

Surgical Treatment of Oral Verrucous Carcinoma

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Background: The aim of this study was to evaluate the outcome of patients with Verrucous carcinoma (VC) of oral cavity treated at the Chung Gung Memory Hospital with respect to the tumor control rates after surgery, the risk of lymph node metastasis and the role of radiation therapy.

Methods: Thirty-eight patients underwent primary treatment for VC of the oral cavity from January 1996 through February 2002. All of the patients had surgery as their primary treatment. In addition, all patients with sufficient details of the therapy and a minimum 1-year follow-up were selected for evaluation of survival and outcomes.

Results: In this study, 94.7% of patients were male and most of them had been exposed to betel nuts, cigarettes, and/or alcohol. The most common site was the buccal mucosa (57.9%), followed by the tongue (13.2%). T3 lesions were the most common type (34.2%). Only two patients had palpable cervical adenopathy during the initial evaluation. Twenty-five patients had free flap for reconstruction. The tumor control rate was 100%. At the time of analysis, no patient had suffered from recurrence in primary site or neck area.

Conclusion: Surgical excision alone was effective for controlling VC, but elective neck dissection was not necessary even in patients in the advanced stages.
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Key words: Verrucous carcinoma, head and neck neoplasms, oral cavity carcinoma.

Verrucous carcinoma (VC) is a variant of squamous cell carcinoma, which is a low-grade malignance that rarely presents with distant metastasis. VC may occur in several locations in the head and neck and in the genitalia. The oral cavity is the most common site of this tumor.⁽¹⁾ The ages range from 50 to 80 years with a male predominance and the median age is 67 years.⁽²⁾ VC may grow very large and can destroy adjacent tissue such as bone and cartilage.⁽³⁾

The diagnosis of VC is established by close communication between surgeons and pathologists.

Surgeons must provide adequate specimens including the full thickness of the tumors and adjacent uninvolved mucosa for correct diagnoses.⁽⁴⁾

Surgery is considered as the treatment of choice.^(1,2) The extent of surgical margin and the adjuvant radiotherapy are still controversial.

Exposure to carcinogens is different between Western countries and Taiwan. The major carcinogens in Western countries come from cigarette smoking and alcohol use, however, in Taiwan, betel nut use is another source in addition to cigarette smoking and alcohol use. The different gene mutations have

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been reported in head and neck cancer comparing with Western countries.⁽⁵⁻⁸⁾ The clinical behavior of VC according to exposure to different carcinogens may be not the same. We present our experience of 38 patients with VC to analysis the patterns of treatment, survival, recurrence, and outcomes.

METHODS

This study consisted of a retrospective review of the medical records and histopathologic material available on all patients who had VCs of the oral cavity treated at the Chung Gung Memory Hospital from 1996 through 2002. We identified 38 patients diagnosed with VC. The patients with hybrid pattern VC (accompanied with SCC) were excluded from this study. All patients were treated with surgery as their initial management. The follow-up time ranged from 13 to 76 months with a median of 37.5 months. The staging work-up and preoperative evaluation included computed tomography of head and neck area, blood chemistry, chest X-ray and complete blood cell count. The clinical stage distributions are shown in Table 1. Among the cases, T3 lesions were the most common (34.2%). Advanced stage (stage III and IV) cases represented 42.1%. Only one patient (6.5%) in this series presented with a T4 lesion and had no cervical metastasis at the time of the initial presentation. The pathologic tumor stages of the specimens were identified according to the American Joint Committee on Cancer staging system, 1997.⁽⁹⁾ The survival rates were calculated using the Kaplan and Meier method.

Table 1. Clinical Stage Distribution

	Stage N		Total
	0	1	
Stage T			
1	14 (36.8%)	0	14 (36.8%)
2	8 (21.1%)	0	8 (21.1%)
3	13 (34.2%)	2 (5.3%)	15 (39.5%)
4	1 (2.6%)	0	1 (2.6%)
Total	36 (94.7%)	2 (5.3%)	38 (100.0%)

RESULTS

Of the 38 patients identified with VCs, 36 (94.7%) were male and only two (5.3%) were female. The age distribution ranged from 27 years to

78 years with a median age of 51.0 years at diagnosis (Fig. 1). The most common site of VC within the oral cavity was the buccal mucosa (57.9%), followed by the tongue (13.2%). The distribution is listed in Table 2.

