Biopsied Oral Soft Tissue Lesions in Kuwait: A Six-Year Retrospective Analysis

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Key Words

Oral biopsies · Oral mucosal lesions · Oral cancer · Prevalence · Kuwait

Abstract

Objectives: The aim of this study was to determine the relative frequency of biopsied oral soft tissue lesions in Kuwait.

Materials and Methods: Biopsy records and microscopic sections of all oral soft tissue biopsies seen in the Department of Histopathology at Al-Amiri Hospital, Kuwait, between January 2004 and December 2009 were reviewed. The biopsies were divided into two major groups; group 1: nonneoplastic lesions, and group 2: neoplastic lesions. Group 1 was subdivided into reactive, inflammatory, cyst/cyst-like, dysplastic, and pigmented lesions. Group 2 was subdivided into epithelial and mesenchymal lesions, and also into benign and malignant lesions. **Results:** Of the 858 biopsies, 732 (85.3%) were nonneoplastic while the remaining 126 (14.7%) were neoplastic. In group 1, more than half of the lesions were within the reactive subgroup ($n = 386$; 52.7%) while in group 2, 94 (74.6%) lesions were epithelial in origin and 32 (25.4%) were mesenchymal. In addition, 70 (55.6%) lesions were malignant and 56 (44.4%) were benign. Of the 858 biopsies, the most common lesions were fibrous hyperplasias: 178 (20.7%); mucocoeles: 110 (12.8%); pyogenic granulomas: 94 (11.0%); squamous cell carcinomas: 56 (6.5%),

and lichenoid mucositis: 49 (5.7%). **Conclusions:** The majority of the lesions were nonneoplastic and were related to local irritation or trauma. Most neoplastic lesions were epithelial in origin. Oral squamous cell carcinoma was one of the most prevalent oral lesions highlighting the importance of prevention, early detection and diagnosis of oral cancer.

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Introduction

The oral mucosa has been considered as a mirror of general health. It can be affected by a wide range of reactive, infectious, cystic, precancerous, and neoplastic lesions and conditions, some of which could pose a significant health problem [1, 2]. While the majority of the non-neoplastic lesions of the oral cavity are limited and harmless, certain lesions are considered premalignant and others can result in serious consequences, even death, if untreated [3]. Benign oral soft tissue neoplasms can also be locally aggressive, and oral malignancies are associated with high morbidity and mortality rates [4, 5].

Histopathologic examination of the oral biopsies is often required to confirm the clinical diagnosis and establish a definitive diagnosis in order to provide appropriate treatment. Collecting data on biopsied oral lesions provides baseline information about the degree of occur-

rence of oral lesions and the extent of the problem prevailing in a certain population. There are several studies from around the world on the relative frequency of biopsied oral mucosal lesions [6–9]. Data regarding biopsied jaw lesions in Kuwait have been reported previously [10], but, to the best of our knowledge, there have been no studies on biopsied oral mucosal lesions. The aim of this study was to determine the relative frequency of biopsied oral soft tissue lesions seen at Al-Amiri Hospital, Kuwait, over a 6-year period.

Materials and Methods

The oral biopsy records of the Department of Histopathology at Al-Amiri Hospital, one of the 5 major referral government hospitals in Kuwait, were reviewed retrospectively for all soft tissue biopsies seen from January 2004 to December 2009. The biopsies included in this study were received from dentists, mainly oral surgeons, in specialty dental centers as well as from the hospital itself. Hematoxylin and eosin-stained sections were reevaluated by 2 pathologists (M.A. and J.M.). Biopsies were divided into 2 major groups; group 1: nonneoplastic and group 2: neoplastic lesions. Group 1 was subdivided into reactive, inflammatory, cyst/cyst-like, dysplastic, and pigmented lesions. Group 2 was subdivided into epithelial and mesenchymal lesions, and also into benign and malignant lesions. Clinical data, i.e. age, sex and location, were collected. Reexcised and recurrent lesions were excluded from the study. Data were recorded and analyzed using the Statistical Package for the Social Sciences for Windows 17.0 (SPSS Inc., Chicago, Ill., USA). The study was approved by the Joint Committee for the Protection of Human Subjects in Research.

