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The relative frequency of odontogenic tumors in the Black Sea region of Turkey: an analysis of 86 cases

Figen ÇİZMECİ ŞENEL[1], Ezher Hamza DAYISOYLU[1], Şafak ERSÖZ[2], Nuray YILMAZ ALTINTAŞ[1], Emre TOSUN[1], Cem ÜNGÖR[1], Fatih TAŞKESEN[1]

Aim: To determine the relative frequency and distribution of different types of odontogenic tumors in southeastern Europe, focusing on the Black Sea region of Turkey.

Materials and methods: In total 1165 oromaxillofacial biopsy records were evaluated for histologic diagnosis of odontogenic tumors over a 7-year period from patients referred to the Department of Oral and Maxillofacial Surgery and Department of Pathology, Karadeniz Technical University, Faculty of Dentistry and Medicine, Trabzon, Turkey.

Results: A total of 86 odontogenic tumors were reported. Malignant transformation only occurred in 6 cases (6.8%), while the others were benign (93.2%). Odontoma was the most common odontogenic tumor (41.8%), followed by keratocystic odontogenic tumor (17.4%), ameloblastoma (12.7%), and odontogenic myxoma (9.3%).

Conclusion: The relative frequencies of odontogenic tumors exhibited variability between geographic regions. In the Black Sea region of Turkey, odontoma and keratocystic odontogenic tumors are the most common benign odontogenic tumors with distinct anatomic predilections.

Key words: Odontogenic tumor, ameloblastoma, keratocystic odontogenic tumor, prevalence

Introduction

Odontogenic tumors (OTs) are rare entities that originate in the odontogenic epithelium and/or ectomesenchymal tissues, which are parts of the tooth-forming apparatus (1). These tumors constitute a heterogeneous group of diseases with diverse clinical and histopathological features (2). The World Health Organization (WHO) classified this group of lesions in 1971 and 1992 (1,3). In 2005, the WHO updated the histological typing of OT, and some pathological entities were changed or new ones introduced. Under this classification, one of the major differences was the parakeratinized variant of odontogenic keratocyst, which is now regarded as keratocystic odontogenic tumor (KCOT) (4,5).

Several reports on the relative frequency of OT occurrence from different parts of the world have been documented (6–11). However, there are only limited data available in the English-language literature on the prevalence of OTs in Turkish population. In 1990, Günhan et al. published a report on OTs in Turkey (12). Afterwards, in 2005, Olgac et al. reported OTs in İstanbul and evaluated diagnoses according to the criteria suggested under the 1992 WHO histological classification (13). However, both of these valuable studies were based on data from similar locations in the western part of Turkey. To our knowledge, there is no information available in the English-language literature on the prevalence of OTs in the eastern part of Turkey, particularly in the Black Sea region.

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[1] Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Karadeniz Technical University, Farabi Campus, Trabzon – TURKEY
[2] Department of Pathology, Faculty of Medicine, Karadeniz Technical University, Farabi Campus, Trabzon – TURKEY
Correspondence: *Ezher Hamza DAYISOYLU, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Karadeniz Technical University, Farabi Campus, Trabzon – TURKEY*
E-mail: edayisoylu@gmail.com

The aim of the present study was to determine the relative frequency of OTs, as assessed by the 2005 WHO classification, in patients from the Department of Pathology, Faculty of Medicine, and the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, at Karadeniz Technical University in Trabzon, Turkey, from 2004 to 2010, and to compare these data with various reports from other geographical regions of the world.

Materials and methods

The histopathology records of the Department of Oral and Maxillofacial Surgery and Department of Pathology, Karadeniz Technical University, Faculty of Dentistry and Medicine, Trabzon, Turkey, were reviewed retrospectively for OTs from January 2004 to December 2010. In the cases of repeated biopsies or recurrent lesions, histological tumor types were compared and considered as a single case. By reviewing the hematoxylin–eosin-stained slides, the diagnoses were re-evaluated according to the 2005 WHO criteria, and OTs were classified into 2 main groups in terms of behavior (benign and malignant) and 3 subdivisions based on the types of odontogenic tissues involved: epithelial odontogenic tumors (odontogenic epithelium with mature fibrous stroma, without odontogenic ectomesenchyme) (EOTs), mixed odontogenic tumors (odontogenic epithelium with odontogenic ectomesenchyme, with/without tissue formation) (MixOTs), and mesenchymal odontogenic tumors (mesenchyme and/or ectomesenchyme, with or without odontogenic epithelium) (MOTs). Despite any methodological errors, approximately 10% of the subjects were randomly selected and evaluated by a different researcher 4 weeks after the initial survey. There was 100% agreement between the investigators.

