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Papillary squamous cell carcinoma of the oral mucosa: a clinicopathologic and immunohistochemical study of 12 cases and literature review

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ABSTRACT

Papillary squamous cell carcinoma (SCC) (PSCC) of the oral mucosa is a relatively rare but distinct variant of SCC of head and neck. The objectives of this study were to describe the clinicopathologic and immunohistochemical features of a series of patients with oral PSCC and to review the literature on this topic. Retrospective review of patients with clinical and pathologic diagnosis of PSCC (n = 12) between 2000 and 2008 in our institution was conducted. The outcome analysis in a mean follow-up of 56 months (range, 24-131 months) was performed. These patients were 7 women and 5 men, and the mean age at diagnosis was 72.9 years (range, 53-83 years). The cheek and the gingiva were the predominant sites of involvement. At the end of follow-up, 4 patients were found to have local recurrence, and 3 were dead of disease. The estimated 3- and 5-year survival was 91.7% and 76.4% for the whole series, respectively. Histopathologically, the papillary pattern consisted of multiple, thin, delicate filiform, finger-like papillary projections with fibrovascular cores. Besides, the exophytic pattern consisted of the broad-based bulbous to "cauliflower-like" exophytic growth with rounded projections. Immunohistochemically, positivity for CKpan, CKhmw (high molecular weight), and p53, yet negativity for CK8, vimentin, desmin, smooth muscle actin, and S-100 was observed in PSCC. In conclusion, 2 specific histopathologic growth patterns of oral PSCC were identified to separate from conventional SCC. Patients with PSCC have a favorable outcome in relation to exophytic nature and limited invasion of the tumor.

1. Introduction

Papillary squamous cell carcinoma (SCC) (PSCC) is a clinically rare variant of SCC of the upper aerodigestive tract mucosa. It was first described by Parkhill [1] in 1968 and was currently included in the World Health Organization (WHO) classification of head and neck tumors as a distinct clinicopathologic entity [1,2]. Papillary squamous cell carcinoma often presents a solitary lesion with an exophytic or papillary growth and with tumor size ranging from 2 mm up to 4 cm. Histopathologically, it is characterized by the finger-like papillary projections with fibrovascular cores or the broad-based bulbous to exophytic growth with rounded projections and malignant nonkeratinizing epithelium with pleomorphic cells and mitotic figures [2–6]. A review of the literature reveals that most of these tumors occur frequently in the larynx and the hypopharynx and that only approximately 70 cases of the oral mucosa (Table 1) have been reported in a few small series and isolated cases [7–15]. The objectives of this study were to describe the clinicopathologic and immunohistochemical features of 12 patients with oral mucosal PSCC in our institution and to review the literature on this topic.

2. Materials and methods

Medical records of 12 consecutive patients with pathologic diagnoses of PSCC according to the WHO classification [2] from 2000 to 2008 were retrieved and reviewed retrospectively in a standard computerized database from Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine. Follow-up information was pursued for these patients. Clinical information was obtained from the patients' charts regarding age, sex, location, life habit, tumor stage, treatment, local recurrence, and outcome at follow-up. Hematoxylin and eosin staining sections were reviewed in all cases. Immunohistochemical staining using the standard streptavidin-biotin-peroxidase method for cytokeratin (CKpan, CKhmw [high molecular weight],

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Table 1
Summary of previously reported cases of oral papillary squamous cell carcinoma in the English language literature

Author	Year	Cases (n)	Age (y)	Sex	Location	Treatment	Follow-up	Outcome
Takeda et al [13]	2001	2	68, 72	M, M	Mouth floor and palate	Surgery	NA	Cure
Khan et al [14]	2005	1	72	M	Gingiva	Surgery (ND)	NA	NA
Marques et al [15]	2009	1	80	M	Tongue	Surgery	6 mo	Cure
Russell et al [11]	2010	18	NA	NA	NA	Surgery	26 mo	REC (n = 3)
Ishiyama et al [12]	1994	Head and neck (n = 52) (oral mucosa, n = 44)	50-69	28 M/24 F	Alveolar ridge (n = 20), cheek (n = 13), mouth floor, or tongue (n = 11)	Surgery (n = 49); radiation (n = 2)	NA	REC (n = 17); DOD (n = 4)

Abbreviations: M, male; F, female; NA, not available; ND, neck dissection; REC, recurrence; DOD, dead of disease.

Table 2
Antibodies for immunohistochemistry

Antibody	Clone	Source	Dilution
CKpan	AE1/AE3	Taiyang, Shanghai, China	1:100
CKhmw	34E12	Taiyang	1:50
CK8	TS1	Gene Tech, Shanghai, China	1:200
Vim	V9	Dako, Copenhagen, Denmark	1:100
SMA	1A4	Dako	1:100
S-100	V1-H14	Dako	1:100
Des	D33	Dako	1:100
p53	DO-7	Dako	1:100

CK8), vimentin (Vim), smooth muscle actin (SMA), S-100, desmin (Des), and p53 was performed. The antibodies, dilutions, and sources are shown in Table 2. The SPSS 16.0 software (SPSS Inc., Chicago, USA) was used to perform statistical analysis and create diagram. Three-year and 5-year survival was calculated by the Kaplan-Meier method. This study was approved by the institutional review board.

