

Case Report

Squamous cell carcinoma arising within verrucous carcinoma of the oral cavity: a case report

Tadashi Terada

Departments of Pathology, Shizuoka City Shimizu Hospital, Shizuoka, Japan

Received November 11, 2011; accepted March 5, 2012; Epub April 16, 2012; Published May 30, 2012

Abstract: The author herein reports a case of squamous cell carcinoma (SCC) arising within verrucous carcinoma (VC) of the hard palate. An 84-year-old woman was admitted to our hospital complaining of oral discomfort. Oral examination revealed a pedunculated verrucous tumor (15 x 15 mm) in the hard palate. A biopsy revealed verrucous tumor. Resection of the lesion with wide margins was performed. Grossly, the palate tumor was pedunculated and verrucous, but a depressed area (8 x 7 mm) was recognized. Microscopically, the verrucous areas showed verrucous proliferation of squamous epithelium with little cellular atypia, and was interpreted as VC without invasion. The depressed lesion was obvious SCC with invasion. There were direct transitions between the VC and SCC. Immunohistochemically, the VC and SCC tumor cells were negative for human papilloma virus antigens. P53 protein was expressed in both VC and SCC, though the expression in SCC was much more strong and broad than that in VC. The Ki-67 antigen was also expressed in the VC and SCC, and Ki-67 labeling index ranged was 12% in VC and 64% in SCC. These findings indicate that SCC may arise within VC.

Keywords: Squamous cell carcinoma, verrucous carcinoma, Ki-67 antigen

Introduction

Verrucous carcinoma (VC) (Ackermann's tumor) is a rare type of low-grade, well differentiated squamous cell carcinoma, and develops mainly in the skin, genitalia, esophagus, and oral cavity. The pathogenesis of VC of the oral cavity is still obscure, but is thought to be associated with human papilloma virus (HPV) [1-3], poor oral hygiene, chewing of tobacco, and use of snuff. Several studies of VC of the oral cavity have been reported [4-6].

Squamous cell carcinoma (SCC) can arise in VC. A review of the literature revealed 4 cases of SCC arising within VC [5, 7-9]. One is oral cavity [5], one is penis [7], one is vagina [8], and the remaining one is skin [9].

Herein, the author reports an old female patient with coexistence of VC and SCC in the same tumor. The author interpreted that SCC developed within a VC.

Case report

An 84-year-old woman consulted to our hospital because of oral discomfort. Oral examination revealed a pedunculated verrucous tumor (15 x 15 mm) in the hard palate. A biopsy revealed a verrucous tumor, and suspected verrucous carcinoma. Resection of the lesion with wide margins was performed.

Grossly, the palate tumor was pedunculated and verrucous, but a depressed area (8 x 7 mm) was recognized (**Figure 1**). Microscopically, the verrucous areas showed verrucous proliferation of squamous epithelium with little cellular atypia (**Figure 2**), and was interpreted as VC. No invasion was recognized in the VC. The depressed lesion was obvious SCC with invasion (**Figure 3**). There were direct transitions between VC and SCC (**Figure 4**).

An immunohistochemical study was performed with the use of Dako Envision method, as previ-

Verrucous carcinomas of oral cavity



Figure 1. Gross findings of the resected palate specimen. There is a verrucous tumor. Foci of the tumor shows depressed lesion (arrow). The verrucous area is verrucous carcinoma, and depressed areas are squamous cell carcinoma.

