

A Retrospective Analysis of Oral Mucosa Pathologies: A Single-Center Trial

Oral Mukozal Patolojilere Ait Retrospektif Klinik Çalışma: Tek Merkeze Ait Sonuçlar

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Özet

Amaç: Oral skuamöz hücreli karsinom dünyada en sık görülen 6. tümör olarak karşımıza çıkmaktadır. Bununla birlikte pek çok hastalık oral mukozada lezyon oluşturabilmektedir. Bu çalışmada 10 yıllık süreçte kendi hasta serimize ait oral mukoza patolojilerini oluşturan lezyonlar histopatolojik tanılarına göre sınıflandırılmış ve tanılarına göre lezyonların yeri, yaş ve cinsiyet dağılımları tespit edilmiş ve malignite ile ilişkileri belirlenmeye çalışılmıştır.

Hastalar ve Yöntem: Çalışmamız 2002-2014 yılları arasında Başkent Üniversitesi, Tıp Fakültesi Konya Uygulama ve Araştırma hastanesi kulak burun boğaz hastalıkları bölümü tarafından tanı amacıyla biopsi alınarak patoloji laboratuvarına gönderilen 288 hastaya ait oral mukoza lezyonunun retrospektif analizini içermektedir. Hastalara ait histopatolojik tanı, yaş, cinsiyet ve lokalizasyon bilgisi patoloji rapor arşivinden elde edilmiştir. İstatistiksel tanımlayıcı analiz SPSS17.0 programı ile yapılmıştır.

Bulgular: Olguların büyük çoğunluğunu benign epitelyal proliferasyon ve reaktif patolojiler oluşturmaktadır (%22,7). Bu grupta en sık skuamöz papillom (n: 31; % 9,9) görülmüş olup bunu fibroepitelyal polip (n:24; %7,7) ve irritasyon fibromu (n:16; %5,1) izlemektedir. Benign patolojiler içerisinde oral mukozal dermatozlar en sık görülen ikinci lezyondur (n:63, % 21,8). Çalışmamızda 288 oral mukozal lezyonun % 15,3'ünü (n:44) malign patolojiler ve % 17,7'sini (n:51) prekanseröz lezyonlar oluşturmaktadır. Skuamöz hücreli karsinom tüm malign patolojilerin %95,5'idir. Tespit edilen premalign lezyonlar; skuamöz hücreli hiperplazi (n:47; 16%), orta dereceli displazi (n:2; % 0,7) ve likenoid displazidir (n:2; % 0,7). Skuamöz hücreli karsinom en sık dudakta lokalizedir. Kadın erkek oranı premalign lezyonlar için hemen hemen eşit olup skuamöz hücreli karsinom erkeklerde biraz daha fazladır (p>0.1).

Sonuç: Skuamöz hücreli karsinom, benign lezyonlar ve premalign lezyonlara göre daha yaşlı hastalarda görülmektedir. Çok geniş spektrumdaki birçok oral mukozal patolojinin benzer bir klinik görüntüsü olması klinisyenleri tanı aşamasında zorlayıcı bir unsurdur. Özellikle malign lezyonlarda erken teşhis hayat kurtarıcı olabilir. Bu nedenle patolojilere yönelik kendi serilerimizi oluşturmak önemlidir. Histopatolojik tanılarına göre sınıflandırılmış lezyonların lokalizasyon, yaş ve cinsiyet gibi bazı klinik özelliklerine göre dağılımını veren bu serimiz klinik tanıda yol gösterici ve kolaylaştırıcı olacaktır.

Anahtar kelimeler: Oral mukoza, kanser, patoloji

Abstract

Aim: Oral cancer is the sixth most common cancer worldwide however a wide range of diseases may affect the oral mucosa. We aim to determine the prevalence of the oral mucosal pathologies in our patient series and discuss the final diagnosis in relation to sex, age and subsite distribution.

