A 10-year study of specimens submitted to oral pathology laboratory analysis: lesion occurrence and demographic features

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Abstract: The purpose of the present paper was to describe the range of lesions histologically diagnosed in an oral pathology laboratory in southern Brazil. A retrospective study of 8,168 specimen analyses recorded between 1995 and 2004 was conducted. The records were retrieved from the Oral Pathology Laboratory, School of Dentistry, Federal University of Rio Grande do Sul, RS, Brazil. A total of 6,831 valid cases (83.63%) were examined. Of these, inflammatory lesions were the most common occurrences (n = 4,320; 63.24%). Benign and malignant tumors accounted for 7.66% (n = 523) and 1.9% (n = 130) of the occurrences, respectively. Significant associations were observed between nonneoplastic proliferative disorders and benign mesenchymal tumors in females, and between squamous cell carcinoma and leukoplakia in males. Most diagnoses were benign in nature and had an inflammatory etiology. The association of some demographic characteristics with the occurrence of lesions suggests that these characteristics should be considered in performing differential diagnoses.

Descriptors: Pathology, Oral; Risk; Epidemiology; Retrospective Study.

Introduction

Biopsy and histopathological analysis are important complementary diagnostic tools that are strongly influenced by clinical data.[1] The literature is vast regarding estimated occurrences of oral lesions such as oral cancer,[2-4] as well as odontogenic[5,6] and salivary gland tumors.[7-10] Contrarily, only few studies have documented the frequency of histologically confirmed lesions in adults,[11-14] and data are particularly scarce in Brazil. For instance, Simões *et al.*[15] and Nascimento *et al.*[16] evaluated 1,040 and 2,147 specimens, respectively, in studies conducted in oral pathology laboratories located in northeastern Brazil. Volkweis *et al.*[17] reported 435 cases from a hospital dental clinic in southern Brazil.

Some oral lesions may exhibit similar clinical features, thus rendering the diagnosis more challenging. For instance, the differential diagnosis between nonneoplastic proliferative disorders (NNPD) and benign mesenchymal tumors, and between leukoplakia and squamous cell carcinoma, often poses challenging situations, requiring prior knowledge of demographic characteristics associated with the occurrence of lesions in order to establish a clinical differential diagnosis.

This study aimed at describing the occurrence of oral lesions diagnosed from specimens submitted to oral pathology laboratory analysis in southern

Brazil over a 10-year period, and to assess demographic characteristics associated with oral lesions exhibiting similar clinical features.

Methodology

Study design and sample

This study retrospectively analyzed oral pathology archives from the School of Dentistry at the Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, southern Brazil. Every year, about 800 specimens are submitted by private and public health dental practitioners, and mostly by undergraduate students of the institution, for histopathological examination. In addition, the laboratory receives specimens obtained for research purposes from experimental studies. Data from 8,168 specimens recorded between 1995 and 2004 were retrieved from the laboratory files and entered into a dataset by a single researcher.

The study excluded 688 (8.42%) research material specimens of the 8,168 recorded in the laboratory files. In addition, 649 specimens (7.95%) from descriptive reports were also excluded from the analysis, on the grounds that the amount of tissue was inadequate for diagnosis. Of a total of 6,831 human specimens, age was specified in 92.5% of cases, and gender was specified in 6,797 cases (99.5%), 62.16% (n = 4,248) of which were females. Data on skin color were available in 6,148 records (90%), and showed that 5,304 individuals (77.64%) were white.

Ethical considerations

The study was approved by the Research Ethics Committee, School of Dentistry, UFRGS, Brazil (protocol no. 269/08).

Classification criteria

Lesions were divided into inflammatory lesions, benign tumors, malignant tumors, and others, using clinical diagnosis together with histological findings obtained from the records.

The group of inflammatory lesions was subdivided into the following categories:

- ***immunologically mediated lesions***, corresponding to lichen planus and pemphigus vulgaris;
- ***NNPD***, including reactional lesions induced by traumatic, chemical, or biological agents, such as inflammatory fibrous hyperplasia, pyogenic granuloma, and peripheral giant cell granuloma;
- ***periapical inflammatory lesions***, corresponding to inflammatory tissue damage induced by a necrotic pulp removed after tooth extraction or apical surgery; and
- others.