All of the patients were treated with surgery alone. Selective regional lymph node dissections were performed in 19 patients (50%) as part of their initial surgical treatment due to advanced T-stage or clinically palpable nodes. Only two patients presented with clinically palpable nodes before surgery. In the remaining 17 patients, the elective neck dissections (all of them were supraomohyoid dissections) were performed. All of the neck specimens were negative for metastasis after detail pathology examination. For the repair of surgical defects, 25 patients (65.8%) had free flap reconstructive surgeries which

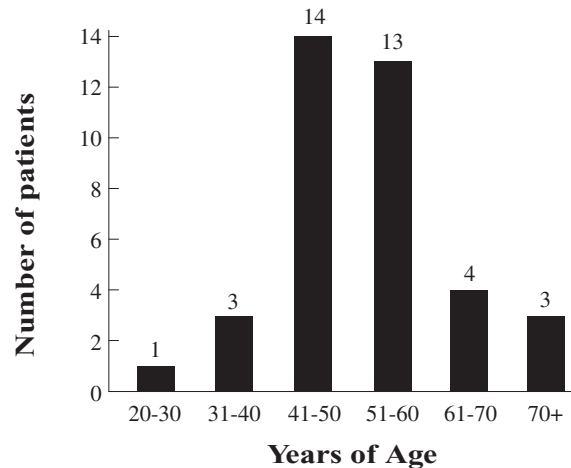


Fig. 1. Histogram showing distribution of patients with verrucous carcinoma by age at time of surgery.

Table 2. Site Distribution

Site	Number	Percentage
Buccal mucosa	22	57.9
Tongue	5	13.2
Lip	4	10.5
Retromolar trigone	3	7.9
Gum	3	7.9
Hard palate	1	2.6
Total	38	100

were performed by a plastic surgeon, one had a split-thickness skin graft, and others had primary closure.

Two patients died during the follow-up period due to secondary lesions. One had tongue based squamous cell carcinoma 6 months after wide excision of the buccal VC and died of sepsis with respiratory failure in chemotherapy. Another one had hard palate cylindrical carcinoma 12 months after excision of the tongue VC, and died of skull based invasion 4 months after diagnosis.

The 3-year overall survival rate was 94.7% and tumor control rate was 100%. The results are shown in Fig. 2. Early stage and advanced stage seem have no impact on occurrence of secondary malignancy in our study. At the time of analysis, no patient had suffered from recurrence in the primary site or neck area.

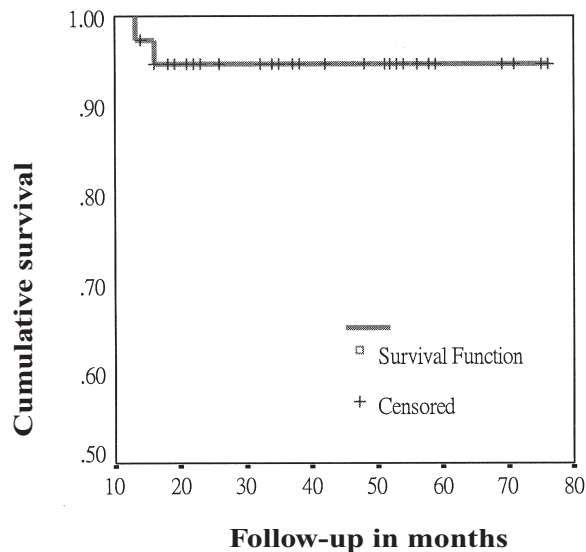


Fig. 2 Kaplan-Meier overall survival for verrucous carcinoma.

DISCUSSION

In our series, VCs of the oral cavity show an overall male predominance (94.7%) and median age of 51 years at diagnosis. The age in this study was younger than that reported in a large study performed in the United States. Koch et al.⁽³⁾ reported the treatment results of a series of 2350 patients with VC in the United States. Sixty percent of the patients were

male and the median age was 67 years at diagnosis. They found that the younger patients had better survival than the older patients.

The association of carcinogen exposure with oral cancer has been reported.⁽⁵⁾ The sources of the carcinogens include tobacco, alcohol, marijuana or cigarette smoking, and betel nuts.^(1,3,6) Due to the differences in carcinogen exposure between Taiwan and Western countries, there are different gene expressions in oral squamous cell carcinoma.⁽⁵⁻⁸⁾ Tobacco exposure had been reported to have a clear association with VC in Western countries.^(3,10,11) In our series, 96% patients had the habit of chewing betel nuts, 92% both chewed betel nuts and smoked cigarettes, and 57.7% consumed alcohol. However, we found no differences in clinical behavior of VC when compared with the data of the Western countries because no neck lymph node metastases or distant metastases were found in this study.^(1,12)

All patients underwent surgery as the primary major treatment in our series. There have been some arguments about the role of radiotherapy in the management of verrucous cancer patients. Some investigators have reported that radiation therapy was not only ineffective in many cases, but also caused anaplastic transformation of the neoplasm,^(3,4,13) leading to rapid metastatic dissemination. However, some recent reports⁽¹⁴⁻¹⁸⁾ have shown different opinions about this issue. They found that patients with VCs had similar responses to radiotherapy as those with well differentiated squamous cell carcinoma. In the report by O'Sullivan and Warde,⁽¹⁴⁾ they proposed that radiotherapy might have a role for organ preservation and reserved surgery as salvage therapy. Only one of our patients with buccal VC and bony invasion pathologically in the ipsilateral mandible received post-operative radiotherapy, but he was diagnosed with secondary SCC of the tongue base at 6 months after radiotherapy.

