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■ Original Article

The demographic and clinicopathological features of salivary gland tumors in Turkey

Türkiye’de tükürük bezi tümörlerinin demografik ve klinikopatolojik özellikleri

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ABSTRACT

Aim: Salivary gland tumors (SGTs) are rare neoplasms thus, the local records are valuable to obtain the epidemiological overview. This study aimed to determine the demographic and clinicopathological features of SGTs in our clinic and compare the findings with the studies from Turkey and all over the world.

Material and methods: The data of 185 patients who underwent surgery for SGT in The Department of Otorhinolaryngology-Head and Neck Surgery of a tertiary referral center between 2012 and 2017 were studied retrospectively. The demographic and clinicopathological features of the patients were recorded.

Results: Among all patients with primary and secondary SGTs, the median age was 53 years, 54.6% of the patients were men. Patients with primary tumor constituted 96.8% of all cases. Malignancy rate was 14. Parotid gland was the most common location (90%). Nearly half of all primary tumors were diagnosed as pleomorphic adenoma (n=84, 46.9%). Mucoepidermoid carcinoma was the most common malign neoplasm of the parotid gland. There were only six patients (3.2%) that had secondary SGT.

Conclusion: Pleomorphic adenoma and mucoepidermoid carcinoma were the most common benign and malign pathologies, respectively. The lowest malignancy rate and the highest rate of warthin tumor of the existing literature were the most conspicuous findings of our study. Although the frequency of the secondary SGTs is low, the possibility of metastasis should be considered especially for the patients above 65 years of age.

Keywords: adenoma, pleomorphic, carcinoma, mucoepidermoid, neoplasm, parotid, salivary gland

ÖZ

Amaç: Tükürük bezi tümörleri (TBT'ler) nadir görülen neoplazmlardır, bu nedenle lokal kayıtlar epidemiyolojik bir bakış açısı elde etmek için değerlidir. Bu çalışma, kliniğimizde opere edilen TBT'lerin demografik ve klinikopatolojik özelliklerini belirlemeyi ve bu bulgular ile Türkiye ve tüm dünyadaki çalışmaları karşılaştırmayı amaçlamıştır.

Gereç ve yöntemler: 2012 ve 2017 yılları arasında bir üçüncü basamak sağlık Merkezinin Kulak Burun Boğaz ve Baş Boyun Cerrahisi Kliniği'nde TBT nedeniyle opere edilen 185 hastanın verileri geriye dönük olarak incelendi. Hastaların demografik ve klinikopatolojik özellikleri kaydedildi.

Bulgular: Primer ve sekonder TBT'li tüm hastalar arasında median yaş 53, hastaların %54,6'sı erkekti. Primer tümörlü hastalar tüm vakaların %96,8'ini oluşturmaktaydı. Malignite oranı 14 idi. Parotis bezi en sık lokalizasyondur (%90). Tüm primer tümörlerin yaklaşık yarısına pleomorfik adenom tanısı kondu (n = 84, %46,9). Mukoepidermoid karsinom, parotis bezinin en sık görülen malign neoplazmi idi. Sekonder TBT'si olan sadece altı hasta (%3,2) vardı.

Sonuç: Pleomorfik adenom ve mukopidermoid karsinom sırasıyla en sık görülen benign ve malign patolojilerdir. Literatürdeki en düşük malignite oranı ve en yüksek warthin tümörü oranı çalışmamızın en çarpıcı bulgularıdır. İkincil TBT'lerin sıklığının düşük olmasına rağmen, özellikle 65 yaşın üzerindeki hastalarda metastaz olasılığı düşünülmelidir.

Anahtar kelimeler: adenom, pleomorfik, karsinom, mukoepidermoid, neoplazi, parotis, tükürük bezi

INTRODUCTION

Salivary gland tumors (SGTs) are rare neoplasms of head and neck region, that constitute 2-6.5% of all head and neck neoplasms [1,2]. The incidence of SGTs was reported as 0.05-2/100,000 in the literature [3]. Not only the incidence but also the pathological distribution was reported to change between distinct ethnic groups and geographical locations [1,4-10]. "Malignancy" term is also disparate for SGTs which was defined as "the benign tumor is less benign and the malign tumor is less malign than the usual ones" by Ackerman and Del Regato in 1970 [11]. Another complexity for SGTs is the histopathological assessment and classification. Although this situation was diminished with the WHO Classification System of Head and Neck Tumors 2005 [2], SGTs show similar histopathological features in between various benign and malign types which create difficulty in diagnosis.

