J Med Sci 2012;32(6):301-303
http://jms.ndmctsgh.edu.tw/3206301.pdf

Rapid Recurrence and Transformation of Verrucous Carcinoma of Lower Lip

Chin-Ta Lin, Shyi-Gen Chen, Tim-Mo Chen, and Shun-Cheng Chang*

Division of Plastic and Reconstructive Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China

We report a 52-year-old male with recurrent verrucous carcinoma of lower lip and rapid transformation into squamous cell carcinomas (SCC) three years after surgery. To date, verrucous carcinoma has been regarded as a variant of well-differentiated SCC, which sometimes shows invasive changes but rarely metastasizes. With this case, we highlight the possibility of early recurrence and rapid transformation into SCC and emphasize the need for surgical resection with adequate margins. To our knowledge, such rapid transformation into SCC merely three months after surgery has never been reported in the literature.

Key words: verrucous carcinoma, squamous cell carcinoma, recurrence, transformation, wide excision

INTRODUCTION

Verrucous carcinoma (VC) of the skin is a rare variant of squamous cell carcinoma (SCC), which shows exophytic nodular growth and is potentially malignant. This tumor is generally recognized as a locally invasive SCC with little propensity for metastasis. Surgical excision seems to be the clear preference for treatment. Although most of the VCs grow slowly, this case showed a different early recurrence and rapid transformation into SCC within three months even after a wide excision with adequate margins.

CASE REPORT

A 52-year-old male presented with a one-year history of recurrent growing verruciform lesion on the lower lip. The patient had smoked half a pack of cigarettes a day for 35 years, but quit smoking one year ago after the malignancy was confirmed. He also had a history of chewing betel nuts in the past and had quit for one year. The first examination a year ago revealed a 30×15 mm verruciform nodule restricted to the lower lip (Fig. 1a) and biopsy report showed verrucous carcinoma (Fig. 2a). There were no clinical findings suggestive of metastasis. Surgical resection and full-thickness skin grafting were

Fig. 1 The picture shows a 30×15 mm verruciform nodule restricted to the lower lip (a) and a recurrent lesion on the lower lip with central ulceration (b).

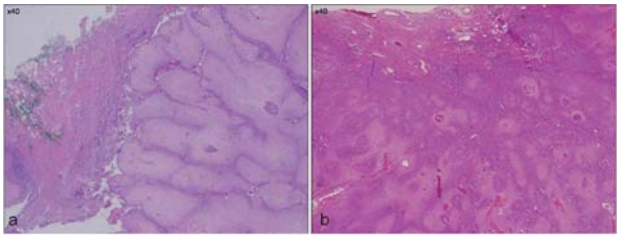

Fig. 2 (a) Verrucous carcinoma is characteristic of hyperparakeratinized epithelium proliferating in a papillary form and extending deep into the connective tissue with broad and bulbous rete ridges showing pushing margins; (b) squamous cell carcinoma is characteristic of a violation of the basement membrane and a downward growth of broad rete pegs and islands of squamous epithelium. (H and E stain, ×40)

Received: April 9, 2012; Revised: July 31, 2012; Accepted: August 22, 2012
*Corresponding author: Shun-Cheng Chang, Division of Plastic and Reconstructive Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, No. 325, Sec. 2, Cheng-gong Road, Taipei 114, Taiwan, Republic of China. Tel: +886-2-87927195; Fax: +886-2-87927194; E-mail: aarondakimo@yahoo.com.tw

performed. Histological examination revealed verrucous carcinoma. Six months after surgery, a growing verruciform lesion of about 20×15 mm was found on the lower lip and the lesion had been successfully treated with a carbon dioxide laser. Three months later, a verruciform lesion of about 30×15 mm was found on the lower lip with central ulceration (Fig. 1b) and biopsy report showed squamous cell carcinoma (Fig. 2b). The patient underwent wide excision, neck lymph node dissection and anterolateral thigh free flap reconstruction with free cut-end margin. Pathologic report showed a picture of SCC with well to moderately differentiated lower lip tissue characterized by verrucous hyperplasia of tumor cell nests showing focal moderate differentiation with stromal invasion at high-power magnification (Fig. 2). The patient was discharged 10 days after surgery. During one-year follow-up, neither recurrence nor metastasis has been detected.