Patients and Methods: This was a cross sectional descriptive study, including 288 patients with oral mucosal pathologies, diagnosed at Baskent University Konya Hospital between January 2002 and December 2014. Data were retrieved from archives of pathology laboratory, retrospectively. A commercially available statistical package (SPSS17.0) was used for descriptive statistical analysis.

Results: The results showed that benign epithelial proliferations and reactive pathologies were the most frequently diagnosed lesion, accounting for 22.7% of the total number of patients. Among this reactive pathologies, squamous papillomas were the most common (n: 31; 9,9%), followed by fibroepithelial polyps (n:24;7,7%) and irritation fibromas (n:16; 5,1%). Oral mucosal dermatoses were the second common benign lesions, accounting for 21,8% (n:63) of all cases. Of the 288 oral mucosal pathologies 15,3% (n:44) were malignant and 17,7% (n:51) were precancerous. Squamous cell carcinoma were comprised of 95,5% of all the malignant lesions. Premalignant lesions were with the following distribution: squamous cell hyperplasia (n:47; 16%), moderate dysplasia (n:2; 0,7%) and lichenoid dysplasia (n:2; 0,7%). Lip was the most frequently involved site for squamous cell carcinoma. The male to female ratio was almost equal in both sex for premalignant lesions however there was slight male predominance for squamous cell carcinoma (p>0.1). Squamous cell carcinoma was commonly seen in the older age group compared to benign and precancerous lesions.

Conclusion: The similar clinical appearance of oral mucosal pathologies in a very wide spectrum is a compelling element for clinicians in the process of diagnosis. Especially in malignant lesions early diagnosis may be life saving. Therefore, it is important to reveal our own series about these pathologies. This study, by demonstrating distribution of histopathologically classified lesions according to some clinical features such as location, age and gender, will guide and facilitate the clinical diagnosis.

Keywords: Oral mucosa, cancer, pathology

INTRODUCTION

A wide range of diseases may cause symptoms in

the oral mucosa. The disease affecting oral mucosa are infections, inflammatory and reactive conditions,

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trauma, immune disorders such as aphthous ulcers in Behcet's syndrome, skin disorders such as lichen planus, bullous dermatose, and tumors. Oral cancer is the sixth most common cancer worldwide, with a fairly high mortality (1). Squamous cell carcinoma (SCC) is the predominant malignancy that occurs in the oral cavity. Early detection and intervention is one of the great determinant of long-term patient survival in oral mucosal cancers. Diagnosis of oral mucosal lesions may be challenging for clinicians, because wide variety of diseases may present with similar appearance. According to the World Health Organization (WHO) classifications of head and neck tumors (2005) "a white patch or plaque that can not be scraped off and can not be characterized clinically or pathologically as any other disease" is defined as leukoplakia. Similarly, those of the red lesion defines as erythroplakia (2). Erythroplakia has higher risk of malignant transformation than that seen with leukoplakia (3). Authors reported that dysplasia ranges from 0.13% to 17.5% in leukoplakia and 14% to 50% in erythroplakia (4). However, any oral lesion such as candidiasis, leukoedema, whitesponge naevus, lichen planus, frictional keratosis, nicotine stomatitis, or malignancies can be seen as white appearance of oral leukoplakia. Therefore, one of the real dangers of oral neoplasm, is that in its early stages, it can go unnoticed. Most oral cavity tumors are diagnosed at an advanced stage, which contributes to the poor overall 5-year survival rate; even in developed countries. Diagnosis of wide variety of lesions that occur in the oral cavity is an essential part of clinical practice. An important element in establishing a diagnosis is knowledge of the lesions relative frequency, or prevalence at one point in time (5). Geographic variations in the prevalence and spectrum of oral lesions have been observed due to variations in culture, habits, environmental pollutants and genetical factors.

In this study we aimed to determine the spectrum of oral mucosal lesions which was diagnosed in our pathology department. We want to obtain data regarding their relation with some spesific features such as age, gender, subsite distribution and prevalence. Thus, such descriptive data may help clinicians in understanding the nature of the lesions.