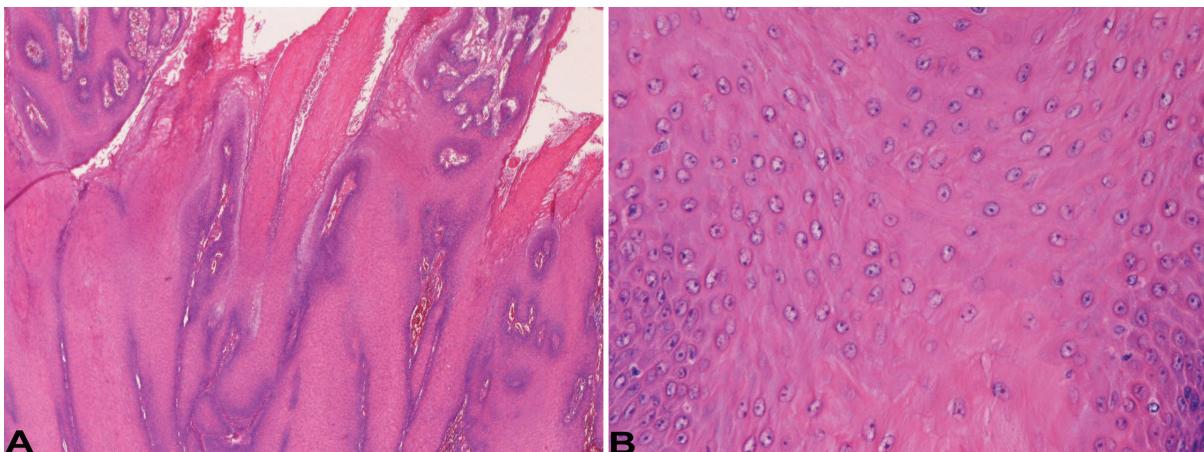


Figure 2. Area of verrucous carcinoma. A. Low power view of verrucous carcinomas. Verrucous proliferation of squamous epithelium is evident. HE, x10 B. The cellular atypia is minimal. HE, x200

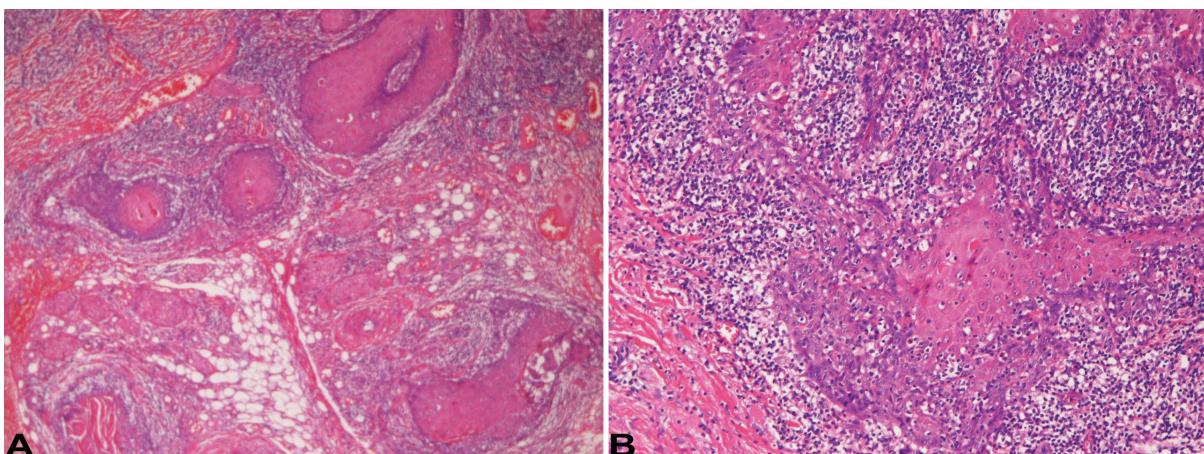


Figure 3. Area of squamous cell carcinoma. A. Low power view demonstrate invasive squamous cell carcinoma. HE, x100. B. High power view shows invasive carcinoma with apparent squamous differentiation. Lymphocytic infiltration is present. HE, x200

ously reported [10, 11]. The antibodies were HPV (polyclonal, Dako), p53 protein (D07, Dako), and Ki-67 (MIB1, Dako). Immunohistochemically, the VC and SCC tumor cells were negative for human papilloma virus antigens. P53 protein was expressed in both VC and SCC, though the expression in SCC was much more strong and broad than that in VC (Figure 5). Ki-67 antigen was also expressed in the VC and SCC, and Ki-67 labeling index ranged was 12% in VC and 64% in SCC (Figure 6).

