

Clinicopathologic features of oral squamous papilloma and papillary squamous cell carcinoma: a study of 197 patients from eastern China

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Abstract

Oral squamous papilloma and papillary squamous cell carcinoma are 2 clinicopathologically distinctive papillary epithelial tumors. The current study aims to compare the clinical and pathologic features of these oral papillary lesions in a patient population from eastern China. A retrospective review in a series of patients with clinical and pathologic diagnosis of oral squamous papilloma (n = 141) and papillary squamous cell carcinoma (n = 56) was conducted. The average age of oral squamous papilloma was 51.0 years (male-to-female ratio, 1.82), with the palate being the predominant site. The average age of oral papillary squamous cell carcinoma was 63.3 years (male-to-female ratio, 1.67), with the gingiva being the predominant site. Multivariate analysis revealed that the elderly patient with papillary lesion (≥ 60 years) was associated with 3.09-fold (95% confidence interval, 1.59–6.03) increased carcinoma risk compared with the nonelderly patient. The lesion located on the gingiva was associated with 4.98-fold (95% confidence interval, 1.96–12.63) increased carcinoma risk compared with other oral sites. Collectively, clinicopathologic features of oral squamous papilloma and papillary squamous cell carcinoma in eastern China were elucidated. Elderly patients with oral papillary lesions located on the gingiva correlate with higher carcinoma risk. It highlights the importance of using a histologic examination to confirm the clinical diagnosis for any suspicious papillary lesions.

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1. Introduction

Oral squamous papilloma is a common benign epithelial tumor, and oral papillary squamous cell carcinoma is an uncommon malignant epithelial tumor. They are oral papillary lesions but clinicopathologically distinctive tumors. Squamous papilloma shares the morphology similarity to papillary squamous cell carcinoma both clinically and histopathologically. They clinically may present a localized

hyperplastic exophytic and papillary projections with finger-like proliferation or cauliflower-like morphology; there are, thus, no striking characteristic features to distinguish malignant papillary squamous cell carcinoma from benign squamous papilloma [1–5].

A review of the literature reveals that the reports focusing on the clinicopathologic feature of oral squamous papilloma are not robust [1–3]. On the other hand, only approximately 70 cases of oral papillary squamous cell carcinoma have been reported in some isolated cases and in a few small series hidden away in several studies on papillary squamous cell carcinoma of the head and neck [6–13]. To date, hardly any reports on the comparative clinicopathologic feature in a series of the 2 papillary lesions have been found in literature, and information on the clinical profiles concerning these

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Table 1
Histopathologic features of the diagnosis of oral squamous papilloma and papillary squamous cell carcinoma

Feature	Squamous papilloma	Papillary squamous cell carcinoma
Low-power view	Papillary fronds or arborizing rete processes	Papillary projections with fibrovascular cores
Surface keratinization	Hyperparakeratosis	Limited and often absent
Stratification	Well ordered	Disordered
Cytologic features of malignancy	Absent	Present
Epithelium pattern	Normal maturation	Immature basaloid cells or more pleomorphic cells
Nuclear pleomorphism	Absent	Marked present
Mitotic figures	May be present but no atypia	Atypia
Margins	Clear	Infiltrating
Invasion	Absent	Present in a part of lesions
Destructiveness	Absent	Present

lesions is missing in China. Because of the clinical and histopathologic resemblance and the rarity of oral papillary squamous cell carcinoma, recognition and accurate diagnosis of the 2 papillary lesions are critical.

We, therefore, retrospectively reviewed a series of patients with clinical and pathologic diagnosis of oral squamous papilloma (n = 141) and papillary squamous cell carcinoma (n = 56) from eastern China to compare their clinicopathologic features and to estimate the relationship between the 2 papillary lesions in the current hospital-based study.

2. Materials and methods

All the medical records of patients with the clinical and pathologic diagnosis of oral squamous papilloma and oral papillary squamous cell carcinoma from January 1994 to December 2010 were retrieved and reviewed retrospectively in a standard computerized database from Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (Shanghai, China). All the study participants underwent biopsy or surgery. The tissue was fixed in formalin, embedded in paraffin, and processed for routine histopathologic examination from hematoxylin-eosin staining sections. Diagnosis of squamous papilloma and papillary squamous cell carcinoma was made based on the World Health Organization criteria [4]. The features of the diagnosis of squamous papilloma and papillary squamous cell carcinoma are listed in Table 1. Information regarding age, sex, lesion site, smoking, and alcohol intake at the time of the initial diagnosis was documented in detail. Because papillary squamous cell carcinoma was predominantly located on the gingiva, lesion sites were grouped as the gingiva and other oral sites for an analysis of carcinoma risk. This study was approved by the institutional review board.

