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Demographic and Histopathological Features of Oral Mucosa Lesions in Kırşehir Region: A Retrospective Cross-Sectional Study

Kırşehir Yöresinde Oral Mukoza Lezyonlarının Demografik ve Histopatolojik Özellikleri: Retrospektif Kesitsel Bir Çalışma

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ABSTRACT Objective: The aim of this study was to evaluate the histopathological findings of the excised lesions from oral mucosa and determine the type and frequency of oral mucosa diseases in Kırşehir region. **Material and Methods:** The histopathology results of 237 patients with oral mucosa lesions who administered to Kırşehir Training and Research Hospital Dermatology Outpatient Clinic and underwent incisional or excisional biopsy between December 2014 and July 2018 were retrospectively evaluated. The demographic characteristics of the patients, disease duration, localisation and frequency of the lesions, the frequency of benign and malignant lesions were recorded. **Results:** Ninety three (39.2%) male and 144 (60.8%) female patients were recruited in our study. The mean age of the patients was 44.33±1.21 years. A total of 237 oral mucosa lesions were detected. The most common benign lesions were intradermal nevi (n=56, 23.6%) followed by inflammatory granulation tissue (n=25, 10.5%), fibromas (n=26, 11%), mucocele (n=21, 8.9%), pyogenic granuloma (n=16, 6.7%), irritation fibromas (n=14, 5.9%), squamous papilloma (n=8, 3.4%), verruca vulgaris (n=6, 2.5%), lichen planus (n=6, 2.5%), hemangiomas (n=5, 2.1%). The most common malignant lesions were squamous cell carcinoma (n=9, 3.8%) and basal cell carcinoma (n=7, 2.9%), followed by lymphoma (n=1, 0.4%) and basosquamous cell carcinoma (n=1, 0.4%). **Conclusion:** In our study, the vast majority (92.8%) of the lesions detected in oral mucosa were benign lesions while malignant lesions constituted a small proportion. Gaining knowledge about the distribution of oral mucosal diseases may contribute to prevention and treatment of these diseases.

Keywords: Oral mucosa; lesion; demographic; biopsy; histopathology; retrospective

ÖZET Amaç: Bu çalışmanın amacı, Kırşehir yöresinde oral mukozadan eksize edilen lezyonların histopatolojik bulgularının değerlendirilerek oral mukoza hastalıklarının tipi ve sıklığının saptanmasıdır. **Gereç ve Yöntemler:** 2014 Aralık-Temmuz 2018 arasında Kırşehir Eğitim ve Araştırma Hastanesi dermatoloji polikliniğine oral mukoza lezyonları nedeniyle başvurup insizyonel ya da eksizyonel biyopsi işlemi uygulanan 237 hastanın lezyonlarının histopatoloji sonuçları retrospektif olarak değerlendirildi. Hastaların demografik özellikleri, hastalık süreleri, lezyonların lokalizasyonları, görülme sıklığı, benign ve malign lezyon sıklığı kaydedildi. **Bulgular:** Çalışmaya 93 (%39,2) erkek, 144 (%60,8) kadın hasta dâhil edildi. Hastaların yaş ortalaması 44,33±1,21 olarak saptandı. Tüm hastalarda toplam 237 oral mukoza lezyonu saptandı. En sık görülen benign lezyonlar intradermal nevüsler (n=56, %23,6) idi. Bunları sırasıyla inflamatuar granülasyon dokusu (n=25, %10,5), fibromlar (n=26, %11), mukosel (n=21, %8,9), piyojenik granüloma (n=16, %6,7), irritasyon fibromu (n=14, %5,9), skuamöz papillom (n=8, %3,4), verruka vulgaris (n=6, %2,5), liken planus (n=6, %2,5), hemanjiyom (n=5, %2,1) takip ediyordu. En sık görülen malign lezyonlar skuamöz hücreli karsinom (n=9, 3.8%) ve bazal hücreli karsinom (n=7, %2,9) olarak saptandı. Bunları lenfoma (n=1, %0,4) ve bazoskuamöz hücreli karsinom (n=1, %0,4) izlemekteydi. **Sonuç:** Çalışmada, oral mukozada saptanan lezyonların büyük çoğunluğu benign lezyonlardı (%92,8). Malign lezyonlar lezyonların az bir kısmını oluşturmaktaydı. Oral mukoza hastalıklarının dağılımıyla ilgili bilgi edinilmesi bu hastalıkların önlenmesi ve tedavisine katkı sağlayabilecektir.

