Original Article

Oral verrucous carcinoma: a retrospective clinical study of 29 Chinese patients

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Abstract: The purpose of this study is to retrospectively describe the clinical features and prognosis of patients undergoing surgical treatment. Between 2002 and 2006, 29 patients diagnosed with oral verrucous carcinoma at Xiangya Hospital, Central South University were included in this study. Each lesion was examined by a single oral pathologist. The patients ranged in age from 29 to 77 years (mean, 51.6 years; SD, 11.8 years), and 24 of the patients are men, giving a 4.8:1 male-female ratio. The frequently sites of oral verrucous carcinoma (OVC) were the lower lip (20.7%), the buccal mucosa (20.7%), the upper and lower jawbones (20.7%), and the gingiva (17.2%). The clinical phenotypes in this group can be classified into three types: exogenic (55.2%), cystoid (20.7%), and infiltrative (24.1%). The survival rate of patients who underwent surgery was 93.1% in 5 years. Recurrence (13.8%) appeared to be related to subtypes of infiltrative and cystoid OVC. Two cases showed risk of cervical lymph node metastasis. Our findings suggest that OVC showed good prognosis in patients who underwent surgical treatment. Infiltrative and cystoid OVC showed aggressive behavior and a high risk of recurrence. Neck dissection, if necessary, may be used with a supra-omohyoid neck dissection (SOHND).

Keywords: Oral verrucous carcinoma, clinical phenotype, prognosis, recurrence

Introduction

Verrucous carcinoma (VC) was first defined by Ackerman in 1948 as an independent solid tumor distinguished from the squamous cell carcinoma (SCC) and hence it known as Ackerman’s tumor [1]. It is an uncommon variant of well-differentiated SCC with the feature of rarity, specific morphology and cyto-dynamics [2]. VC is reported to occur in the larynx, esophagus, skin, scrotum, perineum and so on, while the most frequent occurrence site is oral cavity [3]. The etiology and pathogenesis of oral verrucous carcinoma (OVC) are still uncertain by far. However, literatures showed that the OVC is believed to be markedly correlated with the long-term smoking, chewing tobacco, poor oral hygiene, the human papilloma virus (HPV) and other inducements while the areca-nut has higher potential risk than tobacco [4-9]. The OVC develops slowly and locally with low-grade malignance and high-degree differentiation. It rarely metastasizes but its invasive and proliferative outgrowing clinical nature may induce destroying adjacent tissue like cartilage and bone [2]. Early in 1980, Shear and Pindborg had pointed out that OVC lesions are difficult to be differentiated from verrucous hyperplasia on clinical examination [10]. The OVC is divided into three subtypes: exogenic, cystoid, infiltrative. The cystoid and infiltrative types are often to be confused with cyst of jaw and late periodontitis respectively which may cause serious consequence even death. Several clinical studies of OVC have been reported in other countries while there are few researches performed in China [11, 12]. The primary purpose of this study is to investigate the recurrence rates of the three subtypes of OVC in China and propose reasonable clinical suggestion about the prevention and more suitable treatment of OVC.

Materials and methods

This research got the approval of all subjects and obtained the ethics committee approval in advance. This study consisted of a retrospective review of 29 patients diagnosed with OVC
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retrieved in Xiangya Hospital, Central South University from 2002 through 2006. Each lesion was examined by a single oral pathologist. Every patient conducted the biopsy before operation and it can be observed the typical pathological feature of promoting edge under the light microscopic. Moreover, all patients with verrucous carcinoma were confirmed by the pathological diagnosis after the surgery. In this study, the final diagnosis of oral verrucous carcinoma rests on the histopathological characteristics of these lesions. Biopsy specimen comprising of adjacent normal epithelium is key in distinguishing verrucous hyperplasia from verrucous carcinoma and verrucous keratosis. In verrucous hyperplasia, most of the hyperplastic broadened rete ridges lay above the adjacent normal epithelium. On contrary, verrucous carcinoma exhibits a downward growth pattern of otherwise similar rete ridges. Where-
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**Results**