DISCUSSION

In 1948, the clinicopathological concept of verrucous carcinoma (VC) was first established by Ackerman, who described a variant of squamous cell carcinoma (SCC) of the oral cavity in 31 patients.[1] VC has a characteristic gross appearance of large, exophytic, soft, fungating neoplasms with a pebbly mamillated surface. Microscopically, club-shaped fingers of hyperplastic epithelium gradually pushed rather than infiltrated their way into deeper tissues. The epithelium was well differentiated and the basement membrane remained intact.

The current World Health Organization classification describes VC as a slow-growing variant of SCC with pushing margins.[2] Moreover, oral VC is a phenomenon with slow growth, no metastatic potential and lowest invasive potential, accounting for 2% to 9% of all oral carcinomas.[3,4] VC of the oral cavity is most commonly found on the lower lip followed by the hard palate, inferior gingiva, and buccal mucosa.[5] The etiology of VC is strongly associated with smoking, alcohol, papillomavirus infections, which may play important roles in its pathogenesis.[6,7]

VC has unique biological behavior and is fairly rare compared with the conventional form of SCC.[3] On the other hand, invasive oral SCC is the most common oral cancer, which develops from carcinoma in situ or noninvasive dysplastic precursor lesions.[8] Furthermore, oral SCC has regional lymph node involvement and distant metastatic potential.[4] Owing to different characteristics in terms of invasiveness, metastatic potential, prognosis, and response to conventional treatments, two tumors must be correctly differentiated by pathologist.[3,4]

According to Koch *et al*.[5] and Ferlito *et al*.[9], the correct diagnosis is heavily dependent on close collaboration between clinician and pathologist, and the provision to the latter of a sufficiently large biopsy specimen, because distant metastasis associated with VC can be a consequence of an incorrect diagnosis or of the presence of foci of SCC in lesions with warty features.[9,10] Incomplete resection may lead to multiple recurrences and routine histopathological evaluation fails to identify those tumors that will progress to become biologically aggressive SCC.[11]

Medina et al. have reported the coexistence of foci of less-differentiated squamous carcinoma in 20% of VC of the oral cavity as 'hybrid verrucous-squamous carcinoma'.[12] Anaplastic transformation of VC into squamous cell carcinoma usually occurs following radiation therapy[13], but some authors were also sure that anaplastic transformation could occur not only due to irradiation, but also naturally.[12]

In molecular pathogenesis, the membrane location of the transforming growth factor-β type II receptors (TGF-β R-II) in VC exposes the receptor to the growth inhibitory control of TGF-β and, probably explaining why VC tumors are less aggressive clinically. The marked reduction of membranous TGF-β R-II and their predominant cytoplasmic location diminishes TGF-β growth inhibition and may contribute to the transformation of VC into more aggressive SCC.[11]

According to the treatment results of a series of 2,350 patients with VC by Koch *et al*.[5], those patients with VC of the oral cavity initially treated with surgery had better survival. Wide excision with reconstruction is indeed the treatment of choice for VC of the oral cavity although local recurrences are observed despite of clear surgical margins confirmed by histopathology.[14] While the developed VC with rapid transformation into SCC may be associated with a recurrence which could not be detected early, this aggressive course of VC has to be kept in mind.

In conclusion, although VC does not occur frequently and has excellent prognosis with surgical management, this neoplasm presents a potential for local recurrence that should be considered during surgical planning in the oral cavity. With this case, we highlight the possibility of early recurrence and transformation into SCC and emphasize the need for more aggressive follow-up after surgery.

ACKNOWLEDGMENT

Civilian Administration Division of Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

FINANCIAL DISCLOSURE

None of the contributing authors have any conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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