Results

Of the 1,243 recorded oral biopsies, 858 (69.0%) were oral soft tissue lesions, while the remaining 385 (31.0%) were hard tissue lesions. Of the 858 oral soft tissue lesions, 457 (53.3%) were found in men and 401 (46.7%) in women. The mean age of the patients was 38.9 ± 17.4 years. Of the 858 biopsies, 732 (85.3%) lesions were nonneoplastic (group 1) and the remaining 126 (14.7%) were neoplastic lesions (group 2).

Within the nonneoplastic group (table 1), reactive lesions were 386 (52.7%); inflammatory: 199 (27.2%); cyst/cyst-like: 119 (16.3%); dysplastic: 16 (2.2%), and pigmented lesions: 12 (1.6%). Within the reactive subgroup, the most common cases were fibrous hyperplasias: 178 (46.1%), followed by pyogenic granulomas: 94 (24.4%). Within the inflammatory subgroup, the most common were lichenoid mucositis: 49 (24.6%), followed by nonspecific ulcers: 36 (18.1%). The majority of the cyst/cyst-like

lesions were mucocoeles: 110 (92.4%). Most of the lesions within the dysplastic subgroup were epithelial dysplasias: 14 (87.5%).

Within the neoplastic group (table 2), lesions of epithelial origin were 94 (74.6%) and mesenchymal: 32 (25.4%). Of the neoplastic lesions, the most common were squamous cell carcinomas: 56 (44.4%), followed by squamous papillomas: 16 (12.7%). In addition, 70 (55.6%) lesions were malignant and 56 (44.4%) were benign. Squamous cell carcinomas accounted for the majority (80.0%) of malignant neoplasms. Fifteen salivary gland tumors were found in this study, 12 of which (5 benign and 7 malignant) were from the minor salivary glands.

Of the 858 cases, 171 (19.9%) occurred in the gingiva/alveolar ridge, 174 (20.3%) in the lower lip, 21 (2.4%) in the upper lip, 230 (26.8%) in the buccal mucosa/parotid (cheek), 48 (5.6%) in the palate, 163 (19.0%) in the tongue, and 51 (5.9%) in the floor of the mouth (table 3). Of the buccal mucosa/parotid lesions, 6 lesions were found in the parotid glands; sialadenitis ($n = 2$); benign lympho-epithelial lesion/Sjögren syndrome ($n = 1$); pleomorphic adenoma ($n = 1$); Warthin's tumor ($n = 1$); and mucoepidermoid carcinoma ($n = 1$). Of the lesions in the floor of the mouth, 12 were found in the submandibular glands; sialadenitis ($n = 7$), sialolithiasis ($n = 5$) and 2 cases of sialadenitis were found in the sublingual glands.

Overall, fibrous hyperplasias ($n = 178$; 20.7%) were the most commonly biopsied oral mucosal lesions, followed by mucocoeles ($n = 110$; 12.8%), pyogenic granulomas ($n = 94$; 11.0%), squamous cell carcinomas ($n = 56$; 6.5%), and lichenoid mucositis (lichen planus/lichenoid reaction) ($n = 49$; 5.7%). Fibrous hyperplasias were the lesions most commonly biopsied from the gingiva/alveolar ridge, buccal mucosa and the tongue. The second most common lesions were pyogenic granulomas, biopsied from the gingiva/alveolar ridge; squamous cell carcinomas, biopsied from the buccal mucosa, and nonspecific ulcers, biopsied from the tongue. Mucocoeles and squamous papillomas were the lesions most commonly biopsied from the lower lip and the palate, respectively (table 3).

Discussion

A wide range of lesions were found in this study and most of the biopsies were from the oral mucosa, accounting for slightly more than two thirds of the total, as seen in previous studies [6–8]. More mucosal biopsies were found in men than women. However, Sklavounou-Andrikopoulou et al. [9] observed an equal gender distribu-

Table 1. Frequency of nonneoplastic lesions (group 1) and their distribution according to sex and age (n = 732)