For all patients with OTs, demographic variables including histopathological type, age, sex, and location were recorded. Regarding the site of distribution, the maxilla and mandible were divided into 2 anatomic regions: anterior (from the midline to the distal surface of the second premolar teeth) and posterior (from the mesial surface of the first molar further distally).

Data were analyzed using SPSS for Windows (version 11.5; SPSS, Chicago, IL, USA). Pearson's chi-squared and Fisher's exact tests were used to determine potential differences in the distribution of OTs when stratified by sex and localization. A P value of <0.05 was considered statistically significant.

Results

Frequency

A total of 63,126 biopsies were recorded during the study period in the department of pathology. From these cases, 1165 oral biopsies were received from 2004 to 2010. Among 1165 cases, 86 cases were diagnosed as OTs. The relative frequency of OTs was 0.13% of the total biopsied specimens, and 7.38% of all oral biopsied samples that were encountered in this time period. Of the 86 cases of OTs, 80 (93.2%) were benign and only 6 (6.8%) were malignant.

Table 1 shows the abbreviations, frequency, sex, and male to female ratio of different pathological types of OT listed according to the WHO 2005 OT classification. In summary, 29 cases (33.7%) of these tumors were EOTs, 36 cases (41.8%) were MixOTs, and 15 (17.4%) were MOTs. KCOT (17.4%), odontomas (ODs) (41.8%) (both complex and compound type), and odontogenic myxomas (OMYXs) (9.3%) were the most commonly found EOTs, MixOTs, and MOTs, respectively. The most frequent benign OT was OD (41.8%), followed by KCOT (17.4%), ameloblastomas (AMEs) (12.7%) and OMYXs (9.3%). Primary introsseous squamous cell carcinoma (PIOSCC) (4.6%) was the most frequent malignant OT, followed by ameloblastic carcinoma (AC) (1.1%).

Age and sex

Of the 86 OT patients, 36 were male and 50 were female, resulting in a male to female ratio of 0.7:1.00. Although statistical analysis revealed insignificant differences in the distribution of OTs in relation to sex, a slight female predilection was noted for most of the tumors, except for AMEs and odontogenic fibromas (OFs). Notably, malignant tumors were significantly more common in male than in female patients (male to female ratio of 5.00:1.00).

Table 2 shows the age distribution of OTs. The age of the patients varied from 2 to 78 years, with a mean age of 32.19 years. The peak incidence occurred in

Table 1. Abbreviations, frequency, sex, and male to female ratio of OTs listed according to the WHO.

Tumor type	Abbr	Frequency		Male	Female	M:F ratio
		%	N	N	n	
Benign tumors		93.2%	(80)			
Odontogenic epithelium with mature fibrous stroma, without odontogenic ectomesenchyme	EOT	33.7%				
Ameloblastoma	AME	12.7%	11	8	3	2.6:1
Keratocystic odontogenic tumor	KCOT	17.4%	15	5	10	1:2
Calcifying epithelial odontogenic tumor	CEOT	3.4%	3	1	2	1:2
Odontogenic epithelium with odontogenic ectomesenchyme, with/without tissue formation	MixOT	41.8%				
Odontoma complex	OD-Cx	4.6%	4	1	3	1:3
Odontoma compound	OD-Cd	37.2%	32	11	21	1:2
Mesenchyme and/or ectomesenchyme, with or without odontogenic epithelium	MOT	17.4%				
Odontogenic fibroma	OF-C	4.6%	4	2	2	1:1
Odontogenic myxoma /myxofibroma	OMYX	9.3%	8	3	5	1:1.6
Cementoblastoma	CB	3.4%	3	0	3	0:3
Malignant tumors		6.8%	(6)			
Primary intraosseous squamous cell carcinoma	PIOSCC	4.6%	4	3	1	3:1
Ameloblastic carcinoma	AC	1.1%	1	1	0	--
Fibrosarcoma	FS	1.1%	1	1	0	--
Total		100%	86	36	50	1:1.3

M:F Ratio: Male to Female Ratio Abbr: Abbreviation

the second and third decades of life. EOTs most frequently (48.2%) occurred in the fifth and sixth decades of life, while 58.3% of all MixOTs and 40% of all MOTs were established in the second and third decades. The most frequent OT encountered in the second and third decades was OD, followed by KCOT. The most frequent OTs encountered in the fifth and sixth decades were AMEs and KCOTs, which were equally distributed. However, malignant OTs tended to occur in later decades and had a predilection for patients older than 40 years of age.