A descriptive analysis was performed on clinicopathologic parameters. Statistical analysis was carried out using the χ^2 test and Fisher exact test among qualitative variables and the Student *t* test among quantitative variables. Logistic regression was applied to evaluate odds ratios (ORs) for indication of carcinoma risk. Odds ratio with 95% confidence interval (CI) and *P* values were reported. All

the tests were 2 sided, and *P* values less than .05 were considered statistically significant.

3. Results

3.1. Characteristics of oral squamous papilloma and papillary squamous cell carcinoma

The baseline characteristics of the study subjects are summarized in Table 2. A total of 141 patients with oral

Table 2
Patient baseline characteristics

Characteristic	Squamous papilloma	Papillary squamous cell carcinoma
Total	141	56
Age (y)		
Mean (SD)	51.0 (18.4)	63.3 (12.4)
Range	1-92	35-86
<10	2 (1.4)	–
10-19	6 (4.3)	–
20-29	9 (6.4)	–
30-39	17 (12.1)	1 (1.8)
40-49	27 (19.1)	8 (4.3)
50-59	33 (23.4)	13 (23.2)
60-69	23 (16.3)	14 (25.0)
70-79	14 (9.9)	16 (28.6)
80-89	6 (4.3)	4 (7.1)
≥90	2 (1.4)	–
Not available	2 (1.4)	–
Sex		
Female	50 (35.5)	21 (37.5)
Male	91 (64.5)	35 (62.5)
Site		
Tongue		
Dorsal zone	8 (5.7)	1 (1.8)
Lateral/Ventral zone	32 (22.7)	12 (21.4)
Buccal mucosa	12 (8.5)	14 (25.0)
Gingiva	9 (6.4)	15 (26.8)
Palate	59 (41.8)	6 (10.7)
Mouth floor	1 (0.7)	1 (1.8)
Oropharynx	1 (0.7)	1 (1.8)
Upper lip	8 (5.7)	–
Lower lip	11 (7.8)	6 (10.7)
Life habit		
Smoking	34 (32.7)	10 (21.7)
Alcohol intake	38 (36.5)	12 (26.1)

Values are presented as n (%), unless otherwise indicated.

squamous papilloma were identified for this study, with ages ranging from 1 to 92 years and an average age of 51.0 years at the time of diagnosis. The peak incidence was the fifth decade of life (23.4%). These patients were 50 females and 91 males (male-to-female ratio, 1:1.82). The palate was affected in 41.8% patients with oral squamous papilloma, followed by the tongue (28.4%). Smoking and alcohol intake were involved in 32.7% and 36.5% of patients, respectively. A total of 56 patients with oral papillary squamous cell carcinoma were identified for this study, with ages ranging from 35 to 86 years and an average age of 63.3 years at the time of the diagnosis. The highest incidence occurred in the seventh decade of life (28.6%). There were 21 females and 35 males (male-to-female ratio, 1:1.67). The gingiva was involved in 26.8% of patients with oral papillary squamous cell carcinoma, followed by the buccal mucosa (25.0%). Smoking and alcohol intake were involved in 21.7% and 26.1% of patients, respectively.

Representative histopathology of oral squamous papilloma and papillary squamous cell carcinoma is shown in Fig. 1. Squamous papilloma exhibits well-ordered stratification, normal maturation epithelium, and clear margin with no cytologic features of malignancy in papillary fronds, but papillary squamous cell carcinoma exhibits immature basaloid cells, marked nuclear pleomorphism, numerous atypic mitotic figures, and infiltrating with cytologic features of malignancy in exophytic papillary projections with fibrovascular cores.

3.2. Comparison of oral squamous papilloma and papillary squamous cell carcinoma

To define the differences in clinical parameters between oral squamous papilloma and papillary squamous cell carcinoma, a comparative analysis was performed (Table 3). The average age of the patients with squamous papilloma was 51.0 years compared with that of 63.3 years of the patients with papillary squamous cell carcinoma (Student *t* test, $P < .001$), with a difference in the age group (<60 and ≥ 60 years) (Fisher exact test, $P < .001$). A significant difference in lesion site (Fisher exact test, $P < .001$) was also observed, whereas differences in sex, smoking, and alcohol intake were not observed between the 2 groups.