Diagnosis	n (%) ¹	n (%) ²	Sex		Age, years (mean ± SD)
			male	female	
Reactive					
Fibrous hyperplasia	178 (24.3)	178 (46.1)	88	90	39.2 ± 15.8
Pyogenic granuloma	94 (12.8)	94 (24.4)	54	40	34.8 ± 16.2
Hyperkeratosis	31 (4.2)	31 (8.0)	21	10	48.9 ± 14.8
Giant cell fibroma	22 (3.0)	22 (5.7)	9	13	36.1 ± 17.7
Peripheral ossifying fibroma	19 (2.6)	19 (4.9)	9	10	32.4 ± 9.7
Peripheral giant cell granuloma	12 (1.6)	12 (3.1)	7	5	44.0 ± 21.9
Reactive lymphoid hyperplasia	11 (1.5)	11 (2.8)	6	5	39.1 ± 17.1
Drug-induced gingival hyperplasia	6 (0.8)	6 (1.6)	1	5	30.5 ± 12.3
Epulis fissuratum	4 (0.5)	4 (1.0)	2	2	52.7 ± 18.6
Varix	4 (0.5)	4 (1.0)	3	1	39.5 ± 7.5
Others ³	5 (0.7)	5 (1.5)	3	2	
Subtotal	386 (52.7)	386 (100.0)			
Inflammatory					
Lichenoid mucositis	49 (6.7)	49 (24.6)	28	21	44.0 ± 11.5
Nonspecific ulcer	36 (4.9)	36 (18.1)	19	17	47.1 ± 19.2
Sialadenitis	21 (2.9)	21 (10.6)	12	9	37.0 ± 17.0
Nonspecific mucositis	16 (2.2)	16 (8.0)	9	7	40.1 ± 11.9
Candidiasis	14 (1.9)	14 (7.0)	8	6	51.3 ± 7.4
Pemphigus vulgaris	13 (1.8)	13 (6.5)	3	10	46.8 ± 12.8
Foreign body granuloma	13 (1.8)	13 (6.5)	6	7	39.1 ± 13.6
Sialolithiasis	7 (1.0)	7 (3.5)	5	2	45.3 ± 13.4
Traumatic ulcerative granuloma	6 (0.8)	6 (3.0)	5	1	46.6 ± 15.5
Others ⁴	24 (3.3)	24 (12.0)	12	12	
Subtotal	199 (27.2)	199 (100.0)			
Pigmented					
Melanotic macule	8 (1.1)	8 (66.7)	0	8	35.4 ± 13.8
Amalgam tattoo	4 (0.5)	4 (33.3)	0	4	39.0 ± 6.2
Subtotal	12 (1.6)	12 (100.0)			
Cyst/cyst-like					
Mucocele	110 (15.0)	110 (92.4)	67	43	20.6 ± 12.3
Lymphoepithelial cyst	4 (0.5)	4 (3.4)	3	1	40.0 ± 16.8
Mucous retention cyst	2 (0.3)	2 (1.7)	1	1	63.0 ± 4.2
Ranula	2 (0.3)	2 (1.7)	1	1	31.0 ± 1.4
Nasolabial cyst	1 (0.1)	1 (0.8)	1	0	45.0
Subtotal	119 (16.3)	119 (100.0)			
Dysplastic					
Epithelial dysplasia	14 (1.9)	14 (87.5)	11	3	53.5 ± 10.6
Oral submucous fibrosis	2 (0.3)	2 (12.5)	0	2	35.5 ± 12.0
Subtotal	16 (2.2)	16 (100.0)			
Total	732 (100.0)	732	394	338	

¹ Percentages within group are shown in parentheses and were calculated from a total of 732 nonneoplastic lesions (group 1).

² Percentages within subgroup are shown in parentheses and were calculated based on the subtotal of each subgroup. ³ Verruciform xanthoma (n = 1), traumatic neuroma (n = 1), nodular fasciitis (n = 1), adenomatoid hyperplasia (n = 1) and angina bullosa

(n = 1). ⁴ Abscess (n = 5), erythema migrans (n = 4), actinomycosis (n = 3), tuberculosis (n = 2), mucous membrane pemphigoid (n = 2), benign lymphoepithelial lesion/Sjögren syndrome (n = 2), plasma cell gingivitis (n = 2), Wegener's granulomatosis (n = 1), herpetic stomatitis (n = 1), granulomatous inflammation (n = 1) and erythema multiforme (n = 1).