As the rarity of these neoplasms, the local records are valuable to obtain the epidemiological overview. This study aimed to determine the demographic and clinicopathological features of SGTs in a tertiary referral center and compare the findings with the studies from Turkey and all over the world.

MATERIAL AND METHODS**Cases**

The data of 185 patients who underwent surgery for SGT in The Department of Otorhinolaryngology-Head and Neck

Surgery (ORL-HNS) of a tertiary referral center between 2012 and 2017 were studied retrospectively. The demographic and clinicopathological features of the patients were recorded. Primary and secondary SGTs treated with surgery were included in the study. Primary SGTs were classified histopathologically according to the WHO Classification of Head and Neck Tumors 2005 [2]. The patients with the pathologies as congenital and lymphovascular malformation (hemangioma, lymphangioma, arteriovenous malformation), inflammatory lesions, and the cases with missing data were excluded from the study. None of the patients had a history of prior surgical treatment, radiotherapy (RT) or chemoradiotherapy (CRT) for SGT.

The approval was taken from the local institutional research committee (5417/4). The research was conducted in compliance with the Ethical Principles of the Declaration of Helsinki.

Statistical Analysis

In descriptive statistics related to continuous data; mean, standard deviation, median, minimum, maximum values; number and percentage values were given.

SPSS for Windows, Version 15 Chicago, SPSS Inc. program was used in the statistical analysis.

RESULTS

Among all patients with primary and secondary SGTs, 101 were men (54.6%) and 84 were women (45.4%). The median

Table 1. The demographic and clinicopathological features of patients with primary SGTs

		n (%)
Gender	Male	96 (53.6%)
	Female	83 (46.4%)
Age	0-18	3 (1.7%)
	19-40	34 (19%)
	41-65	127 (70.9%)
	66<	15 (8.4%)
Location	Parotid gland	161 (90%)
	Submandibular gland	11 (6.1%)
	Sublingual gland	-
	Minor salivary gland	7 (3.9%)
Histopathology		
Benign tumors (n=154)	Pleomorphic adenoma	84 (46.9%)
	Warthin tumor	62 (34.6%)
	Basal cell adenoma	6 (3.4%)
	Canalicular adenoma	1 (0.6%)
	Oncocytoma	1 (0.6%)
Malign tumors (n=25)	Mucoepidermoid carcinoma	10 (5.6%)
	Adenoid cystic carcinoma	4 (2.2%)
	Salivary duct carcinoma	2 (1.1%)
	Acinic cell carcinoma	2 (1.1%)
	Myoepithelial carcinoma	2 (1.1%)
	Clear cell carcinoma	1 (0.6%)
	Carcinoma ex pleomorphic adenoma	1 (0.6%)
	Carcinosarcoma	1 (0.6%)
Haematolymphoid tumors	MALT lymphoma	2 (1.1%)
TOTAL		179 (100%)

age of the patients was 53 years, with a range of 2 to 89 years. Out of 185 patients, 179 patients had primary, six patients had secondary tumor (respectively 96.8%, 3.2%); 154 patients had benign, 31 patients had malignant tumor (respectively 83.2%, 16.8%).

Primary SGTs

The demographic and clinicopathological features of patients with primary SGTs are shown in **Table 1**. Among 179 patients with primary SGTs, male: female ratio was 1.16 (96/83), the percentage of the age groups 0-18, 19-40, 41-65 and above 65 years were 1.7%, 19%, 70.9%, and 8.4% respectively. Parotid gland was the most common location with 161 cases (90%). While 123 benign neoplasms (68.7%) originated from the superficial lobe of the parotid, 16 benign neoplasms (8.9%) originated from the deep lobe. When malignant neoplasms were evaluated; 20 malignant neoplasms (11.2%) originated from the superficial lobe of the parotid and two malignant neoplasms (1.2%) from the deep lobe of parotid. The incidences of tumors in other salivary glands were as follows: 11 in the submandibular gland (6.1%) and seven in the minor salivary glands (3.9%). No sublingual SGT was detected.

