

ORAL VERRUCOUS CARCINOMA IN PENINSULAR MALAYSIA

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SUMMARY

Verrucous carcinoma is a form of squamous cell carcinoma which was first described as a distinct clinical and pathological entity by Ackerman in 1948. This study is the first report of 44 cases in Malaysians. Verrucous Carcinoma (VC) formed 1.8 percent of all oral squamous cell carcinoma cases. There was a predominance of males (M:F = 1.4:1). The peak age incidence was between 51 - 70 years (66 percent). The buccal mucosa (43 percent), gingivae (20 percent) and commissures of lips (17 percent) were the commonest sites of involvement. The Chinese who do not chew the betel quid had the least frequency of VC. No case was reported in the Chinese female. The highest frequency of VC was in the Indians who often added tobacco to their betel quids. Although thirty three years have passed since Ackerman's first description of VC it still remains a mystery. Clinicians, pathologists and immunologists in Southeast Asia have the opportunity to study and contribute to a better

understanding of VC which of all variants of oral carcinoma seems to have the best prognosis if diagnosed and surgically excised promptly.

INTRODUCTION

Verrucous carcinoma is a form of squamous cell carcinoma which was first described as a distinct clinical and pathological entity by Ackerman in 1948. Although it has been most commonly reported in the oral cavity, cases involving the larynx, nasal fossa, glans penis, vulva, vagina and scrotum have also been recorded (Kraus and Perez-Mesa, 1966). Verrucous carcinoma differs from the usual oral squamous cell carcinoma in that it is a slow-growing, pearly-white "cauliflower-like" papillary growth (Figs. 1, 2 & 3) which is superficially invasive at least in the course of the disease. Verrucous carcinoma of the buccal mucosa

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Fig. 1 A verrucous carcinoma of the lower lip with a pearly-white "cauliflower-like" papillary growth. The dark brown stain of the surface was caused by the betel quid.

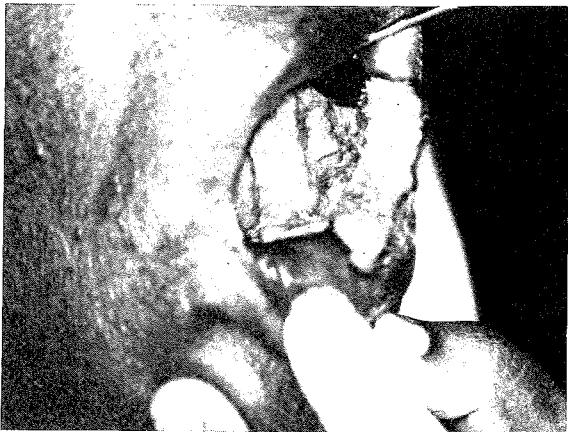


Fig. 2 An extensive verrucous carcinoma involving the left buccal mucosa, commissure of lips and the left mandibular alveolar ridge.



Fig. 5

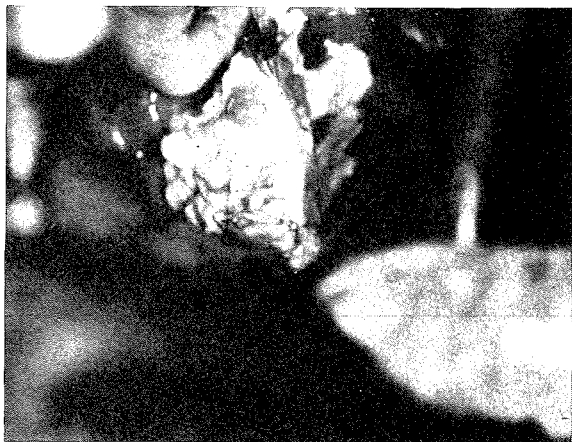


Fig. 3 A verrucous carcinoma of the left buccal mucosa. Adjacent to it is a homogeneous leukoplakia.