Benign tumors were subdivided into mesenchymal, odontogenic, epithelial (lining and glandular), osseous, and nervous tumors. Malignant tumors were subdivided into epithelial (lining and glandular) and mesenchymal tumors. Other diagnoses included:

- ***normal tissue***, corresponding basically to dental follicle;
- ***potentially malignant disorders***, including epithelial morphologic changes (leukoplakia) and actinic cheilitis;
- ***cysts***, including odontogenic, non-odontogenic, and unspecified cysts (inflammatory cysts were classified as inflammatory lesions);
- ***bone-pathology-related***, including peripheral ossifying fibroma, periapical cemental dysplasia, and traumatic bone cyst.

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 16 for Macintosh (SPSS Inc., Chicago, USA). The individual was used as a unit of analysis and the significance level was set at 5%. Individuals were divided into two age groups, using 50 years of age as the cutoff point, and classified as whites or nonwhites, according to self-reported skin color information made available in the records. Occurrence of oral lesions was expressed as an absolute value and percentage per diagnostic category.

Two challenging clinical situations involving differential diagnosis were selected and analyzed separately in order to investigate a possible association between demographic characteristics and oral lesions, as follows:

1. Two groups of oral lesions clinically presenting as exophytic-growing soft tissue nodules comprised of mesenchymal tissue were compared. Demographic characteristics for NNPD were determined using benign mesenchymal tumors (including fibroma, lipoma, hemangioma, lymphangioma, xanthoma, and

spindle cell lesions) as a comparison group.
2. Squamous cell carcinoma and leukoplakia were compared. Demographic risk indicators for squamous cell carcinoma were determined using leukoplakia as a comparison group.

The distribution of subjects with and without a condition, according to gender, age, and skin color was compared using Fisher's exact test. Univariate and multivariate logistic regression models were used to evaluate the association between oral lesions and gender, age, and skin color. Odds ratios (OR) and 95% confidence intervals (95% CI) were reported. Cases with missing data were excluded from the models.

Results

Tables 1 and 2 show the occurrence of oral lesions according to diagnostic category and histopathological report, respectively. Inflammatory lesions were the most common occurrences, diagnosed in 4,320 cases (63.24%). Periapical inflammatory lesions were the most common lesions in the inflammatory group. The second most common lesions were NNPD. In the benign tumor category, mesenchymal tumors (benign mesenchymal tumors) were the most frequently diagnosed. Malignant tumors were observed in 1.9% of cases. Potentially malignant disorders accounted for 2.46% of total cases. The frequency of other histopathological reports is shown in Table 2.

Table 1 - Occurrence of oral lesions according to diagnostic category.

Diagnostic category	Total cases	% of group	% of total
Inflammatory lesions	4,320	100	63.24
Periapical inflammatory lesions	1,932	44.72	28.28
Nonneoplastic proliferative disorder (NNPD)	934	21.62	13.67
Immunologically mediated lesions	59	1.37	0.86
Other inflammatory lesions	1,395	32.29	20.42
Benign tumors	523	100	7.66
Mesenchymal	286	54.64	4.19
Odontogenic	120	22.94	1.76
Epithelial (lining)	91	17.39	1.33
Epithelial (glandular)	14	2.67	0.20
Osseous	7	1.34	0.10
Nervous	5	0.96	0.07
Malignant tumors	130	100	1.90
Epithelial (lining)	114	87.69	1.67
Mesenchymal	10	7.69	0.15
Epithelial (glandular)	6	4.61	0.09
Other diagnoses	1,858	100	27.20
Normal tissue	1,507	81.11	22.06
Potentially malignant disorders	168	9.04	2.46
Cysts	146	7.86	2.14
Bone-pathology-related	37	1.99	0.54
Total	6,831		100

No significant differences were observed in the distribution of NNPD and benign mesenchymal tumors according to age and skin color (Table 3). The percentage of female patients with NNPD was significantly higher than that of those with benign mesenchymal tumors ($p = 0.02$). No multivariate analysis was performed to assess the association between NNPD and benign mesenchymal tumors with demographic characteristics, be-

Table 2 - Most common diagnoses (per diagnostic category) according to histopathological report.