Location

The site distribution of each type of OT is presented in Table 3. The mandible was affected in 47 cases and the maxilla in 39 cases. EOTs and MOTs were most frequently observed in the posterior region of the mandible (maxilla to mandible ratio of 1:2.6 and 1:2.75, respectively), whereas the anterior maxilla region was the predominant site for involvement of MixOTs (maxilla to mandible ratio of 2.6:1.00). In general, there was a predilection for mandibular lesions, except for OD-Cd. AMEs exhibited a significantly high predilection for the posterior region of the mandible, and OD-Cd was notably found in the anterior region of the maxilla. Furthermore, 44.6% of the mandibular tumors were EOTs and 72.2% of the maxillary tumors were MixOTs.

Discussion

OTs infrequently occur in jaw bones derived from the tooth-forming apparatus or associated remnants. Although many classification schemes have been published, there have been many resulting controversies on the diagnosis, classification, terminology and therapeutic challenge of these lesions (7,11,14). In 2005, the WHO published the

Table 2. Age distribution of OTs in decades of life.

Tumor type	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	Total	Age range	Mean age	SD
AME	0	1	1	1	1	5	1	1	11	15–74	49.7	17.2
KCOT	0	4	2	3	1	5	0	0	15	12–59	36.0	17.1
CEOT	0	0	0	1	1	1	0	0	3	36–56	45.6	10.0
OD-Cx	0	1	3	0	0	0	0	0	4	13–26	21.2	5.6
OD-Cd	10	9	8	3	2	0	0	0	32	2–44	19.5	11.2
OF	1	0	1	0	1	1	0	0	4	3–53	31.7	22.5
OMYX	0	4	1	3	0	0	0	0	8	17–40	25.7	8.8
CB	0	0	0	1	0	1	0	1	3	36–78	56.0	21.0
PIOSCC	0	0	0	0	1	1	1	1	4	45–75	59.5	12.3
AC	0	0	0	0	0	1	0	0	1	54	54.0	-
FS	0	0	0	0	1	0	0	0	1	41	41.0	-
Total	**11**	**19**	**16**	**12**	**8**	**15**	**2**	**3**	**86**			

SD: Standard deviation

latest updated edition of the classification of OTs. There were 6 major changes in this scheme from the previous versions: (1) parakeratinized variant of odontogenic keratocyst is now classified as a benign tumor and termed KCOT; (2) adenomatoid odontogenic tumor (AOT) originates from the odontogenic epithelium with mature fibrous stroma and without ectomesenchyme; (3) calcifying odontogenic cyst (COC) is divided into 2 benign and 1 malignant groups; (4) clear cell odontogenic tumor is a malignant lesion and termed clear cell odontogenic carcinoma (CCOC); (5) odontogenic carcinosarcoma is not included due to the lack of evidence for the existence of this type; and (6) some changes were made regarding terminology and subtypings (8,14).

Although the revised definition of the parakeratinized variant of odontogenic keratocyst

Table 3. Site distribution of OTs.

Type of lesion	Maxilla			Mandible				Maxilla to mandible ratio
	A	p	Total	A	P	Total	Total	
AME	2	0	2	1	8	9	11	1:4.5
KCOT	2	3	5	2	8	10	15	1:2
CEOT	1	0	1	0	2	2	3	1:2
OD-Cx	0	2	2	0	2	2	4	1:1
OD-Cd	19	5	24	3	5	8	32	3:1
OF	0	1	1	0	3	3	4	1:3
OMYX	2	1	3	0	5	5	8	1:1.6
CB	0	0	0	0	3	3	3	0:3
PIOSCC	1	0	1	0	3	3	4	1:3
AC	0	0	0	0	1	1	1	0:1
FS	0	0	0	0	1	1	1	0:1
Total	**27**	**12**	**39**	**6**	**41**	**47**	**86**	**1:1.2**

as a KCOT resulted in an increase in the frequency and prevalence of OT, there are limited reports in the English-language literature using the 2005 WHO classification of OTs (7,8,14–16). Furthermore, there are only limited data available in the English-language literature on the prevalence of OTs in Turkish populations. In 1990, Günhan et al. published a report on OTs in Turkey (12). A total number of 409 cases were included from 1973 to 1989 and classified according to the 1971 WHO histological classification scheme (12). Afterwards, in a report on OTs from 1971 to 2003, Olgac et al. evaluated 527 cases in İstanbul according to the criteria suggested for the 1992 WHO histological classification (13). However, both of these valuable studies were based on data from similar locations in the western part of Turkey. Furthermore, there is no information available in the English-language literature on the prevalence of OTs in the eastern part of Turkey, particularly in the Black Sea region. To our knowledge, the present report is the first classification of OTs in this region of the world utilizing the WHO 2005 classification.