Table 2. Frequency of neoplastic lesions (group 2) and their distribution according to sex and age (n = 126)

Diagnosis	n (%) ¹	n (%) ²	Sex		Age, years (mean $\pm$ SD)
			male	female	
Epithelial					
Squamous cell carcinoma	56 (44.4)	56 (59.6)	28	28	53.9 $\pm$ 13.9
Squamous papilloma	16 (12.7)	17 (17.0)	9	7	41.6 $\pm$ 14.7
Mucoepidermoid carcinoma	5 (4.0)	5 (5.3)	3	2	49.0 $\pm$ 12.4
Pleomorphic adenoma	5 (4.0)	5 (5.3)	1	4	36.4 $\pm$ 20.7
Ameloblastoma (peripheral)	3 (2.4)	3 (3.2)	1	2	52.0 $\pm$ 15.7
Verrucous carcinoma	2 (1.6)	2 (2.1)	2	0	59.5 $\pm$ 10.6
Carcinoma ex pleomorphic adenoma	2 (1.6)	2 (2.1)	1	1	35.5 $\pm$ 30.4
Others ³	5 (4.0)	5 (5.3)	4	1	
Subtotal	94 (74.6)	94 (100.0)			
Mesenchymal					
Hemangioma	7 (5.6)	7 (21.9)	4	3	49.7 $\pm$ 16.7
Fibrolipoma	6 (4.8)	6 (18.8)	1	5	41.0 $\pm$ 13.6
Lymphangioma	4 (3.2)	4 (12.5)	3	1	26.8 $\pm$ 17.7
Neurilemmoma	3 (2.4)	3 (9.4)	0	3	15.0 $\pm$ 7.2
Peripheral odontogenic fibroma	3 (2.4)	3 (9.4)	3	0	48.0 $\pm$ 16.1
Neurofibroma	2 (1.6)	2 (6.3)	2	0	41.0 $\pm$ 4.2
Lipoma	2 (1.6)	2 (6.3)	1	1	38.5 $\pm$ 17.7
Lymphoma	2 (1.6)	2 (6.3)	0	2	59.5 $\pm$ 4.9
Others ⁴	3 (2.4)	3 (9.3)	0	3	
Subtotal	32 (25.4)	32 (100.0)			
Total	126 (100.0)	126	63	63	

¹ Percentages within group are shown in parentheses and were calculated from a total of 126 neoplastic lesions (group 2). ² Percentages within subgroup are shown in parentheses and were calculated based on the subtotal of each subgroup. ³ Warthin's tumor

(n = 1), myoepithelioma (n = 1), keratoacanthoma (n = 1), adenoid cystic carcinoma (n = 1) and metastatic carcinoma (n = 1). ⁴ Congenital epulis (n = 1), fibromatosis (n = 1) and malignant giant cell tumor (n = 1).

tion of biopsies in a study limited to Greek children and adolescents while studies on Brazilian elderly populations showed more biopsies in females than males [6, 11]. The higher number of mucosal biopsies from females in these studies was related to cultural bias. In Brazil, women visit dental clinics more frequently, wear more dental prostheses than men, and have more access to oral health care for sociopolitical reasons. Most of the biopsies in our study were from the buccal and labial mucosa, followed closely by the gingiva/alveolar mucosa and tongue. Previous studies have also shown these sites to be common sites of mucosal biopsies [6, 9, 12].

In our study, nonneoplastic lesions were more common than neoplastic lesions, as in several previous studies [1, 6, 7, 9, 11, 13–15]. The reactive lesions comprised more than half of the nonneoplastic group, which is similar to the findings in other studies [9, 11]. Most of these lesions represent an exuberant response to local irritation

and trauma [16]. Local irritants such as calculus have been reported to be highly prevalent among the Kuwaiti population due to inadequate oral hygiene practices and irregular dental visits [17–19]. Fibrous hyperplasia was the most frequently encountered lesion in our study, and was the most commonly biopsied lesion from the gingiva/alveolar mucosa, buccal mucosa and tongue; these findings are similar to that of previous studies [1, 6, 20]. These studies have also shown fibrous hyperplasia to be more common in the 4th and 5th decades of life [1, 20]. In our study the mean age of occurrence was 39.2 years.