According to the assessment of the histopathology of the primary SGTs; benign tumors constituted 86% of all primary tumors. Nearly half of all primary tumors were diagnosed as PA (n=84, 46.9%). Warthin (WT) tumor was the second most common histopathology (n=62, 34.6%) in all tumors. The malignancy rate of all primary SGTs was 14% (25/179). Mucoepidermoid carcinoma was the most common malignant SGT (n=10, 5.6%). Adenoid cystic carcinoma was the second most common malignant pathology (n=4, 2.2%).

When considering the histopathological distribution of primary SGTs according to the location; parotid gland was the most common location for almost all histopathological types. As the most common pathology, PA commonly originated from the superficial lobe of the parotid (n=63, 40.9% of all benign neoplasms). In one case with PA, benign metastasis was detected in a lymph node. When only benign neoplasms were taken into consideration, the incidences of other locations were; six from the deep lobe of the parotid (3.9%), 11 from submandibular (7.1%), four from minor SGs of the hard palate (2.6%). The only location of WT and all other remaining benign pathologies was parotid. While 55 WT (35.7%), four basal cell adenoma (2.6%), one canalicular adenoma (0.6%) originated from the superficial lobe of the parotid; seven WT (4.5%), two basal cell adenoma (1.3%), one oncocytoma (0.6%) originated from the deep lobe of the parotid. All submandibular gland pathologies (7.1%) were benign and diagnosed as pleomorphic adenoma.

MEC was the most common malignant neoplasm of the parotid gland and had a 36% incidence when only malignant pathologies were taken into consideration. Among ten cases of MEC, six cases were low-grade and four were high-grade.

In our series, there were three patients (12%) that had malignant minor SGTs: one MEC and one adenoid cystic carcinoma that were both located in the hard palate and one acinic cell carcinoma of the nasal mucosa. All other malignant SGTs (88%) were located in the parotid gland (**Table 2**).

The histopathological distribution of primary SGTs according to the age groups is shown in **Table 3**. The most common age group of both benign and malignant cases were between 41-65 years of age (71.4%, 64% respectively).

Table 2. The histopathological distribution of primary SGTs according to the location

	Parotid	Submandibular	Minor glands
BENIGN TUMORS			
Pleomorphic adenoma	69 (44.8%)	11 (7.1%)	4 (2.6%)
Warthin tm	62 (40.2%)	-	-
Basal cell adenoma	6 (3.9%)	-	-
Canalicular adenoma	1 (0.6%)	-	-
Oncocytoma	1 (0.6%)	-	-
n (% of benign tumors)	139 (77.7%)	11 (7.1%)	4 (2.6%)
MALIGN TUMORS			
Mucoepidermoid Ca	9 (36%)	-	1 (4%)
Adenoid Cystic Ca	3 (12%)	-	1 (4%)
Ductus cell Ca	2 (8%)	-	-
Acinic cell Ca	1 (4%)	-	1 (4%)
Myoepithelial Ca	2 (8%)	-	-
Clear cell Ca	1 (4%)	-	-
Ca Ex Pleomorphic Adenoma	1 (4%)	-	-
Carcinosarcoma	1 (4%)	-	-
Maltoma	2 (8%)	-	-
n (% of malign tumors)	22 (88%)	-	3 (12%)
TOTAL (n=179/ 100%)	161 (89.9%)	11 (6.1%)	7 (3.9%)

Secondary SGTs

There were only six patients (3.2%) that had secondary SGT. Parotid was the only salivary gland in which malign metastasis was detected. SCC of skin was the most common secondary neoplasm of the parotid gland (n:3, 50%), the other diagnoses were the metastasis of 1 malignant melanoma, 1 rhabdomyosarcoma, 1 nasopharynx carcinoma. The most common age group was above 65 years of age (83%).

DISCUSSION

Histopathologically distinct tumors arise from salivary glands infrequently. Not only the low frequency but also the difficult histopathological assessment, diverse biological behavior, and unknown etiology complicate the approach to the SGTs [8, 12]. Epidemiological studies from all over the world reflect this diversity (**Tables 4 and 5**).

This study reviewed the demographic and clinicopathological data of 185 patients with both primary and secondary SGTs diagnosed at a tertiary referral center. In the present study, the majority of the demographic features of the cases were similar to the previous studies.