Anahtar Kelimeler: Oral mukoza; lezyon; demografik; biyopsi; histopatoloji; retrospektif

Oral mucosa is the mucosal tissue that lines the oral cavity. Oral mucosa can be affected by many cutaneous diseases including drug reactions as well as systemic diseases and genetic syndromes. Physical examination of oral mucosa is therefore essential in diagnosing various diseases. In this study, we aimed to determine the prevalance of oral mucosa lesions in Kırşehir region.

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MATERIAL AND METHODS

The histopathology results of the biopsy specimens of the patients on whom incisional or excisional biopsy was performed between December 2014 and July 2018 in our tertiary center were retrospectively reviewed. The study was conducted in accordance with the principles set forth in the Helsinki Declaration 2008. The study protocol was approved by the Ahi Evran University Ethics Committee (date: September 25, 2018, no: 2018-17/146). The histopathological diagnoses, demographic data, disease durations and lesion localizations were recorded. Descriptive statistical analysis was used to analyse the data obtained. The data were expressed as mean±standard deviation or as a number percentage.

RESULTS

Ninety three (39.2%) male and 144 (60.7%) female patients were recruited in our study and oral mucosa lesions were significantly more common in females than males. The mean age of the patients was 44.33±1.21 years. A total of 237 oral mucosa lesions were detected. Benign lesions constituted the majority of the lesions, only 7.2% of the lesions were malignant. Of the benign lesions, 25.4% were intradermal nevi (n=56). Squamous cell carcinoma (SCC) was the most common malignant lesion (n=9), (52.9%).

The other lesions included inflammatory granulation tissue (n=25), fibroma (n=26), mucocele (n=21), pyogenic granuloma (PG) (n=16), irritation fibromas (n=14), squamous papilloma (n=8) verruca vulgaris (n=6), lichen planus (LP) (n=6), hemangiomas (n=5), chronic sialadenitis (n=2), cavernous hemangioma (n=1), lichenoid dysplasia (n=1), actinic keratosis (n=4), compound nevi (n=3), arteriovenous malformation (n=3), trichilemmal cyst (TC) (n=1), seborrheic keratosis (n=2), epidermal cysts (n=3), fibroepitelial polyps (n=3), pemphigus vulgaris (n=1), dermatofibroma (n=1), giant cell granuloma (n=1), fibrous papule (n=1), trichoblastoma (n=1), lymphangioma circumscriptum (n=1), granulomatous cheilitis (GC) (n=1), inverted follicular keratosis (n=1), cheilitis (n=3), myxoma (n=1), peripheral ossifying fibroma (n=1), radicular cyst (n=1), schwannoma (n=1), neuroma (n=1), squamous cell cancer (n=9), basal cell carcinoma (BCC) (n=7), basosquamous cell carcinoma (n=1), and lymphoma (n=1) were detected (Table 1, Table 2).

DISCUSSION

Oral mucosa can be the localization of various lesions including vascular lesions, ulcerations, pigmentations, and exophytic lesions. In our study, oral mucosa lesions were more common in female population than males. In a study by Castellanos and Díaz-Guzmán, where patients presenting for dental consultation were included, a male predominance was detected.[1] However, since a particular group administrating for dental care was included, it was suggested that the results of this study may not reflect the results of an open population.

In our study, melanocytic nevi, which were localized on the lip-skin border consituted a considerable amount (24.9%) of all lesions followed by fibromas and mucocels. Castanellos and Díaz-Guzmán reported that the three most common oral mucosal lesions were leukoedema, traumatic ulceration and frictional keratosis while Espinoza et al. reported denture stomatitis, irritative hyperplasia and oral mucosal varicosities as the most common lesions in their study which was performed in the patients aged over 65. Differing from these studies, the inclusion of the lesions located on lip-skin border might have led to the high frequency of melanocytic nevi in our study.[1,2]

In our study, dermal nevi constituted 94.9% of the total number of nevi and 58.9% of dermal nevi were localized on the upper lip skin. Concordant with the study by Ghosh et al., a female predominance was seen in the patients with dermal nevi in our study.[3] In that study, lip was found as the second most common localization of dermal nevi after cheek.[3] Our study also confirmed that lip skin is a common localization for dermal nevi. The high frequency of dermal nevi in female population may be related to increased awareness of skin lesions in female population due to higher cosmetic concerns.