The detailed multi-aspect statistical information of each subject with OVC is showed in Table 1. Observation from this series showed that OVC occurred more often in male patients (n=24, 82.8%) than in female patients (n=5, 17.2%) which is corresponding to previous researches [15]. The mean age of the women is 48.5±5.76 (range 38 to 52 years) and that of men is 52.25±12.66 (range 29 to 77 years) during this oral diagnosis. The data analysis of gender combined with age is performed in Figure 1. Approximately 70% OVC patients are located in the group rang between fifth and sixth decades years. The common sites of the OVC development were the lower lip (20.7%), the buccal mucosa (20.7%), the jawbone (20.7%) and the gingiva (17.2%) which totally account for 79.3%. There also exist six jawbone lesions, including 4 (66.7%) involved maxillary bone and 2 (33.3%) involved the mandible. In addition, one case of ameloblastoma was observed in verruous carcinoma. All the OVC patients can be classified into three types: exogenic (n=16, 55.2%), cystoid (n=6, 20.7%), and infiltrative (n=7, 24.1%) which were showed in Figure 2. The rate of recurrence (n=4, 13.8%) appeared to be related to OCV subtype: The rates of recurrence of infiltrative and cystoid OVC were 28.6% and 33.3%, respectively (Table 2). The rare of survival differed significantly between the infiltrative and exogenic groups (P<0.05) and between the cystoid and exogenic groups (P<0.05). No significant differences in rates of recurrence were observed between the cystoid and infiltrative groups (P=0.157). All patients were subject to surgical resection. The survival rate was 93.1% (n=27) during 5 years. Six patients showed submaxillary regional lymph node involvement upon palpation. These patients underwent supra-omohyoid neck dissection. One of these patients was dead after 1 year and the other patient was dead after 3 years. Both showed considerable risk of cervical lymph node metastasis.

**Discussion**

VC is classified as a verrucous variant of squamous cell carcinoma because of its microscopic and clinical features, which include the ability to invade and compress the underlying stroma with pushing margins [16]. Since 1981, several studies of OVC have been performed in many different countries, and most of them have taken age and gender into account [4, 11, 17]. These tumors occur more often in male patients than in female patients. The data collected in the present study showed that OVC tended to occur at a slightly earlier age (mean, 51.6 years), and the prevalence rate (82.6%) of man was significant higher than previous researches. Rekha et al. reported that, out of 133 patients, mean age of OCV occurrence was around 53 and more involved in buccal mucosa [11]. The predominance of jawbone involvement (20.7%) was evident. One case was ameloblastoma arising from within verruous carcinoma. Although hybrid verrucous carcinoma of the oral cavity has been demonstrated several times, no case of both ameloblastoma and OVC in the same patient has yet been reported in the literatures [18-20]. Several efficient therapy protocols have been employed to the OVC disease, including lasers, chemotherapeutics, and radio therapeutics [21-23]. And a few retrospective studies have reported that surgery is still the optimal choice.
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In the present work, all patients underwent surgery and the survival rate was high (93.1%) within 5 years. This supports the conclusion that surgery fosters a higher survival rate among OVC patients than other treatments. The clinical feature criteria of OVC were established by Ackerman and verified by other studies [1, 24, 25]. The 29 patients evaluated in this study were classified into three types, as suggested in previous studies.

The reported recurrence rate of OVC varies in previous studies and only a few of researches refer to the OVC recurrence. However, both cystoid and infiltrative OVC were observed to be inclined to recur in this study. In a stereological study, more large and irregular nuclei could be observed in the cystoid and infiltrative OVC than in exogenic OVC. This was found to be related to the progression and poor prognosis [26, 27]. In the present work, clinical outcome was consistent with a previous three-dimensional study. Besides, other mechanisms should be evaluated in further studies. Few of OVC involve cervical lymph node metastasis [28]. Elective neck dissection is not necessary even in patients at advanced stages [6]. Two patients (Patient ID: 1 and 20) with the enlargement of clinically palpable lymph nodes who performed supra-omohyoid neck dissection in this research. The OVC both recurred after the initial resection on these two patients and they had the symptom of cervical lymph node metastasis. The patients eventually died even suffered the radical neck dissection during the second operation due to the recurrence. The primary treatment of the cystoid and infiltrative OVC should be implemented by a wide excision of the mass and supra-omohyoid neck dissection which may prevent the recurrence of the OVC.

Conclusions

OVC showed a good prognosis with surgical treatment. Infiltrative and cystoid OVC presented with aggressive characteristics and may have a high risk of recurrence. Supra-omohyoid neck dissection (SOHND) may be useful in many such cases.

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Disclosure of conflict of interest

None.

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