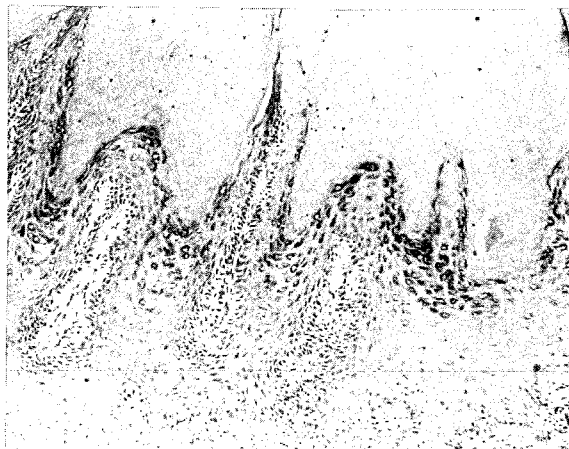


Fig. 6

Figs. 4, 5 and 6 Photomicrographs showing verrucous carcinoma. The surface epithelium is thrown into papillary folds with abundant keratin or parakeratin cells in the folds. The bulbous rete ridges reach to about the same depth. Unlike other carcinomas in the case of verrucous carcinoma the basement membrane is intact. H & E. Fig. 4 (orig. mag. x 10). Figs. 5 & 6 (orig. mag. x 25).

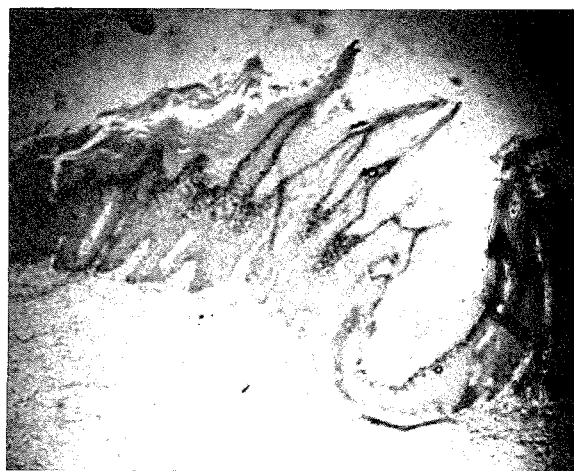


Fig. 4

may grow through the cheek to appear on the skin surface or grow out to form a mass underneath the mandible. Verrucous carcinoma when confronted with bony structures such as the mandible tends to destroy the bony tissue on a broad front, eroding with a sharp margin rather than infiltrating into the marrow spaces. Metastases is indeed rare. Verrucous carcinoma is often amenable to simple local excision because of its relative non-aggressive and protracted course.

Verrucous carcinoma has a predilection for occurrence in elderly males, the majority of whom

TABLE I
ORAL VERRUCOUS CARCINOMA —
DISTRIBUTION BY RACE, SEX AND AGE GROUPS OF 44 PATIENTS

AGE	MALAYS		CHINESE		INDIANS		OTHERS		TOTAL	PERCENTAGE
	M	F	M	F	M	F	M	F		
31 - 40	-	1	-	-	1	-	-	-	2	4.6
41 - 50	-	-	-	-	2	3	1	-	6	13.6
51 - 60	3	4	1	-	4	5	-	-	17	38.6
61 - 70	4	2	-	-	5	1	-	-	12	27.3
71 - 80	1	-	2	-	1	2	-	-	6	13.6
81 - 90	1	-	-	-	-	-	-	-	1	2.3
TOTAL	9	7	3	-	13	11	1	-	44	100%
PERCENTAGE	20.5%	15.9%	6.8%	-	29.5%	25%	2.3%	-	-	100%

M : F = 1.4:1

are tobacco chewers although some are smokers or snuff dippers, and it develops most frequently on the buccal mucosa and gingiva. Microscopically, the lesion appears deceptively benign and is frequently misdiagnosed as pseudoepitheliomatous hyperplasia, leukoplakia, a well differentiated squamous cell carcinoma, some benign papillary process or a viral growth, unless the pathologist is totally familiar with the entity. (Figs. 4, 5, & 6).