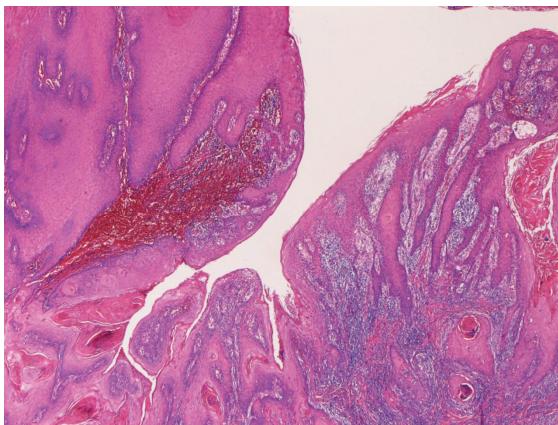


Figure 4. The gradual transition between verrucous carcinoma (left) and squamous cell carcinoma is recognized. HE, x10

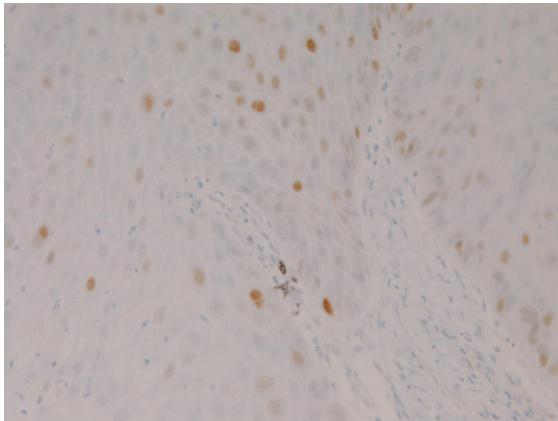


Figure 5. p53 expression in the squamous cell carcinoma area. X200

The surgical margins of the resected specimen were negative for atypical cells. The patient is now free of tumors, and followed up 13 months after the operation.

Discussion

The VC of the present case showed verrucous proliferation of squamous epithelium with little cellular atypia. No invasion was seen. The histology of the present tumors fulfills the criteria of VC. VCs of the present case are different from verrucous hyperplasia, proliferative verrucous leukoplakia, and well differentiated papillary squamous cell carcinoma with regard to the histology and immunohistochemistry [12]. The SCC of the present study was typical invasive

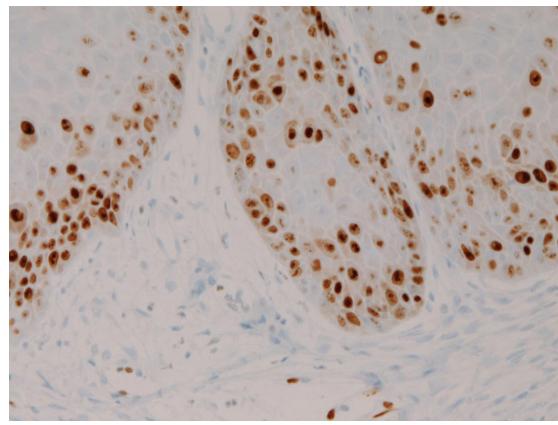


Figure 6. Ki-67 expression in the squamous cell carcinoma area. The labeling index is high. X 100.

SCC.

Of particular interest is that the present case showed coexistence of VC and SCC. The tumor area was larger in VC than in SCC. The VC showed no invasion, but SCC was invasive. The VC and SCC were located within a tumor. Gross and microscopic findings apparently showed SCC within VC, and a gradual transition between the VC and SCC was present. These findings indicate that SCC arose within VC in the present study. To the best of the author's knowledge, there are only 4 reports of SCC arising within VCs [5, 7-9]. One is oral cavity [5], one is penis [7], one is vagina [8], and the remaining one is skin [9]. Medina et al. [5] reported that they, for the first time, documented the coexistence of foci of less-differentiated SCC within VC of the oral cavity. However, a literature review by the author revealed no coexistence between VC and SCC in other papers. In any way, the present findings indicate that SCC can occur within VC in the oral cavity.

The expression of p53 protein and Ki-67 antigen in VC has been reported [13, 14]. The present cases showed p53 protein in VC and SCC. Ki-67 antigen labeling was relatively high in VC and very high in SCC. The expression of p53 and relatively high Ki-67 labeling support the low grade malignant natures of the VCs of the present case. The high p53 expression and high Ki-67 labeling in the present SCC shows that the SCC was relatively high grade SCC.