Among 185 patients, the primary SGTs constituted the major part of the cases (n=179, 96.8%). The male: female ratio of the primary SGTs was 1.16 (96/83) in the present series. In the literature, except the study from Latin America-Mexico [6] which revealed the ratio as 0.57, there is no evident predominance in the gender distribution and the ratio ranges between 0.81-1.23 [1,5,7-10].

The most common age groups of both benign and malign pathologies were 41-65 age group (71.4%, 64% respectively), compatible with the literature [1, 4-8].

The most common histopathology was PA, accounting for 46.9% of all tumors and 55.5% of benign tumors. PA is a benign neoplasm of epithelial and myoepithelial cells, arranged in various morphological patterns [8]. PA is inalterably the most common pathology of SGTs in the literature, its frequency ranges between 40.9% and 65.6%. WT was the second most common benign histopathology

Table 3. The histopathological distribution of primary SGTs according to the age groups

	0-18	19-40	41-65	65<
BENIGN TUMORS				
Pleomorphic adenoma	2 (1.3%)	30 (19.5%)	46 (29.9%)	6 (3.9%)
Warthin tm	-	-	58 (37.7%)	4 (2.6%)
Basal cell adenoma	-	1 (0.6%)	5 (3.2%)	-
Canalicular adenoma	-	-	1 (0.6%)	-
Oncocytoma	-	-	-	1 (0.6%)
n (% of benign tumors)	2 (1.3%)	31 (20.1%)	110 (71.4%)	11 (7.2%)
MALIGN TUMORS				
Mucoepidermoid Ca	-	1 (4%)	8 (32%)	1 (4%)
Adenoid Cystic Ca	-	1 (4%)	2 (8%)	1 (4%)
Ductus cell Ca	-	-	2 (8%)	-
Acinic cell Ca	1 (4%)	-	1 (4%)	-
Myoepithelial Ca	-	-	1 (4%)	1 (4%)
Clear cell Ca	-	-	1 (4%)	-
Ca Ex Pleomorphic Adenoma	-	-	-	1 (4%)
Maltoma	-	1 (4%)	1 (4%)	-
Carcinosarcoma	-	-	1 (4%)	-
n (% of malign tumors)	1 (4%)	3 (12%)	16 (64%)	4 (16%)
TOTAL	161 (89.9%)	11 (6.1%)	7 (3.9%)	179 (100%)

Table 4. Summary of the epidemiological studies of primary SGTs from different countries in last 10 years

Study	n	Malignancy rate (%)	M/F ratio	PA (%)	WT (%)	MEC (%)	ACC (%)
Tian et al. 2010 (China) (4)	6982	32.1	1.06	47	13.8	9.6	9.8
Luksic et al. 2012 (Croatia) (1)	779	35.8	1.01	47.2	11.2	8.6	12.1
Fonseca et al. 2012 (Brazil) (5)	493	25.2	0.81	63.7	7.3	7.9	4.5
Meija-Velazquez et al. 2012 (Mexico) (6)	360	23.1	0.57	65.6	5.6	4.7	5.0
Lawal et al. 2013 (Nigeria) (7)	413	53.5	1.02	40.9	0	14.8	22.5
Vasconcelos et al. 2017 (Brazil) (8)	109	44.3	0.94	44.3	14.6	4.6	12.8
Ant et al. 2019 (Turkey)- Current study	179	14	1.16	46.9	34.6	5.6	2.2

Table 5. Summary of the epidemiological studies of primary SGTs from Turkey

Study	n	Malignancy rate (%)	M/F ratio	PA (%)	WT (%)	MEC (%)	ACC (%)
Kara et al. 2010 (9)	125	24	0.86	64	4.8	2.4	8.8
Kizil et al. 2013 (10)	510	31.0	1.23	45.3	17.8	5.7	17.6
Ant et al. 2019 - Current study	179	14	1.16	46.9	34.6	5.6	2.2

(n=62, 34.6%), consistent with the literature. The frequency of WT of this study was the highest (34.6%) of the literature which ranges between 0 and 17.8% (**Tables 4** and **5**). The frequency of WT in the studies from Africa was seen to be lowest as 0% in the study by Lawal et al. [7], compared with the studies from Europe and Asia [1, 4, 7, 9, 10]. The only location of WT was the parotid gland. Despite the general knowledge that; WT – papillary cyst adenolymphomatosum originates from superficial lobe which harbors lymph nodes, 7 WT (4.5%) originated from deep lobe of the parotid. In the study by Colella et al. [13] the frequency of deep lobe originated WT was also reported as 4%.