Diagnoses	Total cases	% of group	% of total
Inflammatory lesions	4,320	100	63.24
Periapical inflammatory lesion	1,932	44.72	28.28
Inflammatory hyperplasia	719	16.64	10.53
Mucocele	185	4.28	2.71
Pyogenic granuloma	166	3.84	2.43
Pericoronitis	108	2.50	1.58
Giant cell lesion	49	1.13	0.72
Lichen Planus	28	0.65	0.41
Benign tumors	523	100	7.66
Fibroma	216	41.30	3.16
Papilloma	76	14.53	1.11
Keratocystic odontogenic tumor	38	7.27	0.56
Hemangioma	34	6.5	0.50
Odontoma	30	5.74	0.44
Malignant tumors	130	100	1.90
Squamous cell carcinoma	113	86.92	1.65
Undifferentiated malignant neoplasms	8	6.15	0.12
Mucoepidermoid carcinoma	4	3.08	0.06
Plasmacytoma	1	0.77	0.01
Lymphoma	1	0.77	0.01
Adenocarcinoma	1	0.77	0.01
Adenoid cystic carcinoma	1	0.77	0.01
Basal cell carcinoma	1	0.77	0.01
Normal tissue	1,507	100	22.06
Dental follicle	1,425	94.56	20.86
Potentially malignant disorders	168	100	2.46
Epithelial morphological changes (leukoplakia)	152	90.48	2.23
Actinic cheilitis	16	9.52	0.23
Cysts	146	100	2.14
Odontogenic	122	83.56	1.79
Unspecified	16	10.96	0.23
Nonodontogenic	8	5.48	0.12
Bone-pathology-related	37	100	0.54
Peripheral ossifying fibroma	15	40.54	0.22
Benign fibro-osseous lesion	11	29.73	0.16
Traumatic bone cyst	9	24.32	0.13
Periapical cemental dysplasia	2	5.41	0.03

Table 3 - Distribution of subjects with exophytic-growing oral nodules (nonneoplastic proliferative disorder and benign mesenchymal tumors), leukoplakia and squamous cell carcinoma according to demographic characteristics.

Demographic characteristic	Nonneoplastic proliferative disorder	Benign mesenchymal tumor	p*	Leukoplakia	Squamous cell carcinoma	p*
	n (%)	n (%)		n (%)	n (%)	
Age						
30-49 years	116 (15.5)	29 (13.2)		20 (14.6)	6 (6.0)	
≥ 50 years	632 (84.5)	191 (86.8)	0.45	117 (85.4)	94 (94.0)	0.06
Gender						
Male	184 (24.6)	73 (33.2)		70 (51.1)	72 (72.0)	
Female	564 (75.4)	147 (66.8)	0.02	67 (48.9)	28 (28.0)	0.001
Skin color						
White	652 (87.2)	194 (88.2)		123 (89.8)	88 (88.0)	
Nonwhite	96 (12.8)	26 (11.8)	0.73	14 (10.2)	12 (12.0)	0.68
Total	748 (100.0)	220 (100.0)		137 (100.0)	100 (100.0)	

* Fisher's exact test.

Table 4 - Univariate logistic regression analysis of the association between nonneoplastic proliferative disorder and demographic characteristics (benign mesenchymal tumor as a comparison group).

Demographic characteristic	OR (95% CI)	p
Age		
30-49 years	1	
≥ 50 years	1.21 (0.78 – 1.87)	0.40
Gender		
Male	1	
Female	1.52 (1.10 – 2.11)	0.01
Skin color		
White	1	
Nonwhite	0.91 (0.57 – 1.45)	0.69

CI = confidence interval; OR = odds ratio

Table 5 - Logistic regression analysis of the association between squamous cell carcinoma and demographic characteristics (leukoplakia as a comparison group).

Demographic characteristic	OR (95% CI)	p
Adjusted estimates		
Age		
30-49 years	1	
≥ 50 years	2.95 (1.12 – 7.79)	0.03
Gender		
Male	1	
Female	0.39 (0.22 – 0.68)	0.001

CI = confidence interval; OR = odds ratio.

cause only gender was found to be significantly associated with the occurrence of NNPD (OR = 1.52, p = 0.01; Table 4).