3. Results

3.1. Clinical findings

The baseline characteristics of the study subjects are summarized in Table 3. Of the 12 patients with PSCC, 7 women and 5 men were identified. The mean age at diagnosis was 72.9 years (range, 53-83 years). The lesions of 4 cases were located on cheek; 3, on the gingiva; 2, on the lower lip; 1, on the palate; 1, on the tongue; and 1, on the mouth floor. There were 2 smokers and 3 alcohol users. Clinical symptom of chief complaint was presented with pain mass or painless mass. The mean course of that was 10.7 months (range, 2 weeks to 36 months). The pT1, 2, and pT3, 4, of clinical stage was seen in 7 and 5 cases, respectively. Clinical evidence of regional lymph node metastasis was present in 1 patient. All patients were treated with surgical excision, and selective neck dissection was performed in 8 patients. At the end of follow-up (mean, 56 months; range, 24-131 months), 4 patients were found to have local recurrence, and 3 were dead of disease. The estimated 3- and 5-year survival was 91.7% and 76.4% for the whole series, respectively (Fig. 1).

3.2. Microscopic findings

The representative histopathology and immunohistochemistry of PSCC are illustrated in Fig. 1. Histopathologically, 2 specific growth patterns were identified to separate from conventional SCC. The papillary pattern consisted of multiple, thin, delicate filiform, finger-like papillary projections with fibrovascular cores (Fig. 2A). The exophytic pattern consisted of the broad-based bulbous to "cauliflower-like" exophytic growth with rounded projections (Fig. 2B). Malignant epithelium was observed to have an increased nuclear-to-

Table 3
Summary of clinicopathologic and immunohistochemical data of the present 12 cases of oral papillary squamous cell carcinoma

No.	Age (y)/sex	Location	Clinical symptom	Clinical course (mo)	Smoking	Alcohol intake	T	N	M	Tumor stage	Primary treatment	Outcome at follow-up (mo)	Immunohistochemical findings
1	83/F	Palate	Pain mass	36	No	No	3	0	0	III	Surgery	REC at 20 mo, DOD at 24 mo	CKpan, CKhmw, p53 (+); CK8, Vim, SMA, S-100 (−)
2	86/F	Cheek	Pain mass	6	No	No	2	0	0	II	Surgery (ND)	REC at 53 mo, DOD at 68 mo	CKpan, p53 (+); CK8, Vim, SMA, S-100 (−)
3	53/M	Cheek	Pain mass	12	No	Yes	3	0	0	III	Surgery (ND)	Alive at 78 mo	CKpan, CKhmw (+); CK8, Vim, SMA (−)
4	63/M	Gingiva	Painless mass	0.5	No	No	2	0	0	II	Surgery (ND)	REC at 28 mo, alive at 36 mo	CKpan, p53 (+); CK8, Vim, SMA, S-100 (−)
5	63/M	Lower lip	Painless mass	1	Yes	Yes	2	0	0	II	Surgery	Alive at 88 mo	CKpan, CKhmw (+); CK8,Vim, SMA, Des (−)
6	67/F	Cheek	Painless mass	1	No	No	3	0	0	III	Surgery (ND)	Alive at 40 mo	CKpan, p53 (+); CK8, Vim, SMA, S-100 (−)
7	72/M	Month floor	Painless mass	6	Yes	Yes	4	0	0	IV	Surgery (ND)	Alive at 36 mo	CKpan, CKhmw (+); CK8, Vim, SMA, S-100 (−)
8	74/F	Lower lip	Painless mass	1	No	No	1	0	0	I	Surgery	Alive at 30 mo	CKpan, p53 (+); CK8, Vim, SMA, Des, S-100 (−)
9	76/M	Gingiva	Pain mass	1	No	No	1	0	0	I	Surgery	DOD at 48 mo	CKpan, p53 (+); MDM2, Vim, SMA, OC (−)
10	78/F	Tongue	Painless mass	36	No	No	1	0	0	I	Surgery (ND)	Alive at 131 mo	CKpan, p53 (+); CK8, Vim, SMA, Des, S-100 (−)
11	82/F	Gingiva	Painless mass	4	No	No	1	1	0	III	Surgery (ND)	Alive at 30 mo	CKpan, p53 (+); CK8, Vim, SMA, Des, S-100 (−)
12	78/F	Cheek	Painless mass	24	No	No	4	0	0	IV	Surgery (ND)	REC at 55 mo, alive at 63 mo	CKpan, CKhmw, p53 (+); CK8, Vim, SMA, Des (−)

Abbreviations: M, male; F, female; ND, neck dissection; REC, recurrence; DOD, dead of disease; MDM2, murine double minute 2; OC, osteocalcin.