Mucocoele was the second most frequent mucosal lesion as in the study by Tay [15]. Mucocoeles, which are pseudocysts lined by granulation tissue and are related to local trauma, were the most common cyst/cyst-like lesions. True epithelium-lined cysts of developmental origin such as mucous retention cysts were relatively rare as seen in previous reports [7, 14]. Consistent with other studies,

Table 3. Site distribution of all biopsied lesions (n = 858)

Diagnosis	Site							n (% of total)
	gingiva	lower lip	upper lip	cheek	palate	tongue	floor of mouth	
Fibrous hyperplasia	46	22	3	61	3	41	2	178 (20.7)
Mucocele		90		4		12	4	110 (12.8)
Pyogenic granuloma	43	12	5	12	6	14	2	94 (11.0)
Squamous cell carcinoma	11			22	4	16	3	56 (6.5)
Lichenoid mucositis	1	3		36	1	8		49 (5.7)
Nonspecific ulcer	2	6	1	7	1	17	2	36 (4.2)
Hyperkeratosis	6	7	1	2	6	8	1	31 (3.6)
Giant cell fibroma	2	2		7	2	9		22 (2.6)
Sialadenitis		5	1	4	1	1	9	21 (2.4)
Peripheral ossifying fibroma	19							19 (2.2)
Nonspecific mucositis		6	1	5	2	2		16 (1.9)
Squamous papilloma	1	1		3	8	3		16 (1.9)
Candidiasis				6	1	7		14 (1.6)
Epithelial dysplasia		1	1	4	1	7		14 (1.6)
Pemphigus vulgaris	1	2		9	1			13 (1.5)
Foreign body granuloma		1	1	6	3	1	1	13 (1.5)
Peripheral giant cell granuloma	12							12 (1.4)
Reactive lymphoid hyperplasia				2		2	7	11 (1.3)
Melanotic macule	1	1	2	2	1	1		8 (0.9)
Sialolithiasis		2					5	7 (0.8)
Hemangioma	1	2	1	3				7 (0.8)
Drug-induced gingival hyperplasia	6							6 (0.7)
Traumatic ulcerative granuloma				2		3	1	6 (0.7)
Fibroilipoma		1		5				6 (0.7)
Abscess	4						1	5 (0.6)
Mucoepidermoid carcinoma				1	1	2	1	5 (0.6)
Pleomorphic adenoma			1	2	2			5 (0.6)
Epulis fissuratum				4				4 (0.5)
Varix		2	1			1		4 (0.5)
Erythema migrans						4		4 (0.5)
Amalgam tattoo	2			2				4 (0.5)
Lymphoepithelial cyst						2	2	4 (0.5)
Lymphangioma				2		1	1	4 (0.5)
Peripheral ameloblastoma	3							3 (0.3)
Neurilemmoma				2		1		3 (0.3)
Peripheral odontogenic fibroma	3							3 (0.3)
Actinomycosis				2			1	3 (0.3)
Others ¹	7	8	2	13	4		8	42 (4.9)
Total	171 (19.9)	174 (20.3)	21 (2.4)	230 (26.8)	48 (5.6)	163 (19)	51 (5.9)	858 (100)

¹ Tuberculosis (n = 2), mucous membrane pemphigoid (n = 2), benign lymphoepithelial lesion/Sjögren syndrome (n = 2), plasma cell gingivitis (n = 2), mucous retention cyst (n = 2), ranula (n = 2), oral submucous fibrosis (n = 2), verrucous carcinoma (n = 2), carcinoma ex pleomorphic adenoma (n = 2), neurofibroma (n = 2), lipoma (n = 2), lymphoma (n = 2), verruciform xanthoma (n = 1), traumatic neuroma (n = 1), nodular fascitis (n = 1), adeno-

matoid hyperplasia (n = 1), angina bullosa (n = 1), Wegener's granulomatosis (n = 1), herpetic stomatitis (n = 1), granulomatous inflammation (n = 1), erythema multiforme (n = 1), nasolabial cyst (n = 1), Warthin's tumor (n = 1), myoepithelioma (n = 1), keratoacanthoma (n = 1), adenoid cystic carcinoma (n = 1), metastatic carcinoma (n = 1), congenital epulis (n = 1), fibromatosis (n = 1), malignant giant cell tumor (n = 1).

mucocles were more common on the lower lip and in the younger age group (mean age = 20.6 years) [9, 12–14]. This may be explained by the fact that both the younger age group and the lower lip are more prone to trauma.