PATIENTS AND METHODS

The study consisted of 288 patients who were examined at otorhinolaryngology department and underwent oral mucosal biopsies at Baskent University

Hospital, between 2002 and 2014. All pathology records diagnosed in pathology department at the same hospital were retrospectively evaluated.

Oral mucosal lesions were divided into 7 groups as "reactive, inflammatory and infectious, benign epithelial proliferations, dermatoses, benign tumors, premalignant lesions and malignant tumors". The World Health Organisation (WHO), "head and neck tumors histological classification of tumors" was used to subcategorize the histopathologic diagnosis of tumors. Tumours of the oral cavity may be either epithelial, mesenchymal, or haematolymphoid. The epithelial tumours were classified as those originating within the epithelial lining of the oral cavity and those derived from salivary gland tissue. In premalignant lesions, oral epithelial dysplasia were graded to traditional three-tiered grading system (mild, moderate, severe). Odontogenic cysts and odontogenic tumors were not included in the study group.

The data including sex, age and subsite localization were recorded according to histopathologic diagnosis of oral mucosal lesions from pathology reports. The "SPSS 17.0 for Windows" was used to perform descriptive statistical analysis.

RESULTS

From January 2002 through December 2014, 288 oral mucosal lesions have been detected. Of the 288 oral mucosal pathologies 67% (n:193) were benign; 17,7% (n:51) were precancerous and 15,3% (n:44) were malignant. The most common benign oral lesions were benign epithelial proliferations and reactive pathologies. Among these benign reactive pathologies, squamous papillomas (figure 1) comprised the majority of the lesions (n:31; 9,9%), followed by fibroepithelial polyps (n:24; 7,7%) and irritation fibromas (n:16; 5,1%). Oral mucosal dermatoses were the second common oral benign lesions, accounting for 21,8% (n:63) of all cases. Lichen planus (n:45; 14,4%) was the most common dermatoses, affecting the oral mucosa and is followed by bullous dermatoses (n:9; 2,9%). Among bullous dermatoses, pemphigus vulgaris accounts for 1.9% (n:6). In the malignant group, SCC comprised 95,5% (n:42) of all the malignant lesions (figure 2), in lesser numbers, malignant melanoma % 0,6 (n:2). The precursor lesions of the SCC had the following distribution: squamous cell hyperplasia (n:47; 16%) (figure3), moderate dysplasia (n:2; 0,7%) (figure 4) and lichenoid dysplasia (n:2; 0,7%). The distribution

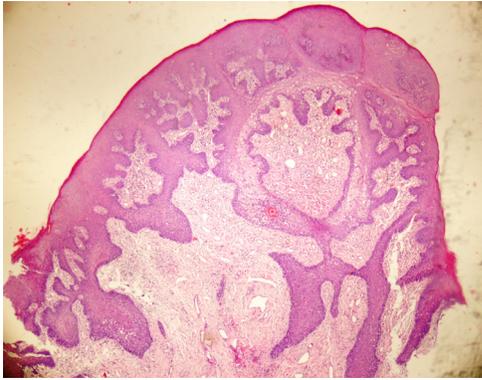


Figure 1. Squamous papillom is a lesion which is characterized finger-like projection lined by stratified squamous epithelium and contains a thin central connective tissue.

of all the lesions according to histopathological diagnoses has been listed in Table 1.

On the basis of site involvement; the majority of the benign lesions localized in buccal mucosa (n: 64; 22,2%) and were followed by the lip (n:52; 18,1%), tongue (n: 36; 12,5%), uvula (n:19; 6,6%), soft palate (n:3; %1) and floor of the mouth (n:3; %1). Squamous papillomas mostly localized in uvula (n:19/31; 61%), fibroepithelial polyps in tongue (n:13/24; 54%) and irritation fibromas in the buccal mucosa (n:10/16; 62,5%). Lichen planus (n: 25/46; 54%) and pemphigus vulgaris (n:6/6; 100%) commonly occurred in the buccal mucosa. Sites for SCC were lip (n:31; 10,8 %), followed by tongue (n:9; 3,1%). On the other hand, sites for premalignant lesions were lips (n:13; 4,5%), buccal mucosa (n:16; 5,6%), tongue (n:14; 4,9%), gingiva (n:6; 2,1%), soft palate (n:1; 0,3%), and hard palate (n:1; 0,3%). Table 2 shows the site of oral lesions in our patient group .