Koch et al.⁽³⁾ suggested that patients with oral cavity VC treated with surgery first had better survival. In this study, we treated all of the patients with surgery first and two-third patients received free flap reconstruction. The tumor control rate was 100%. Our data support that surgery should be the first choice for treatment of oral cavity VC. Another reason for the good tumor control may have been because we selected "very pure" VC and excluded all patients with hybrid patterns from this study.

Verrucous hyperplasia was the initial pathologic diagnosis in 60% of our cases. The diagnoses of VC in these patients were proved by pathologic report of a further deep incisional biopsy or wide excision. The problems in diagnosing VC are discussed in many reports in the literature.^(1-3,19) VC exists within the histologic continuum ranging from benign squamous hyperplastic lesions to invasive squamous cell carcinoma.⁽³⁾ 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.^(3,20) When VC was highly suggested by clinical appearance, patients should undergo deep incisional biopsies under general anesthesia.

Ferlito and Recher⁽¹³⁾ reported that neck dissection is not indicated in laryngeal VC because laryngeal VC has so far never metastasized to the cervical lymph nodes or to other organs. Neck dissection is also a concern in patients with oral cavity VCs. In this retrospective study, 19 (50%) patients underwent elective neck dissections. Due to the incidence of hybrid patterns of VC was as high as 20%,^(1,3) when the hybrid pattern of VC was suggested, we performed wide excision of the tumor and elective neck dissection as the primary treatment after an explanation and having consensus of the patient. The other reason is that it is difficult to perform a second neck operation for a patient with hybrid pattern of VC after free flap reconstruction. In addition, complete functional neck dissection rarely induces negative functional or cosmetic consequences to patient according to a report by Larson et al.⁽²¹⁾ They determined that functional neck dissection can serve as a biopsy procedure or alternative to elective neck irradiation. All of the pathologic reports of nodal metastasis in this pure VC series were negative, including the two patients initially presented with clinical neck nodes metastases.

The 25 cases with large defects after tumor ablation were reconstructed using microvascular free flap. The benefits of the free flap reconstruction are to preserve the oral cavity and/or oropharynx functions including chewing, swallowing, and articula-

tion and to decrease the limitation of surgical excision.⁽²²⁾

The median follow-up time in this study was 37.5 months. It may have been too short for following patients with head and neck tumors. However, as shown in Figure 2, tumors reached stable tumor control rates within 2 years, and the two cases with secondary lesion occurred within 2 years. However, more time is needed to follow up these patients for secondary and recurrent lesion.

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. The most frequently involved site of the oral cavity in our series was the buccal mucosa, followed by the tongue. Surgical excision alone was effective for treating patients with VC, and elective neck dissection was not necessary to achieve the results. The hybrid patterns of VC in our database need further study to compare the clinical behavior of patients with VC with that reported in Western countries.

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口腔疣狀癌之手術治療結果

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背景：報告口腔疣狀癌患者於林口長庚醫院接受手術治療之結果，藉以評估手術之腫瘤控制率、頸部淋巴廓清術及放射線治療的角色。

方法：於1996年至2002年共收集了38例於林口長庚醫院接受手術切除並追蹤滿一年之口腔疣狀癌患者，用以探討其手術治療結果及存活率。

結果：本篇研究中，94.7%為男性且大部份(95%)曾有嚼食檳榔、抽煙及喝酒之習慣。頰粘膜為口腔中最易發生疣狀癌之地方；腫瘤大小分期以T3者最多，佔34.2%。僅有2例於最初臨床診斷時發現頸部淋巴結腫大，50%之患者接受了頸部淋巴廓清術，但病理報告中並無發現淋巴轉移。25例於術後接受顯微游離皮瓣之整形重建手術。手術之腫瘤控制率為100%，於分析之時並無發生腫瘤復發或頸部淋巴轉移之狀況。

結論：手術切除為治療口腔疣狀癌最有效的方法，但頸部淋巴廓清術則不需要為常規施行即使是晚期之腫瘤，且不建議於術後追加放射線治療。

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關鍵字：疣狀癌，頭頸部腫瘤，口腔癌。

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