In our study, the second most common lesion detected was fibromas (11%). In a study by Torres-Domingo, fibromas were the most common mucosal lesion in oral mucosa.[4] Buccal mucosa is reported to be a common site for fibromas. Consistently, in our

TABLE 1: The distribution of benign lesions in the study population.

Type of lesion	The number of patients	Percentage (%)	Gender		Localization
			Male	Female	
Benign lesion					
Dermal nevi	56	23.6	14	42	33 upper lip 23 lower lip
Compound nevi	3	1.3	1	2	Upper lip
Actinic cheilitis	4	1.7	1	3	1 upper lip 3 lower lip
Inverted follicular keratosis	1	0.4	0	1	Upper lip
Arteriovenous malformation	3	1.3	1	2	1 lower lip 2 upper lip
Pemphigus vulgaris	1	0.4	0	1	Buccal mucosa
Hemangiomas	5	2.1	4	1	3 upper lip 1 lower lip 1 tongue
Inflammatory granulation tissue	25	10.5	12	13	6 lower lip 8 tongue 2 upper lip 1 floor of month 1 mandibula 7 buccal mucosa
Irritation fibromas	14	5.9	2	12	10 buccal mucosa 2 lower lip 2 tongue
Dermatofibroma	1	0.4	1	0	Upper lip
Giant cell granuloma	1	0.4	1	0	Maxilla
Cavernous hemangioma	1	0.4	0	1	Upper lip
Epidermal cyst	3	1.3	1	2	2 lower lip 1 tongue
Chronic sialadenitis	2	0.8	0	2	1 lower lip 1 palatum
Fibroepitelial polyps	3	1.3	3	0	3 upper lip
Lichen planus	6	2.5	3	3	4 buccal mucosa 1 upper lip 1 lower lip
Lichenoid dysplasia	1	0.4	1	0	Buccal mucosa
Mucosel	21	8.9	13	8	2 upper lip 17 lower lip 1 floor of mouth 1 buccal mucosa
Peripheral ossifying fibroma	1	0.4	1	0	Palatum
Radicular cyst	1	0.4	0	1	Maxilla
Schwannoma	1	0.4	0	1	Tongue
Granulomatous cheilitis	1	0.4	0	1	Upper lip
Fibrous papule	1	0.4	0	1	Lower lip
Fibroma	26	11.0	5	21	12 buccal mucosa 5 tongue 4 lower lip 4 upper lip 1 palatum

continue →

TABLE 1: The distribution of benign lesions in the study population (*continued*).

Type of the lesion	The number of patients	Percentage (%)	Gender		Localization
			Male	Female	
Benign lesion					
Neuroma	1	0.4	1	0	Upper lip
Seborrheic keratosis	2	0.8	1	1	1 upper lip 1 lower lip
Squamous papilloma	8	3.4	2	6	3 tongue 1 palatum 2 upper lip 2 buccal mucosa
Trichilemmal cyst	1	0.4	0	1	Upper lip
Trichoblastoma	1	0.4	1	0	Upper lip
Verruca vulgaris	6	2.5	4	2	4 upper lip 1 lower lip 1 tongue
Myxoma	1	0.4	0	1	Buccal mucosa
Lymphangioma circumscriptum	1	0.4	1	0	Lower lip
Pyogenic granuloma	16	6.7	6	10	3 lower lip 4 tongue 1 palatum 1 buccal mucosa 7 upper lip

TABLE 2: The distribution of malignant lesions in the study population.

Type of the lesion	The number of patients	Percentage (%)	Gender		Localization
			Male	Female	
Squamous cell carcinoma	9	3.8	9	0	7 lower lip 2 upper lip
Basal cell carcinoma	7	2.9	2	5	2 lower lip 4 upper lip
Lymphoma	1	0.4	1	0	Floor of mouth
Basosquamous cell carcinoma	1	0.4	1	0	Lower lip

study 46.1% of the fibromas were localized on buccal mucosa followed by 19.2% on the tongue, 15.4% lower lip, 15.4% upper lip and 3.8% on the palatum. In the histology of fibroma, a nodular mass of fibrous connective tissue consisting of collagen fibers, fibroblasts and overlying keratinized squamous epithelium is seen. Irritation fibroma is induced by local trauma or chronic irritation.[5,6] Similar to the study by Naderi et al., 78.5% of the patients diagnosed with irritation fibroma consisted of female patients.[5,6] Fibromas are generally seen in the fourth decade of life.[7] In our study, the mean age of the patients was 49±1.2 years (9-75).

