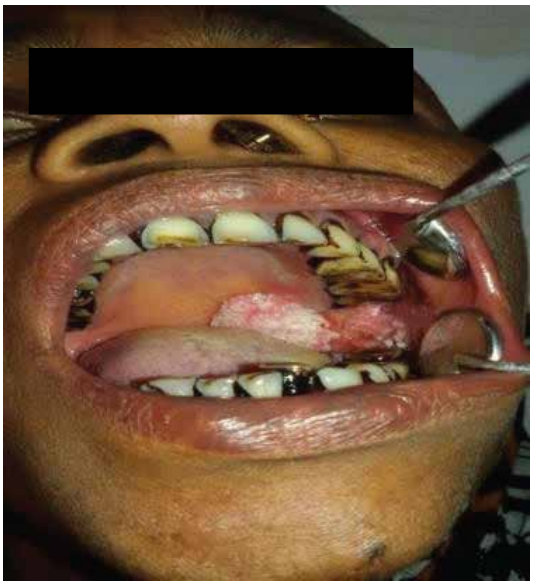


Figure 2: Verrucous type

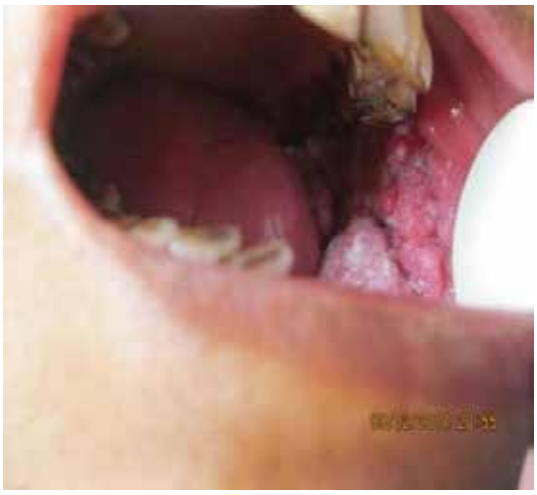


Figure 3: Ulcerative type

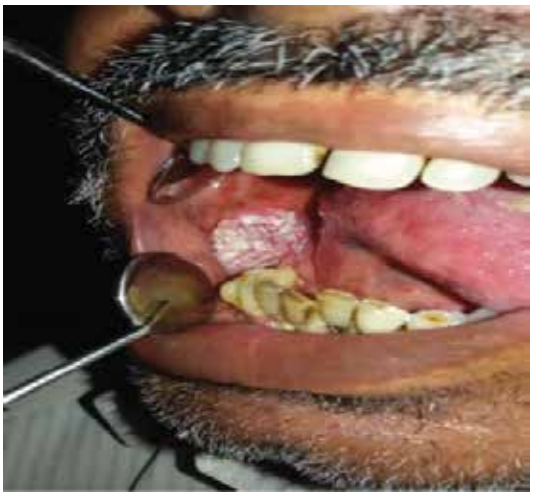


Figure 4: Ulcero-proliferative type

The presence of leukoplakic lesions and poor oral hygiene may also act as predisposing factors.[14]Rohan et al., recorded in their 101 cases, 33.7% present leukoplakiaact as a predisposing factor.[25]Demian et al., also recorded the clinical association with leukoplakia and OVC is significant since untreated

longstanding leukoplakia could progress to a verrucous cancer in time.[26] 56.2% of PVL lesions can transform to squamous cell carcinoma orverrucouscarcinoma.[27] Oral verrucous hyperplasia (OVH) is a histological entity and precursor of oral verrucous carcinoma (OVC)that was first described by Shear and Pindborg.[23]

Verrucous' terminology is applied for lesions that show exophytic, keratotic surfaces, made of blunt or sharp epithelial projections, filled with keratin invaginations, but without clear fibro vascular cores.[7]The verrucous surface is the most characteristic feature of verrucous lesions (OVH and OVC lesions). Clinically, distinguishing OVH from OVC lesions is often difficult.[28]There have been few clinicopathological studies in the literature on OVH and OVC, Wang *et al.*, Rohan*et al.*, RekhaAngadi and Zhu *et al*.[25,28,29,30] In generally, OVH is superficial

lesion, adjacent to normal epithelium and does not extend into deeper tissues, whereas OVC spreads more deeply .[31]

PVL presentation as cauliflower like and most common in buccal mucosa, palate, gingiva andtongue.[32] Histologically, in early lesions of PVL present only hyperkeratosis, then over time they may progress to become verrucous and commonly show variable degrees of epithelial dysplasia and a sudden change from hyperparakeratosis to hyperorthokeratosis, associated withverruciform or ridged surfaces.[33] But overall OVC has a better prognosis compared to other carcinomas.[7]

In this study the most common site of lesion wasbuccal mucosa 46.7%, followed by multiple site (lower alveolus, buccal sulcus, and floor of the mouth) of oral cavity which is 20.0%, palate 13.3%, tongue 6.7%, floor of the mouth 6.7% and retro molar trigon was 6.7%. The most common site for OVC is the buccal mucosa. Yeh et al., Rohan*et al.*, and Rekha and Angadi, also show similar presentation of their study.

However, the most affected areas in Alkan*et al's*study were the mandibular area followed by buccalmucosa,[14] and the predominant site of OVC lesions in Zhu *etal's*study was lower lip.[28]Jacobson et al., Regezi., Yoshimura., and Hashibe et al., suggest that verrucous carcinoma had predilection for the oral cavity; in particular the buccal mucosa and the lower alveolus.[23,28,36,37] Shear &Pindborg., suggested OVC develop at the site where the betel quid & tobacco was placed habitually.[23]Fonts et al., Yeh C J. andAlperAlkan., found in their study that 41.6% cases OVC present in retro molar & mandibular posterior alveolar crest area.[10,14,34]

In this study the most common morphological presentation of OVC was both proliferative and verrucous each of which comprising 6 (40.0 %) of the sample. Followed by ulcerative type which is 13.3% and ulcer proliferative type is 6.7%. QianPeng et al., present his review article as the OVC are exophytc, cystoid and infiltrative types.[38] Tang et al also divided OVC into three types: exogenic type, cystoid type, and infiltrative type. The exogenic type of OVC is characterized by exophytic growth, cauliflower-like warty lesion and slow tumor growth. However, the other two types of OVC grow rapidly, forming bean dreg-like white dry keratosis, accompanying poor prognosis compared to the exogenic type of OVC.[39]Rohan et al., also recorded proliferative, verrucous, ulcerative, ulceroproiferrative & infiltrative/sub mucous type of OVC in there study of 101 patient.[25] Yoshimura &Vivekanando et al., also recorded the similar presentation of OVC in their study.[36,40] OVC present both benign and malignant processes, malignant ovc contain small foci of squamous cell carcinoma, which are known as a "hybrid" forms of verrucouscarcinoma.[9]

Generally speaking, the accurate histological classification of squamous mucosal lesions with an exophytic growth pattern is often difficult and requires experience.[41] Hence, OVC clinico-histopathological diagnosis is usually exclusionary and extremely problematic.[30]

Conclusion:

Verrucous carcinoma present with different special morphological presentation with local invasiveness and non-metastasizing behavior. Most commonly seen with in buccal mucosa of oral cavity, and distinguishing of OVC from other exophytic lesions such as OVH, PVL is often difficult to clinicians, and also furthermore, distinguishing of different morphological presentation of OVC from classical (grade-I) OSCC is a common problem for pathologists due to poorly-defined diagnostic criteria. Thus both clinicians and pathologists must be careful about warty and exophytic lesions of oral cavity, and communicate with each other for better diagnosis.

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