Several reports from different countries exhibited considerable geographic variation in the frequency of OTs (10–12,17,18). The relative frequency of OTs in the present study was 0.13% of the total biopsied specimens and 7.38% of all oral lesions recorded from January 2004 to December 2010. This incidence is much higher than Middle Eastern (1.9%) (6), Asian (3.9%) (7), South American (1.82%) (10,15), and North American (1.55%) (11) series, but lower than a South African (9.6%) (19) series. These differences may be the result of 2 main reasons: (1) higher numbers of reactive and inflammatory lesions are subjected to microscopic examination in developed countries, whereas only patients with incapacitating symptoms presented to the hospitals in developing countries; and (2) our department serves as a referral center for oral and maxillofacial surgery and pathology for the population of the Black Sea region, Eastern Turkey, and thus there are a significant number of diagnostically or therapeutically difficult cases from this region. Furthermore, the relative frequency of OTs among the total biopsied specimens was lower than that of a European (0.8%) (13) series, and there were insufficient data on the total oral biopsied specimens in the study from the western part of Turkey (12,13).

With a total of 80 recorded cases (93.2%), this study confirms that benign tumors are the most frequently observed OTs, in accordance with previous reports from Iran, China, Egypt, India, Mexico, and the United States, while only 6 cases (6.8%) were malignant. Of these benign tumors, 29 cases (33.7%) were EOTs, 36 (41.8%) were MixOTs, and 15 (17.4%) were MOTs. MixOTs were the most frequent subdivision of OTs in agreement with previous reports from Mexico, the United States, the western part of Turkey, and Estonia, but in contrast to series from China, Egypt, Brazil, and Libya (7,8,10,13–16,20,21). Table 4 shows the distribution and comparison of OTs in selected studies from various countries based on the types of odontogenic tissues involved.

In the present study, OD (OD-Cx and OD-Cd, together) was the most frequent OT, followed by KCOT, AME, and OMYX, in that order. Relatively high frequencies of OD were in agreement with previous reports from North America, South America, Asia, and Europe (10,11,21–23). According to series from Middle Eastern, Asian, and African populations, AME was the most frequent OT (6,8,9,13,14,17–19), with KCOT becoming the most frequent OT in more recent reports (7,15,16,20). Together, these 3 types of lesion constituted more than half of all the OTs identified in this study, which was in agreement with the recent literature (7,8,14–16,20). Table 5 shows the distribution and comparison of the 4 most common OTs in selected series from various countries.

ODs are usually discovered during routine radiographic examination and do not cause pain; therefore, treatment of this OT is generally provided by dentists or oral surgeons and pathological examination is underestimated (22–26). However, OT treatment is concentrated in our department in this region, and therefore, a higher frequency of OD may be reported in comparison to the western part of Turkey (12,13). Surgical specimens that are not sent for diagnosis may also produce inaccurate estimates of the frequency and recurrence rate of these lesions (10,27–29).

Regarding sex, 66.6%, 66.6%, and 51.7% of MixOTs, MOTs, and EOTs were identified in females, respectively. Of the 86 OTs, 36 were found in male patients and 50 were found in female patients, resulting in a male to female ratio of 1:1.38. Although

Table 4. Comparison of OTs in selected studies from various countries.

Author	Country	EOT	MixOT	MOT	Maxilla:Mandibula	Male:Female
Present study	Turkey	33.7%	41.8%	17.4%	1:1.2	1:1.3
Luo et al.[7]	China	77.7%	10.3%	5.8%	1:3.5	1.3:1
Tawfik et al.[8]	Egypt	68.4%	15.8%	12.2%	1:3.5	1.2:1
Taylor et al. [10†]	Mexico	31.6%	45%	19.9%	1:1	1:1.2
Buchner et al.[11†]	United States	14.2%	80.8%	4.6%	1:1.2	1:1
Günhan et al.[12†]	Turkey	41.5%	25%	32%	1:2	1:1
Olgac et al. [13†]	Turkey	34.0%	35.1%	30.8%	1:2	1:1.1
Jing et al. [14]	China	80.7%	8.9%	6.9%	1:3.5	1.4:1
Osterne et al. [15]	Brazil	58.3%	25.4%	14.6%	1:2.1	1:1.6
Avelar et al. [16]	Brazil	61.5%	30.5%	8%	1:2	1:1.3
Gehani et al. [20]	Libya	61.4%	27.5%	10.7%	1.2	1.3:1
Tamme et al.[21†]	Estonia	26.6%	52%	20%	1:1.6	1:1.7