The percentage of females with squamous cell carcinoma (28%) was lower than that of those with leukoplakia (48.9%) (p = 0.001, Table 3). There were no significant differences in the distribution of carcinoma and leukoplakia, according to age and skin color. In the multivariable logistic regression model (Table 5), significant associations were observed for age and gender. Females had a 61% lower chance of developing squamous cell carcinoma than males (p = 0.001). Patients over 50 years of age were 2.68 times more likely to have squamous cell carcinoma than younger individuals (p = 0.03).

Discussion

The present study demonstrated that the overall distribution of lesions analysed in a Brazilian oral pathology laboratory was similar to that observed in other laboratories in the United Kingdom,[11] United States of America[12-14] and Brazil.[15-17] Most specimens analyzed in this reference oral pathology laboratory were diagnosed over a 10-year period as inflammatory lesions or normal tissue. Benign and malignant tumors were found in only 7.66% and 1.9% of specimens, respectively.

The majority of specimens analyzed corresponded to inflammatory lesions, corroborating data from pre-

vious studies.[11-17] Periapical inflammatory lesions and NNPD were the most frequent lesions in this diagnostic category. The frequency of periapical inflammatory lesions was similar to that reported by Jones and Franklin[11] and Baskar,[14] but much higher than that described by Weir *et al*.,[12] Simões *et al*.,[15] Nascimento *et al*.[16] and Volkweis *et al*.[17] This finding may be related to the profile of our sample, in which most patients sought tooth extraction as a treatment for decayed teeth usually associated with periapical inflammatory lesions. Moreover, it is important to emphasize that specimen sources vary considerably among oral pathology laboratories. Weir *et al*.[12] reported that 80% of their sample was obtained from a private office, which could affect the pattern of lesion occurrence. Unfortunately, comparisons with other studies are difficult, because this information is usually not provided.[11,15,16]

Inflammatory hyperplasia was the major entity found among NNPD cases, which is consistent with data from other studies.[11,13,16] The slightly higher prevalence of this pathological condition may be explained in part by the high prevalence of edentulous individuals in Brazil,[18] who tend to use the same prosthesis over decades or resort to low-cost prosthetic rehabilitation[19] under inappropriate conditions because of their low socioeconomic status.

Females had a higher occurrence of NNPD and benign mesenchymal tumors than males. These data may reflect the fact that women seek oral health services more often than men, in accordance with epidemiological studies reporting that males generally have a poorer health status than females.[20] Women were also more likely to have NNPD than men, when compared to benign mesenchymal tumors, a finding that may be attributed to a high frequency of prosthesis use among women, as demonstrated in a previous study conducted in the same geographic region.[19]

Fibroma was the most frequent diagnosis in the benign tumor group, supporting previous findings reported in the literature.[12,15] In contrast, Jones and Franklin[11] reported a high occurrence of squamous papillomas and a low proportion of fibromas.[11] These contradictory findings may be attributed to differences in the immunological profile of the populations, since squamous papillomas are associated to human papillomavirus,[21] and also to the histopathological criteria used for oral fibroma.[22]

Malignant tumors accounted for 1.9% of specimens, which is in accordance with previous reports.[12,13,16] Men older than 50 years of age were more closely associated with squamous cell carcinoma when leukoplakia was used as a reference group, reinforcing associations observed in previous studies.[13] This association is probably an effect of long-term exposure to risk factors such as tobacco and alcohol. Although men were more likely to have squamous cell carcinoma than women, it has been demonstrated that the male-female ratio disparity has decreased over the past years, probably because of a change in women's behavior in relation to smoking and alcohol consumption.[23,24]

It has been demonstrated that some factors, such as age, gender, socioeconomic status, prosthesis use, smoking and alcohol consumption, may be associated to oral lesions.[19] Unfortunately, these data are frequently not informed by surgeons when histopathological evaluation is requested. The associations related to gender and age observed in the present study could be explained by the cumulative effects of smoking and alcohol consumption. Since information regarding behavioral factors was not available in the files of the Laboratory, we were unable to evaluate these factors in the present study.

Conclusion

In conclusion, most diagnoses were benign in nature and had an inflammatory etiology. Age and gender may be considered demographic characteristics to be used for the differential diagnosis of major oral lesions.

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