In our study, 21 (8.8%) patiens were diagnosed with mucocele, the third most common lesion detected in our study. Mucocele is a mucus-filled, soft-textured, transparent, bluish, cystic swelling. Extravasation type mucocele occurs as a result of spillage of saliva into the soft tissue due to salivary gland duct damage and the lower lip is the most frequent localization of mucocele as it is more prone to trauma.[8] Retention type mucocele is caused by blockage of the salivary gland ducts and can be seen in any localization in oral cavity. The extravasation type (84.48%) was more common than the retention type

(15.52%). The most common affected site was lower lip (36.20%) followed by ventral surface of the tongue (25.86%).[9] In our study, concordantly, the vast majority of the lesions 19 (90.4%) were of extravasation type and localized on the lower lip.

In our study, the histopathology results of 25 patients were consistent with granulation tissue. Granulation tissue formation is an important stage in wound healing and raising a possibility of a traumatic etiology. Lesions of traumatic origin have been commonly reported in oral mucosa. In a study by Castellanos and Díaz-Guzmán, traumatic ulcer and traumatic erythema were among the most common lesions in oral mucosa.[1] The high proportion of granulation tissue (10.5%) that we detected in our study reveals the importance of traumatic etiology in the development of oral mucosa lesions.

PG was also among the most common lesions detected in our study. Altough the etiology is not clear, chronic low-grade irritation, traumatic injury, hormone effect, and reactions to grafts have been suggested to play a role in the development of PG.[10,11] Gingiva is the most common localization, PG can be also seen on the lips, tongue, buccal mucosa and palate. Consistently maxillary gingiva (43.7%) was the most common localization in our study.[10] The mean age of the patients was 37.1±4.21, 62.5% of the patients (n=10) were female patients supporting the role of hormonal influences in PG development.

GC is a very rare disorder with unknown etiology characterized by recurrent swelling of the labial tissue. GC has been associated with Crohn's disease, sarcoidosis, genetic, possibly some allergic reactions and odontogenic infections.[12] However, in a case series by Martínez Martínez et al., none of the GC patients had an accompanying disease suggesting that GC is an independent orofacial granulomatous disease mostly not accompanied by other systemic diseases.[12] GC mostly affects upper lip and the lower lip is less frequently affected.[13] In our study, GC was detected in only one female patient and was localized on upper lip and was not associated with any systemic disease.

Dermatofibroma is a benign fibrohystiocytic mesencymal tumor presenting as a firm, red nodule, most commonly seen on extremities. Dermatofibromas are rarely seen in oral mucosa. Tongue, gingiva, mandibula, maxilla, upper and lower lip localizations have been reported previously.[14] Prolonged sun exposure, traumatic injuries and chronic infections have been proposed in the pathogenesis of oral mucosa dermatofibromas.[14] In our study, the localization of dermatofibroma was upper lip.

Inverted follicular keratosis is a neoplasm of follicular origin that arises from the infundibular portion of the hair follicle.[15] The most common localization is head-neck region in 90% of patients, and elderly males are frequently affected.[16] Concordantly our patient diagnosed with inverted follicular keratosis was a 67-year-old male patient. The etiopathogenesis is not clear, some studies reported that human papilloma virus antigen was detected in cases with inverted follicular keratosis.[17] Mohamed et al. reported a 55 year old female patient with inverted follicular keratosis of the upper lip.[15] Similarly in our study, the lesion was localised on the upper lip.

Oral LP (OLP) is a chronic inflammatory disease with unknown etiology. OLP can present as white striations, plaques, erythema, and erosions. Buccal mucosa, tongue and gingiva are commonly affected.[18] In our study, 6 patients were diagnosed with LP; 4 were localized on the buccal mucosa. 1 on the upper lip and 1 on the lower lip. Although LP on buccal mucosa is frequently encountered, LP on the lip localization has been reported in only a few case reports.[19-21] Lupus erythematosus, actinic cheilitis and early carcinoma in situ are in the differential diagnosis of LP in this localization.[21] LP localized on lip area is generally associated with intraoral lesions. However, Cecchi and Giomi also reported a patient developing cutaneous LP after LP development on the lip.[21]

Basosquamous carcinoma (BSC) is a rare subtype of BCC. Ultraviolet (UV) radiation, aging, and tobacco exposure are suggested to play a role in the development of BSC. BSC often simulates BCCs clinically and morphologically, but BSC is more aggressive and metastasis has been reported in 17.9% of cases.[22-24] BSC mainly affects male patients older than 60 years and localized on the upper face. In our study, a 81-year-old patient was diagnosed with BSC which was localised on the lower lip. BSC is mainly

localized on head and neck and lip is a rare localization of BSC.[24] Our case underlines that BSC should be kept in the differential diagnosis of ulcerated lesions on the lips.