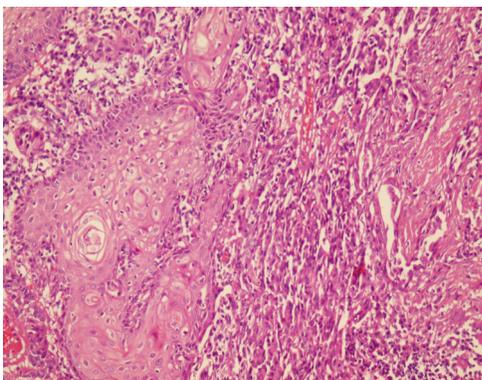


Figure 2. Squamous cell carcinoma showing malignant islands with keratin pearl formation and infiltrating cord of atypical cells.

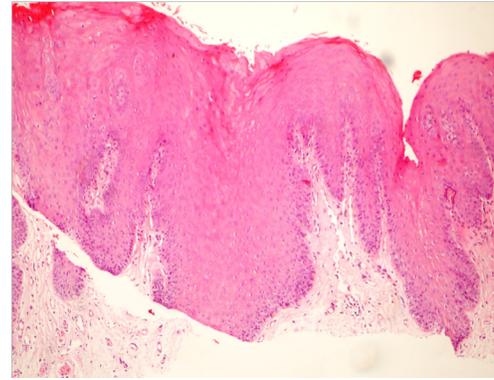


Figure 3. Squamous cell hyperplasia, with thickening of the epithelial layer and numerous folds.

Of the 288 patients 43,82% were males (n:126) and 56,3% were females (n:162). Benign lesions affected female at about 60,6 % (n: 117), and male at about 39,4% (n:76). 51% (n:26) of precancerous lesions affected male, and 49% (n: 25) affected female. Of the 42 patients presenting with SCC, 22 (52,5%) were male and 20 (47,5%) were female. Percentages and number of benign, precancerous, and malignant lesions according to location are given in table 2. The specific characteristics of the study population such as frequency, age, and gender are presented in Table 3.

DISCUSSION

This study revealed that benign oral pathologies are significantly more common than the malignancies. The spectrum of oral lesions in our population showed 67% benign lesions of various etiology and 15,3% malignant lesions in the form of SCC and malignant

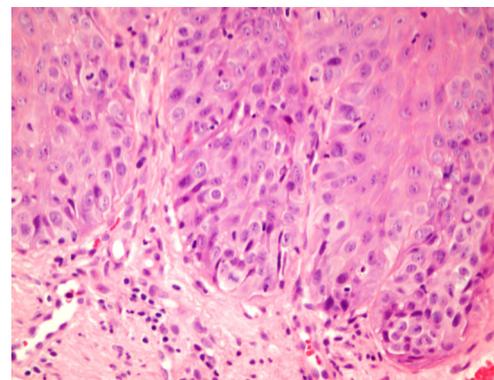


Figure 4. Moderate epithelial dysplasia. There is considerable cytological atypia which extends into the middle third of the epithelium. The lesion also demonstrates increased and abnormal mitoses in the basal layers.