The malignancy rate of the primary SGTs was 14% (25/179). This rate was the lowest malignancy rate in the literature which ranged from 23.1% to 53.5% (**Tables 4** and **5**). Not only the geographical and racial variations, but also the structure of the clinics that the studies were performed affect this rate. Dental and oral surgery clinics in the world mainly deal with minor SGTs which have higher malignancy rates [10] however, these clinics are not common in Turkey. Additionally, the second referral centers in Turkey mainly deal with benign pathologies and refer the cases with malign pathologies to the tertiary referral centers. The center where the study was performed is mainly an oncological hospital, and the Otorhinolaryngology, Head, and Neck Surgery Department had the maximum number of surgery of SGTs per year when compared with the literature from Turkey. Thus we claimed that this study which had the 5 years section of the cases represent the demographic and clinicopathological features of salivary gland tumors in Turkey.

MEC was the most common malign SGT, representing 5.6% of all tumors and 40% of malign tumors. ACC was the second most common malign pathology (n=4, 2.2%). Despite the other studies from Turkey, ACC was the most common malign SGT, followed by MEC (**Table 5**). The predominance

of ACC was described in the majority of the studies except the study conducted in Brazil (**Table 4**). The finding suggesting the geographic and racial variations in the frequency of malignant SGTs should be confirmed with the various epidemiological studies.

The most common location was the parotid gland with 161 cases (90%) as the majority of the studies on SGTs in the literature, including those from Turkey. However, the frequency of the parotid location in this study (90%) was higher than the literature which was reported between 60 and 80% [1, 4-10]. This finding was consistent with the lowest malignancy rate of the study (14%) compared with the literature.

The frequency of deep lobe location of benign neoplasms was 10.4% (16/154) while the frequency was 8% (2/25) for malign neoplasms. The location in the superficial or deep lobe of the parotid gland does not seem to affect the possibility of malignancy. However the operative risks as facial paralysis, bleeding, hematoma etc. must be predicted to be increased with the deep lobe location of the tumor and the patient should be informed about these risks. The frequency of deep lobe location of benign neoplasms was reported as 14.7% in the study by Kizil et al. [10] and 21% in the study by Musani et al. [14].

The only pathology of the submandibular gland was pleomorphic adenoma (7.1%). The only benign pathology of the minor salivary glands was also pleomorphic adenoma. The pleomorphic adenoma constituted 100% and 57% of submandibular and minor salivary gland tumors, respectively. In the literature, this rate was reported between 40% and 60% [7, 8]. Although the rate of minor salivary gland was compatible with the literature, the rate of submandibular gland was higher.

The malignancy rate of the minor salivary glands was 42.8% (3/7) and, the rate was 50% for oral cavity. In the study by

Kizil et al., the malignancy rate was reported as 52%. Hard palate was the most common location of all minor SGTs, as stated in the same study [10].

In this study, no sublingual pathology was detected as reported in the studies by Fonseca et al. and Vasconcelos et al. [5, 8]. In the other studies, the rate of sublingual location was so low as less than 1% [1, 4, 6, 7].

Secondary SGTs constituted 3.2% of the cases. Malign metastasis of a secondary tumor to the salivary glands was detected only in the parotid gland. When the cases were examined, it was seen that apparent mass was detected with US, CT or MRI in all patients preoperatively. This situation leads to questioning the effectiveness of prophylactic parotidectomy with the presence of advanced radiological techniques. The most common group constitutes the patients above 65 years of age with neglected SCC of the skin. Therefore, the patients above 65 years of age should be evaluated in terms of secondary tumors of the parotid.

In conclusion, SGTs were more located in the major salivary glands than minor salivary glands. PA and MEC were the most common benign and malign pathologies, respectively. The most conspicuous findings of our study were the lowest malignancy rate and the highest rate of WT of the existing literature. Although the frequency of the secondary SGTs is low, the possibility of metastasis should be considered especially for the patients above 65 years of age.

DECLARATION OF CONFLICT OF INTEREST

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