The most characteristic feature of oral squamous papilloma and papillary squamous cell carcinoma lesions is the papillary appearance. Clinically, distinguishing papillary squamous cell carcinoma from the hyperplastic papillary lesions is often difficult. To evaluate the carcinoma risk of patients with oral papillary lesions, clinical parameters were analyzed by using the logistic regression model (Table 3). On univariate analysis, sex, smoking, and alcohol intake were not significantly associated with carcinoma risk. The elderly patient (≥ 60 years) was associated with 3.23-fold (95% CI, 1.70–6.14; $P < .001$) increased carcinoma risk compared with the nonelderly patient. The lesion located on the gingiva was associated with 5.37-fold (95% CI, 2.19–13.17; $P < .001$) increased carcinoma risk compared with

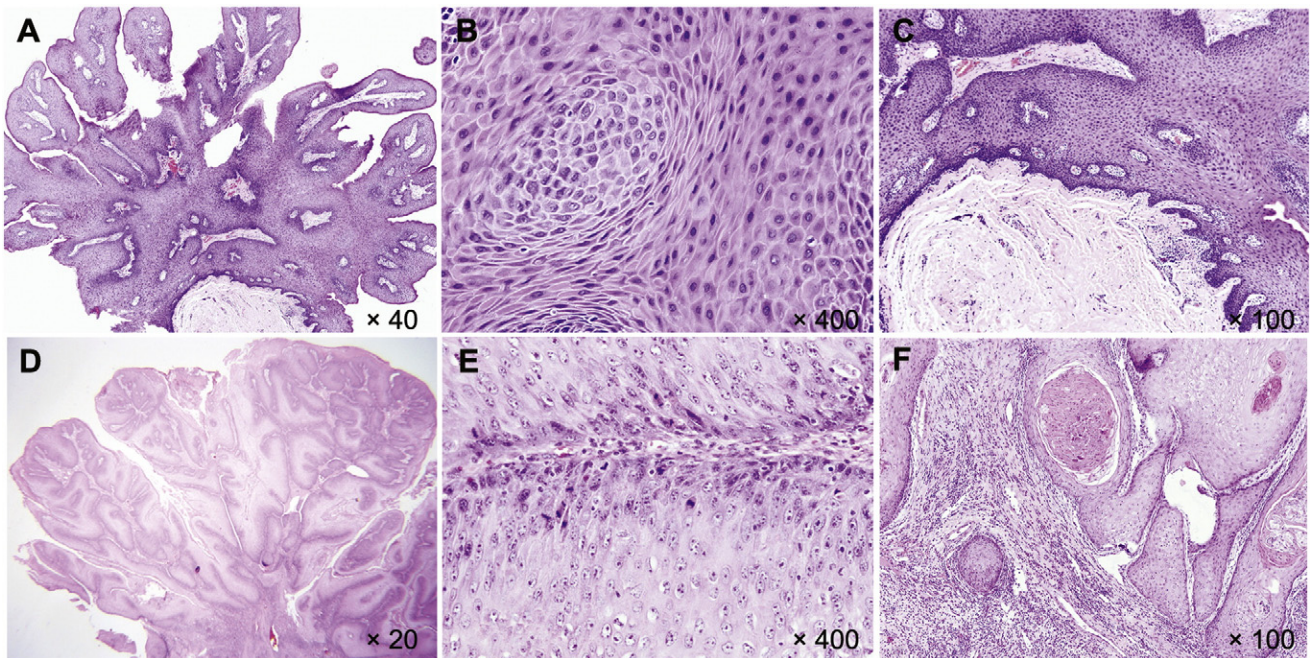


Fig. 1. Representative histopathology of oral papillary lesions. (A) Low-power view showing squamous papilloma with papillary fronds and arborizing rete processes. (B) Squamous papilloma with normal maturation epithelium. (C) Squamous papilloma with clear margins. (D) Low-power view showing papillary squamous cell carcinoma with exophytic papillary projections with fibrovascular cores. (E) Papillary squamous cell carcinoma with malignant epithelium with nuclear pleomorphism and mitotic figures. (F) Papillary squamous cell carcinoma with a microinvasive component.