Pyogenic granuloma ranked third among oral mucosal lesions, confirming studies from Singapore, Greece, Brazil and Thailand, which have also reported it to be one of the most common oral mucosal lesions [6, 9, 13, 15]. It was mostly found on the gingiva, which is similar to previous studies [1, 7, 13, 20]. Gingival irritation that results from poor oral hygiene may be a precipitating factor for the striking gingival predilection.

Lichenoid mucositis was the most common lesion in the inflammatory subgroup. It represents a cell-mediated immune response to an unknown cause; some cases are induced by a variety of medications or dental restorative materials [21]. The commonly affected sites are the buccal mucosa followed by the tongue, which was also observed in our study. It is a common mucosal pathology in adult patients [1] as in our study, where the mean age was 44 years.

In our study, the prevalence of epithelial neoplasms was notably higher than that of mesenchymal neoplasms. Squamous cell carcinoma was the most common epithelial neoplasm, accounting for more than three-fourth of all malignancies; the mean age of the patients was 53.9 years. These findings are in agreement with most previous studies [1, 2, 6, 7, 11, 15]; however, studies restricted to pediatric population showed that epithelial malignancies were less common than mesenchymal malignancies [9, 12, 14]. This is probably due to the low frequency of squamous cell carcinoma in the pediatric population as it is associated with multiple abnormal cellular events that result from chronic and excessive exposure to carcinogens, found mainly in tobacco and alcohol, over an extended time period [3].

The prevalence of oral squamous cell carcinomas was higher than that of dysplastic lesions, indicating a delay in the detection or diagnosis of suspicious oral lesions. It is generally accepted that the development of oral cancer is preceded by an identifiable precursor lesion [22–24]. Failure of the dentists to conduct a systematic oral examination could explain the delay in the detection of such lesions. In addition, failure of the general dental practitioners to refer suspicious oral lesions to oral surgeons for further investigations (biopsy) could be a possible reason for the delayed diagnosis. Another possible explanation could be that many patients in Kuwait seek dental care only when they have pain [19]. Most oral precancerous and early cancerous lesions are not painful

and, hence, go undetected as the patients either delay in seeking dental care or fail to comply with the dentist's decision to biopsy [3].

The finding that malignant neoplasms were more common than benign neoplasms is in contrast to other studies [6, 12]. However, in those studies, fibromas, which occurred at a high frequency, were considered as benign neoplasms and not as reactive lesions. Fibrous hyperplasia (fibroma), which was the most common lesion in our study, was included with the reactive lesions instead and squamous papilloma was the most common benign neoplasm. In addition to being the most common benign neoplasm, it was also the most common benign neoplasm of epithelial origin, similar to the findings reported in most previous studies [1, 6, 7, 9, 12–15]. It was also more frequently found on the palate as seen in the reports by Dhanuthai et al. [13] and El-Gehani et al. [25].

In our study, pleomorphic adenoma, the most common benign salivary gland neoplasm, ranked second to papilloma as reported by Jones and Franklin [1]. The most frequent malignant salivary gland neoplasm was mucoepidermoid carcinoma similar to the findings of Dhanuthai et al. [13] and Jones and Franklin [1, 14]. Malignant minor salivary gland tumors (58.3%) were found to be more frequent than benign tumors, which is in agreement with the findings of Lukšić et al. [26] (59.0%), Jaber [27] (61.3%) and Adeyemi et al. [28] (62.0%).

Conclusions

This study provided important baseline data about the frequency and distribution of histologically diagnosed oral soft tissue lesions in Kuwait. The majority of the lesions were nonneoplastic and associated with local irritation or trauma. Most neoplastic lesions were epithelial in origin. Oral squamous cell carcinoma was one of the most prevalent oral mucosal lesions, even more than dysplastic epithelial lesions, thereby indicating the importance of the dentist's role in educating the patients in order to prevent oral cancer, and the need to look for and follow-up suspicious lesions to establish early diagnosis.

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