Table 1. Distribution of the oral mucosal lesions according to histopathological diagnoses

		n	%
Infections, inflammatory conditions and reactive pathologies	Fibroepithelial polyp	24	7,7
	Traumatic (irritation) fibroma	16	5,1
	Ulcer, Granulation tissue	5	1,6
	Condyloma acuminatum	4	1,3
	Chronic inflammation	3	1
	Verruca Vulgaris	2	0,6
Benign Epithelial Pathologies	Squamous papillom	31	9,9
	Keratoacanthoma	3	1
	Papillary hyperplasia	3	1
Soft tissue	Hemangioma	14	4,5
	Pyogenic granuloma	9	2,9
	Lymphangioma	1	0,3
	Lipoma	1	0,3
Dermatoses	Lichen planus	45	14,4
	Bullous dermatoses (nonspecific)	9	2,9
	Pemphigus vulgaris	6	1,9
	Cicatricial pemphigoid	3	1
Epithelial precursor lesions	Squamous cell hyperplasia	46	14,7
	Moderate dysplasia	2	0,6
Malignant	Squamous cell carcinoma	42	14,5
	Malignant Melanoma	2	0,6
Others	Mucocele	6	1,9
	Pleomorphic adenoma	1	0,3
	Mature cystic teratom	2	0,6

melanoma. More than 90% of all oral cancers are SCC in the worldwide (5,6). Similar to the literature, our results showed that SCC comprised 95,5% of all the malignant lesions. It is known to be more common in older individuals and especially in men. However in our study, female to male ratio was almost equal. Increased tendency in females was reported in many publications. The authors thought that changing habits may lead to this outcome. The increase in females like in most European countries largely reflects the ongoing tobacco epidemic (7).

In the present study we found that 70% of SCC were localized in the lip. Although there are similar observation reported from different countries (8-10), some studies showed that the most commonly affected anatomic sites were the tongue, the floor of the oral cavity and buccal mucosa (11-15). The study from Turkey, similar to us, authors reported that the lip was the most common site for SCC followed by buccal mucosa, by anterior 2/3rd of tongue and floor of mouth (16). Exposure to different risk factors may be responsible for this regional variation. It is noticed that SCC frequently seen in buccal mucosa in Asian populations, due to betel quid/tobacco chewing habits (5).

Carcinogenesis is a slow multi-steps process, based on progressive accumulation of genetic events leading to the selection of clonal populations of transformed epithelial cells (17). According to the WHO, the steps of the transformation from normal epithelium to carcinoma is as follows: squamous cell hyperplasia, mild dysplasia, moderate dysplasia, severe dysplasia and carcinoma in-situ (2). Presence of oral epithelial dysplasia is the most important prognostic factor for malignant transformation. Dysplasia is present in a minority of leukoplakia but it is a consistent finding in erythroplakia. Although the features of a lesion, such as borders, site, size may be important in determining the malignancy potential, any lesion even a small cancer can mimic benign lesions. Therefore biopsy and histopathological examination is necessary for exact diagnosis. In the current study we found dysplasia in only 1,5% of all our specimens. It is interesting to note that both dysplasia and SCC mostly presented at lip. This finding may support stepwise progression in carcinogenesis and oral lesions in lip region should be more carefully evaluated by the clinicians.

The risk factors of oral SCC has been well presented. The use of tobacco and alcohol is strongly

Table 2. Site of oral mucosal lesions according to benign, precancerous and malignant pathologies.

Localization	Benign		Precancerous		Malignant	
	n	%	n	%	n	%
Lip	52	18,1	13	4,5	31	10,8
Buccal	64	22,2	16	5,6	1	0,3
Tongue	36	12,5	14	4,9	9	3,1
Uvula	19	6,6	0	0	0	0
Gingiva	15	5,2	6	2,1	0	0
Soft Palate	3	1,0	1	0,3	0	0
Hard Palate	1	0,3	1	0,3	2	0,7
Floor of mouth	3	1,0	0	0	1	0,3

linked to malign transformation. Other risk factors are familial cancer syndromes such as Li-Fraumeni syndrome, Lynch syndrome, and environmental factors such as diet (deficient in iron) and infectious diseases (Epstein Bar Virus (EBV) and Human Papilloma Virus (HPV)).