Table 3
Comparison of oral squamous papilloma and papillary squamous cell carcinoma (PSCC)

Patients	Squamous papilloma (n = 141)		PSCC (n = 56)		Univariate LRA		Multivariate LRA	
	n (%)		n (%)	P	OR (95% CI)	P	OR (95% CI)	P
Age (y)								
Mean (SD)	51.0 (18.4)		63.3 (12.4)	<.001				
Range	1-92		35-86					
Age group (y)				<.001				
<60	94 (67.6)		22 (39.3)		1.00 (reference)		1.00 (reference)	
≥60	45 (32.4)		34 (60.7)		3.23 (1.70-6.14)	<.001	3.09 (1.59-6.03)	.001
Sex				.870				
Female	50 (35.5)		21 (37.5)		1.00 (reference)			
Male	91 (64.5)		35 (62.5)		0.92 (0.48-1.74)	.788		
Site				<.001				
Others	132 (93.6)		41 (73.2)		1.00 (reference)		1.00 (reference)	
Gingiva	9 (6.4)		15 (26.8)		5.37 (2.19-13.17)	<.001	4.98 (1.96-12.63)	.001
Smoking				.243				
Never	70 (67.3)		36 (78.3)		1.00 (reference)			
Past and present	34 (32.7)		10 (21.7)		0.57 (0.25-1.29)	.177		
Not available	37		10					
Alcohol intake				.261				
Never	66 (63.5)		34 (73.9)		1.00 (reference)			
Past and present	38 (36.5)		12 (26.1)		0.61 (0.28-1.32)	.213		
Not available	37		10					

LRA, logistic regression analysis.

that located on the other oral sites. To further assess the influence of each factor, we did a multivariate analysis. Age and lesion site retained statistical significance. The carcinoma risk of the elderly patients (≥ 60 years) was higher than that of the nonelderly patients (adjusted OR, 3.09; 95% CI, 1.59-6.03; $P = .001$). Lesion located on the gingiva was associated with increased carcinoma risk compared with that located on the other oral sites (adjusted OR, 4.98; 95% CI, 1.96-12.63; $P = .001$).

4. Discussion

The current study attempts to elucidate the clinicopathologic features and assess the relationship between the 2 oral papillary lesions in a series from one source of 141 patients with squamous papilloma and 56 patients with papillary squamous cell carcinoma. Multivariate regression analysis revealed that age and lesion site at the diagnosis were significantly associated with carcinoma risk in oral papillary lesions.

Previous findings revealed that oral squamous papilloma is common in children and in adults in the third to fifth decades of life, and there is an almost equal sex incidence with a slight male predominance [4]. We observed that oral squamous papilloma is common in adults in the fourth to sixth decades but uncommon in children, and the males obviously outnumbered the females (male-to-female ratio, 1.82:1). These are probably because of the differences in ethnic populations and geographical areas. Oral squamous papilloma was predominantly located on the palate and tongue in our study, in accordance with the previous reports [1-4].

On the other hand, we found that oral papillary squamous cell carcinoma occurs predominantly in the males in the sixth and seventh decades of life, which is in agreement with the demographic features of head and neck papillary squamous cell carcinoma [4-12]. Oral papillary squamous cell carcinoma was predominantly located on the gingiva and buccal mucosa in our study, in conformity with the observations of previous studies [8,10].

It is particularly note worthy that we evaluate the clinical parameters in carcinoma risk of the oral papillary lesions. We found that the carcinoma risk in elderly patients was higher than in nonelderly patients, which may be related to genetic susceptibility contributing to the phenotype [14,15]. Despite abundant data related to overall oral squamous cell carcinoma (OSCC), limited information is available with respect to OSCC development of the gingiva specifically. We found that oral papillary lesion located on the gingiva was associated with a much higher carcinoma risk compared with other sites, which is similar to the result of the study on malignant transformation of oral verrucous leukoplakia in our institution [14]. The exact etiology of OSCC of the gingiva is unknown, although predisposing factors include tobacco and alcohol use [16]. However, the association between tobacco and alcohol use and carcinoma risk was not observed in our study. Further studies are required to assess the roles of the potential risk factors for oral papillary lesions. Biopsy for histopathologic examination is currently recommended to exclude papillary squamous cell carcinoma from oral papillary lesions. Because patients older than 60 years and with lesions located on the gingiva had a much higher carcinoma risk, we further recommend routine biopsy to rule out papillary squamous cell carcinoma from these

patients with papillary lesions. Taken together, age and lesion site may be used as significant factors for carcinoma risk assessment in patients with oral papillary lesions.

In summary, the current investigation was a clinicopathologic study of patients with oral papillary lesions. The clinicopathologic features of oral squamous papilloma and papillary squamous cell carcinoma in eastern China were elucidated. A point to highlight was that we evaluate the clinical parameters in carcinoma risk of oral papillary lesions. Patients older than 60 years and with lesions located on the gingiva had a much higher risk of carcinoma. It highlights the importance of using a histopathologic examination to confirm the clinical diagnosis for any suspicious these papillary lesions.

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