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Original Article

Comparison of the histologic risk assessment model between lower lip and oral squamous cell carcinoma

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ABSTRACT

Introduction: The histologic risk assessment (HRA) grading system was proposed as a practical measure to predict clinical outcome and its effectiveness has been shown in several studies. It has been suggested that the HRA model might exhibit differences among various oral subsites. The aim of the present study was to compare this system between squamous cell carcinomas (SCCs) of the lower lip (LL) and oral cavity.

Materials and methods: All primary SCCs located in the LL and oral cavity were retrieved and graded using the HRA model. Data regarding risk score (RS), perineural invasion (PNI), lymphocytic infiltration (LI) and worst pattern of invasion (WPOI) were compared between LL and oral SCCs using χ^2 analysis ($P < 0.05$).

Results: There were a total of 33 LLSCCs, of which 15, 8 and 10 were categorized as low-risk (RS = 0), intermediate-risk (RS = 1–2) and high-risk (RS $\geq$ 3) tumors, respectively. Corresponding values in the 48 oral SCCs were 7, 15 and 26 cases. Significant differences in RS ($P = 0.00$), LI ($P = 0.01$) and WPOI ($P = 0.01$) were observed between LL and oral tumors.

Conclusions: The HRA model could be included among the various factors suggested to be different between lip and oral SCCs. Low-risk tumors were more prevalent in the lip which corroborates the less aggressive nature of these cancers. Considering the significantly higher LI in LL SCCs, inflammation may be regarded as an important factor in regulating the invasive behavior of these tumors.

1. Introduction

For several decades, efforts have been made to improve the prediction of oral squamous cell carcinoma (SCC) prognosis in order to advance the management of patients afflicted with this disease. In this journey, various laboratory techniques and molecular factors have been employed but one of the most simple and inexpensive methods has been the evaluation of histopathologic characteristics of carcinoma cells on plain hematoxylin and eosin-stained sections, i.e. grading [1].

SCC grading has a long history in head and neck pathology; Broders was one of the first investigators to introduce a histologic quantitative system for lip cancer which was based on the resemblance of the neoplasm to its parent tissues [2]. Over the following years, several cellular and morphological features were contemplated in the development of subsequent grading systems. In 1973, Jacobsson et al. [3] proposed a grading system which was later modified by Fisher [4], Lund et al. [5,6], Willen et al. [7] and Anneroth et al. [8] who finally classified oral SCCs according to neoplastic cell features and histopathologic characteristics of the tumor-host relationship. The criteria used in this classification included keratinization degree, nuclear pleomorphism, number of mitoses, invasion pattern, depth of invasion and leucocytic infiltration. Bryne et al. [9], in 1992, recommended analysis of the neoplastic invasive front and proposed a modification of the grading system suggested by Anneroth et al. [8], while the World Health Organization (2005) [2] based its grading system on Broders' classification. In 2005, Brandwein-Gensler et al. [10] examined the relationship of various histologic variables in relation to prognosis and presented a histologic risk scoring system which in contrast to former classification schemes was non-linear [11,12].

Among the various grading systems, the histologic risk model, proposed by Brandwein-Gensler et al. [10] has shown the most promise in assessing overall survival and local recurrence [2]. This model has been validated in several cohorts in different

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Table 1
Histologic grading system proposed by Brandwein-Gensler et al [10,12].

Histologic parameter	Score	Type/pattern	Specification
Perineural invasion	0	None	No perineural invasion
	1	Small nerves	Tumor cells traveling alongside or within small nerves (< 1 mm diameter)
	3	Large nerves	Tumor cells traveling alongside or within large nerves (≥ 1 mm diameter)
Lymphocytic infiltration	0	Continuous band	Dense lymphoid tissue at tumor-host interface containing a minimum of one lymphoid nodule (inflammatory cells covering ≥ half of a × 20 field) in each LPF[a]
	1	Large patches	One or more lymphoid nodules with intervening areas of non-inflammatory tissue in more than one LPF
	3	Limited to none	Possibility of scattered inflammatory cells, but no definitive lymphoid nodule
Worst pattern of invasion	0	1	Broad pushing tumor border
		2	Pushing "finger-like" growths
		3	Separate islands containing > 15 cells
	1	4	Single infiltrating tumor cells, strands or small neoplastic islands (≤ 15 cells)
	3	5	Neoplastic satellites or lymphovascular emboli or PNI with ≥ 1 mm distance from tumor border or between each other (× 20)

[a] LPF: low power field (× 4).

populations [11–15]. When considering subsites, a difference in the distribution of risk categories has been observed between the tonsil and oral cavity [11,12]. However histologic risk assessment (HRA) has not been adequately compared between different oral locations [10]. Considering the reports that have indicated a number of differences between oral and lip tumors [16,17], we aimed to compare the histologic risk assessment (HRA) model between these two sites.

2. Material and methods

Patient pathology files archived in our Institution during a ten-year period, were reviewed and those with a diagnosis of intraoral and lower lip SCC were considered for further evaluation. Only stage 1 primary tumors treated with excisional biopsy were selected for histologic analysis and those with lymph node metastasis, tumor dissemination, previous chemo/radiotherapy and concurrent tumors in other locations were excluded from the study sample. Based on the information provided under the "block list" of the gross description section in the pathology reports, all hematoxylin/eosin-stained slides were retrieved and in cases lacking one or more slides, paraffin blocks were sectioned and stained with hematoxylin and eosin. Using a double-headed microscope (BX51, Olympus, Japan), two oral and maxillofacial pathologists examined all specimens in order to confirm the diagnoses and only cases which obtained the agreement of both observers and those with sufficient amount of connective tissue beyond the tumor-host interface were chosen for grading. According to the histologic risk assessment model established by Brandwein-Gensler et al. [10], worst pattern of invasion (WPOI) and lymphocytic infiltration (LI) were scored at the tumor-host interface and perineural invasion was assessed throughout the specimen (Table 1) and all scores were summed to determine the histologic risk score (RS). Cases where the sum of all points reached 3–9, were considered as high-risk, those with a final score of 1 or 2 were regarded as intermediate-risk and samples which received an RS of 0 were classified as low-risk tumors. Observers were blind to the tumor subsite and using the same double-headed microscope, both had to agree on the neoplastic grade. In cases where there was no consensus, the tumors were precluded from the study sample. The protocol of this study was approved by the Ethics Committee of our Institution.

3. Statistical analysis

Statistical analysis was performed using χ^2 and P values of less than 0.05 were considered significant.

4. Results

A total of 81 cases satisfied the strict inclusion and exclusion criteria employed in this study, of which 33 occurred in the lower lip and 48 in the oral cavity.

In the lower lip group, 15, 8 and 10 cases demonstrated risk scores of 0 (low-risk), 1–2 (intermediate-risk) and ≥ 3 (high-risk), respectively. Of the 48 oral SCCs, seven were grouped as low-risk, 15 as intermediate-risk and 26 as high-risk patients. A significant difference was observed between the RSs of lower lip and oral SCC tumors ($P = 0.00$).

Table 2
Histologic variable scores according to tumor subsite.

Histologic variable	Score	No. of lower lip cases	No. of oral cavity cases	P value
Perineural invasion	0	24	27	0.14
	1	9	17	
	3	0	4	
Lymphocytic infiltration	0	20	13	0.01
	1	6	14	
	3	7	21	
Worst pattern of invasion	0	26	24	0.01
	1	5	21	
	3	2	3	

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