Although oral SCC principally affects patients over 50 years of age, in developing countries oral cancer presents at younger ages than those in high-income countries (18). We found that 73,2% of SCC patients were over 50 years old. Fourth and seventh decades of life are reported to be the mean ages for the first precursor lesion, but in the developing world it is found 5–10 years earlier (19). In the present study, a neglectable number of patient has been diagnosed with oral precancerous lesion before 40 years-old (2 squamous cell hyperplasia and 1 dysplasia in the second decade). In addition there were no SCC patients younger than third decade.

Another point of our findings is that mucocel, fibroepithelial polyp and pyogenic granuloma can be seen in pediatric age. We also found that hemangiomas, irritation fibromas and fibroepithelial polyps can be present in any age. Among benign lesions mucocele was the only lesion determined before age 40 .

Malignant melanoma was the second type of malignancy in the oral mucosa in this study. Mucosal melanomas of the head and neck comprise just over 1% of all melanomas and of these about 50% arise in the oral cavity. Although a uniform age distribution from 20–80 years, they arise in adults with an average age of about 55 (2). In most large series there is a male predominance. Although we have limited number of patient, similar to literature our patients were male and between 45- 63 years old.

Beside malignancies, the oral mucosa is also one of the most commonly affected area for dermatosis,

Table 3. Specific characteristics of oral mucosal lesions. (n:number of patients)

Frequency	Benign		Precancerous		Malignant	
	n	%	n	%	n	%
	193	67,0	51	17,7	44	15,3
Age (year)	n	%	n	%	n	%
1-10	3	1	0	0	0	0
11-20	10	3	3	1	0	0
21-30	21	7	0	0	0	0
31-40	24	8	4	1	0	0
41-50	35	12	11	3,8	4	1
51-60	39	13,5	14	4,9	6	2
61-70	36	12,5	10	3,5	14	4,9
71-80	19	6,5	8	2,7	10	3,5
81-90	6	2	1	1	9	0,3
91-100	0	0	0	0	1	1
Gender	n	%	n	%	n	%
Female	117	60,6	25	50	20	45,5
Male	76	39,4	26	50	24	54,5

inflammatory and reactive conditions, and viral diseases. In the present study, benign epithelial proliferations and reactive pathologies such as squamous papilloma and irritation fibroma were the first two common benign lesions. Similar to literature, we found that squamous papillomas mostly occurred in young to middle aged adults. Although papillomas are not considered to be associated with a risk of malignant transformation, of those with HPV related may be at increased risk for malignant transformation (20). HPV can be found in oral lesions of different clinical appearances and significance, ranging from benign warts to malignant neoplasms. In the study we found 4 patient with condyloma acuminatum which composed of 1,3% of all cases. Although condyloma acuminatum is considered the HPV-induced benign epithelial hyperplasia of the oral mucosa, HPV immunohistochemistry had not been applied before. On the other hand, in another studies, authors described that 25.9% of the tumors had detectable HPV 35.6% of those in the oropharynx and 23.5% in the oral cavity lesions (21,22). Nevertheless, the role of HPV in oral carcinogenesis is still controversial (23).

Oral mucosal dermatoses were the second major group of disease in our study population. Among oral inflammatory dermatoses, lichen planus was more common than bullous disease. Our findings are also in agreement with general nature of oral lichen planus which is most prevalent among women between ages in the fourth to fifth decades of life, and the buccal mucosa being the most common site. We found that 54% of lichen planus occurred in the buccal mucosa. In this study, gingiva was seen to be a rare localization of lichen planus, with an exception that all of the cicatricial pemphigoid cases were of gingival origin.

In conclusion, oral mucosal lesions can be detected by visual inspection. Although they are quite varied in appearance, a small cancer can mimic most of the other benign lesions commonly seen in oral cavity. Clinically, early-stage SCC and epithelial dysplasia may manifest as erythroplakia or leukoplakia. However, especially in malignant lesions early diagnosis may be life saving. Therefore, it is important to reveal our own series about these pathologies. This study, by demonstrating distribution of histopathologically classified lesions according to some clinical features such as location, age and gender, will guide and facilitate the clinical diagnosis.

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