BCC involving the oral mucosa is rare. In a study by Silapunt et al., 14 of the 18 cases of mucosal BCCs were localized on the upper vermilion lip, 4 were located on the lower lip.[25] In our study, of the 7 BCCs detected, 2 were localized on the lower lip and 5 on the upper lip. In a study by Rowe et al., upper lip BCCs were found to be more common in female patients and female/male ratio of the patients treated with Mohs surgery was found as 3.5/1 suggesting that female patients are at a higher risk than male patients.[26] The reason of female predominance of BCC on the upper lip has not been clearly indentified, the protective role of terminal hairs of male upper lip, the anatomic differences between genders posing female lips more to sun exposure and use of cosmetics have been put forward waiting to be confirmed by further studies.[26] Similarly, female predominance was observed in our study as female/male ratio of the patients was found 3/2.

Lip SCC (LSCC) is a common oral malignancy, and accounts for approximately 25-30% of all oral SCCs.[27] LSCC involves the lower lip in about 90% of cases and chronic exposure to UV plays a major role in the etiology.[28] Oral leucoplakia, erythroplakia, LP, actinic cheilitis and photosensitive diseases like xeroderma pigmentosum, lupus erythematosus and albinism are the predisposing diseases for SCC.[29] In our study, 8 of SCCs were located on the lower lip, 1 was on the upper lip. All the cases of SCCs developed on the basis of actinic cheilitis.

Seborrheic keratosis are very common lesions of the skin. Trunk and face are the most common localizations, but oral region is rarely involved. In a study by Ntomouchtsis et al., 5 cases of seborrheicc keratosis localized on lips have been reported.[30] In our study, two cases of seborrheic keratosis one localized on the upper and the other on the lower lip skin have been detected.

TCs arise from the outer root sheath epithelium of the hair follicle.[31] To the best of our knowledge, the current literature includes only two case reports of intraoral TCs located on upper and lower lip mucosa.[32] In our study, one case was diagnosed with TC which was localised on the upper lip.

Trichoblastomas are solitary, small, well circumscribed tumors developing from hair germ. The most common localizations are face, scalp, neck, trunk, proximal extremities and perianal region.[33] Histopathologically symmetrical growth, smooth borders, follicular germinative cells, stroma consisting fibrocytes, thick or fibrillary collagen are seen. In our study trichoblastoma was detected in one patient and on the skin of the upper lip. To our knowledge, trichoblastoma in oral region has not been reported in literature until now.

Marginal zone lymphoma is an indolent B cell lymphoma which arises from post germinal center marginal zone B cells in lymph nodes and extranodal tissues. Oral mucosa-associated lymphoid tissue (MALT) lymphoma is a rare entity and persistent immune stimulation caused by chronic infection or inflammation is noted in the etiopathogenesis. In the literature, one case with MALT lymphoma on the hard palate and parotid gland has been previously reported.[34] In our study, one patient was diagnosed with marginal zone lymphoma and the lesion was localized on the floor of the mouth.

The retropective nature and restricted number of patients were among study limitations.

CONCLUSION

In this study, in which we analysed the histopathological results of oral mucosa lesions, the vast majority of the excised lesions were benign. The most common benign lesion was dermal nevus. The malignant lesions constituted a small proportion of the total lesions with SCC being the most frequent. The malignant lesions cumulated in older age, possibly as a result of cumulative UV exposure. Knowing the distribution of benign and malignant oral mucosal diseases may help to develop strategies to prevent and treat these diseases.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Emine Müge Acar, Asuman Kilitci;* ***Design:*** *Emine Müge Acar, Asuman Kilitci;* ***Control/Supervision:*** *Emine Müge Acar;* ***Data Collection and/or Processing:*** *Emine Müge Acar;* ***Analysis and/or Interpretation:*** *Emine Müge Acar, Asuman Kilitci;* ***Literature Review:*** *Emine Müge Acar, Asuman Kilitci;* ***Writing the Article:*** *Emine Müge Acar;* ***Critical Review:*** *Emine Müge Acar, Asuman Kilitci;* ***References and Fundings:*** *Emine Müge Acar, Asuman Kilitci;* ***Materials:*** *Asuman Kilitci.*

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