MATERIAL AND METHODS

This study was based on the records of the Department of Stomatology, Institute for Medical Research, Kuala Lumpur and for the years 1967 - 80. Only histologically confirmed verrucous carcinoma cases and patients reported for the first time were included in this study. In all 44 patients were reported. The total number of squamous cell carcinoma cases reported during this period was 2491. Thus verrucous carcinoma formed 1.8 percent, of all oral squamous cell carcinoma cases. For the anatomical charting of verrucous carcinoma the topographical classification of Roed-Petersen and Renstrup (1969) dividing the oral mucosa into 43 well-defined regions was used. For purposes of histological diagnosis the criteria spelt-out in the WHO Histological Typing of Oral And Oropharyngeal Tumours (Wahi, *et al*, 1971) was used.

RESULTS AND DISCUSSION

Although oral squamous cell carcinoma has the highest frequency in Southeast Asia there is indeed a lacuna with regard to the distribution of

verrucous carcinoma in Asians. Cooke (1969) reported 29 cases of verrucous carcinoma in Papua-New Guineans. Except for Landy and Whites (1961) report of 25 cases of verrucous carcinoma in females almost all the other reports in Caucasians have shown a predominance of males (Shafer, 1972). In our series too there was a predominance of males (M:F = 1.4:1). (Table I).

In Caucasians the peak age incidence has generally been over 60 years. The peak age incidence among the Papua-New Guineans was between 40 - 50 years. In our series the peak age incidence was between 51 - 70 years (66 percent).

As reported in the earlier studies the buccal mucosa (43 percent), gingivae (20 percent) and commissures of lips were also (17 percent) the commonest sites for verrucous carcinoma even in Malaysians. (Table II). Just as in oral squamous cell carcinoma the high frequency of involvement of these anatomical sites would strongly suggest a site correlation between the habit of keeping the betel-quid at a specific site and the development of carcinoma. What factors determine whether a person who is a betel quid chewer develops an ordinary squamous cell carcinoma or a verrucous carcinoma are totally unknown.

The Chinese who do not chew the betel quid had the least frequency of verrucous carcinoma. No case was reported in the Chinese female. In the Chinese male there were only three cases (7 percent). The betel quid consists of a young leaf of the betel vine (*Piper betel*), sliced betel nut (the fruit of the betel palm, *Areca catechu*) and slaked stone lime. The Malays, in addition, add "Getah

TABLE II
ORAL VERRUCCOUS CARCINOMA —
DISTRIBUTION BY RACE, SEX AND ANATOMICAL SITES

SITE	MALAYS		CHINESE		INDIANS		OTHERS		TOTAL	PERCENTAGE
	M	F	M	F	M	F	M	F		
Buccal Mucosa	6	6	1	-	5	7	1	-	26	43.3
Gingivae	4	1	1	-	3	3	-	-	12	20.0
Commissures (lips)	2	3	-	-	-	4	1	-	10	16.7
Palate	1	-	-	-	2	1	-	-	4	6.7
Lips	1	-	-	-	-	2	-	-	3	5.0
Tongue	-	1	1	-	-	-	-	-	2	3.3
Pterygo-Mandibular plicar region	1	1	-	-	-	-	-	-	2	3.3
Floor of Mouth	1	-	-	-	-	-	-	-	1	1.7
TOTAL	16	12	3	-	10	17	2	-	60*	100%

* The total number of anatomical sites exceeded the total number of patients for the carcinoma extended to involve more than one anatomical site in some patients.

Gambir" which is extracted from the shrub *Uncaria gambir*. The delicacy of flavour of this product depends upon its catechin content. The leaves are bound, steamed, and then small amounts of boiling water are allowed to trickle through. On cooling, catechin crystallizes out, leaving the more soluble and bitter catechin tannic acid in solution. Usually a little bran is added and the bran-catechin mixture made into cakes. The higher frequency of verrucous carcinoma in the Malays is due to the betel quid chewing habit. The frequency of verrucous carcinoma in the Malay male was 21 percent and in the Malay female it was 16 percent. Unlike the Indians, the Malays do not add tobacco to their betel-quids.