In summary, the author demonstrated a case of

VC, within which SCC arose.

Address correspondence to: Dr. Tadashi Terada, Department of Pathology, Shizuoka City Shimizu Hospital, Miyakami 1231 Shimizu-Ku, Shizuoka 424-8636, Japan Tel: +81-54-336-1111; Fax: +81-54-334-1173; E-mail: piyo0111jp@yahoo.co.jp

References

- [1] Fujita S, Senba M, Kumatori A, Hayashi T, Ikeda T, Toriyama K. Human papillomavirus infection in oral verrucous carcinoma: genotyping analysis and inverse correlation with p53 expression. *Pathobiology* 2008; 75: 257-264.
- [2] Stankiewicz E, Kudahetti SC, Prowse DM, Ktori E, Cuzick J, Ambrosine L, Zhang X, Watkin N, Corbishley C, Berney DM. HPV infection and immunohistochemical detection of cell-cycle markers in verrucous carcinoma of the penis. *Mod Pathol* 2009; 22: 1160-1168.
- [3] Shroyer KR, Greer RO, Fankhouser CA, McGuirt WF, Marshal R. Detection of human papilloma DNA in oral verrucous carcinoma by polymerase chain reaction. *Mod Pathol* 1993; 6: 669-672.
- [4] McCoy JM, Waldron CA. Verrucous carcinoma of the oral cavity: a review of forty nine cases. *Oral Surg Oral Med Oral Pathol* 1981; 52: 623-629.
- [5] Medina JE, Dichtel W, Luna MA. Verrucous-squamous cell carcinoma of the oral cavity: a clinicopathologic study of 104 cases. *Arch Otolaryngol* 1984; 110: 437-440.
- [6] Kamath VV, Varma RR, Gadewar DR, Muralidhar M. Oral verrucous carcinoma: an analysis of 37 cases. *J Craniomaxillofac Surg* 1989; 17: 309-314.
- [7] Youngberg GA, Thornthwaite JT, Inoshita T, Franzus D. Cytologically malignant squamous cell carcinoma arising in a verrucous carcinoma of the penis. *J Dermatol Surg Oncol* 1983; 9: 474-479.
- [8] Haidopoulos D, Diakomanolis E, Rodolakis A, Voulgaris Z, Vlachos G, Michalas S. Coexistence of verrucous and squamous carcinoma of the vulva. *Aust N Z J Obstet Gynaecol* 2005; 45: 60-63.
- [9] Shimizu A, Tamura A, Ishikawa O. Invasive squamous cell carcinoma arising from verrucous carcinoma: recognition of verrucous carcinoma of skin as an *in situ* carcinoma. *Eur J Dermatol* 2006; 16: 439-442.
- [10] Terada T, Kawaguchi M. Primary clear cell adenocarcinoma of the peritoneum. *Tohoku J Exp Med* 2005; 206: 271-275.
- [11] Terada T, Kawaguchi M, Furukawa K, Sekido Y, Osamura Y. Minute mixed ductal-endocrine carcinoma of the pancreas with predominant intraductal growth. *Pathol Int* 2002; 52: 740-746.
- [12] Murrah VA, Batsakis JG. Proliferative verrucous leukoplakia and verrucous hyperplasia. *Ann Otol Rhinol Laryngol* 1994; 103: 660-663.
- [13] Saito T, Nakajima T, Mogi K. Immunohistochemical analysis of cell-cycle-associated proteins p16, pRb, p53 and Ki-67 in oral cancer and pre-cancer with special reference to verrucous carcinoma. *J Oral Pathol Med* 1999; 28: 226-232.
- [14] Drachenberg CB, Blanckaert R, Ioffe OB, Ord RA, Padadimitriou JC. Comparative study of invasive squamous cell carcinoma and verrucous carcinoma of the oral cavity: expression of bcl-2, p53, and HER2/neu, and indexes of cell turnover. *Cancer Detect Prev* 1997; 21: 483-489.