The highest frequency of verrucous carcinoma was reported in the Indian male (13 patients/30 percent) and in the Indian female (11 patients/25 percent). This racial predominance is approximately similar to the frequency of oral squamous cell carcinoma in Malaysians. Oral squamous cell carcinoma formed 31 percent in the Indian female and 29 percent in the Indian male (Ramanathan and Lakshimi, 1976). This would therefore indicate that the addition of tobacco to the betel-quid increased the risk of developing

verrucous carcinoma in much the same manner as in oral squamous cell carcinoma. Our observations would corroborate the earlier studies in Caucasians correlating verrucous carcinoma with tobacco-chewers. Moreover it would also imply, just like oral squamous cell carcinoma, verrucous carcinoma must be most frequent in Southeast Asia where the habit of chewing betel quid is very popular. There is therefore a real need for both pathologists and clinicians in Southeast Asia to be aware of the presence of verrucous carcinoma.

In 32 (72 percent) of our patients the verrucous carcinoma involved one anatomical site at the time of diagnosis. In 6 (14 percent) of our patients the verrucous carcinoma extended to involve one more adjacent anatomical site and in another 6 (14 percent) of our patients it extended to involve two or more adjacent anatomical sites. This would emphasize not only the slow indolent nature of spread of verrucous carcinoma but also the excellent prognosis with surgery for growths diagnosed early and treated promptly.

Shafer (1972) has recently made a crystal-clear appraisal of two cloudy and controversial aspects of verrucous carcinoma viz, (1) treatment with radiotherapy and (2) its relationship to the so-called

oral florid papillomatosis. The treatment of verrucous carcinoma has been by surgery, radiotherapy or a combination of the two. In recent years there have been several reports of patients with oral verrucous carcinoma treated with radiotherapy in which the tumour has subsequently, usually quite promptly, undergone anaplastic transformation, invaded and metastasized, killing the patients rather rapidly. Shafer (1972) after reviewing the literature on this modality of treatment concluded that at least in some cases it appears that the treatment of oral verrucous carcinoma by ionizing radiation is followed by the evolution of a highly anaplastic carcinoma with an extremely different and rather aggressive biologic behaviour. Shafer furthermore added that considering the large number of cases reported in the literature, treated with radiation and without this transformation, it must be concluded that it is a relatively rare phenomenon and the factors that contribute or are related to the transformation are totally unknown.

Rock and Fisher (1960) originally used the term oral florid papillomatosis to describe the occurrence of multiple confluent squamous cell papillomas of the oral cavity and pharynx. These cauliflower-like growths have been considered by some to be wholly benign neoplasms although others consider them premalignant. Considerable confusion has existed in as much as the clinical photographs and photomicrographs of most of the published cases of oral florid papillomatosis appear quite characteristic of oral verrucous carcinoma. Many investigators today who have had experience with both lesions described as oral florid papillomatosis and as oral verrucous carcinoma believe that this represents one and the same tumour. Shafer (1972) has emphasized that there does not appear to be any justification for the continued use of the term oral florid papillomatosis in as much as it does not truly describe the carcinomatous nature of this distinct entity.

Although thirty three years have passed since Ackerman's description of verrucous carcinoma as a distinct clinical and pathological entity, it still remains a mystery. As to why betel-quid chewing, tobacco-chewing, snuff-dipping and heavy tobacco smoking in a majority of cases causes squamous cell carcinoma, and in a small number of cases verrucous carcinoma, is unknown. As to why the treatment of verrucous carcinoma with radiotherapy in some instances leads to the evolution of a highly anaplastic carcinoma with an

extremely different and rather aggressive biologic behaviour is totally unknown. The constant frequency of involvement of the buccal mucosa, gingivae and commissures of lips by verrucous carcinoma in patients through out the world with different oral habits is indeed intriguing. Although the ordinary squamous cell carcinoma and the verrucous carcinoma arise from one and the same oral squamous epithelium the clinical behaviour and prognosis of the two are so contrasting like night and day that the explanation remains a mystery. Clinicians, pathologists and immunologists in Southeast Asia have the opportunity to study and contribute to a better understanding of verrucous carcinoma which of all variants of oral carcinoma seems to have the best prognosis if diagnosed and treated promptly.

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