† KCOT not included

statistical analysis revealed insignificant difference in the distribution of OTs in relation to sex ($P > 0.05$), a slight female predilection was noted for most of the tumors, except for AMEs and OFs. This result was in agreement with reports from Iran, Mexico, and Brazil (6,10,15,16), but conflicted with data from China, Egypt, and India (7–9,17). Notably, malignant tumors were significantly more common in male than in female patients in accordance with the literature (male to female ratio of 5.00:1.00). Günhan et al. reported an insignificant male predilection for OTs, whereas Olgac et al. noted a female predominance for OTs, consistent with our results (12,13) (Table 5).

Table 2 shows the age distribution of patients with OTs in decades of life. The age of the patients varied from 2 to 78 years, with a mean age of 32.19 years. In the present study, 96.5% were older than 5 years of age, which strengthens the impression that the majority of OTs arise from quiescent cell remnants of the tooth germ (17,22–25,30). Peak incidence occurred in the second and third decades of life. Furthermore, EOTs were most frequent (48.2%) tumors identified in the fifth and sixth decades of life, while 58.3% of MixOTs and 40% of MOTs were established in the second and third decades of life, respectively. The most frequent OT encountered in the second and third decades was OD, followed by KCOT. The most frequent OTs encountered in the fifth and sixth decades were AMEs and KCOTs, which were equally distributed. The higher prevalence in elderly people can mainly be attributed to the multicystic epithelial character of EOTs (12,21).

The patients with ODs ranged in age from 2 to 44 years, with a mean age of 19.7 years. The age range of males with ODs was between 9 and 30 years (mean age: 12.8 years), whereas this range was between 2 and 44 years (mean age: 23.2 years) for females. Of the OD patients, 86.1% were less than 30 years old; these results were also inconsistent with the previous series from Asia, South America, North America, and North Africa (6–8,10,11,14,15,18,20,29).

KCOT, the second most frequent tumor type, was observed in the patient age range of 12 to 59 years, with a mean age of 36.0 years. The mean patient age was higher than that seen for patients with the other benign OTs, except for AME patients, with an age range from 14 to 75 years (mean age: 49.7). Although the mean age of KCOT patients was similar to recently published results (7,8,14–16,20), the mean age for AME patients was in contrast to studies from industrialized countries (7,10,11,14), and, furthermore, was inconsistent with studies from

Table 5. Distribution and comparison of the 4 most common OTs in selected series.

Author	Country	AME	KCOT	OD*	OMYX	Male: Female	Maxilla: Mandibula
Present study	Turkey	12.7	17.4	41.8	9.3	1:1.3	1:1.2
Luo et al.[7]	China	36.5	38.7	6	2.6	1.3:1	1:3.5
Tawfik et al.[8]	Egypt	41.5	19.5	13.4	8.5	1.2:1	1:3.5
Taylor et al.[10†]	Mexico	23.7	-	34.6	17.7	1:1.2	1:1
Buchner et al.[11†]	United States	11.7	-	75.9	2.2	1:1	1:1.2
Günhan et al.[12†]	Turkey	36.5	-	18	12.5	1:1	1:2
Olgac et al.[13†]	Turkey	25	-	21	16	1:1.1	1:2
Jing et al.[14]	China	40.3	35.8	4.7	4.6	1.4:1	1:3.5
Osterne et al.[15]	Brazil	29.1	28.1	19.4	7.0	1:1.6	1:2.1
Avelar et al.[16]	Brazil	23.7	30	22.1	6.3	1:1.3	1:2
Gehani et al.[20]	Libya	22.3	35.1	19.5	3.3	1.3:1	1.2
Tamme et al.[21†]	Estonia	25.3	-	34.6	12	1:1.7	1:1.6

* OD-Cx and OD-Cd together
† KCOT not included
Abbreviations as in Table 1.

the developing parts of the world, such as India and Nigeria (17,19,25). The reasons for delayed diagnosis time were considered to be the reasons discussed in the Frequency section of the discussion. However, dysplastic changes tended to occur in later decades and had a predilection for patients greater than 40 years of age, which was in agreement with the literature (7,8,11,15,16,18,20,31).

Regarding location, 54.6% of all OTs were observed in the mandible, whereas 45.3% were located in the maxilla. Table 3 shows the distribution of OTs based on location. EOTs and MOTs were most frequently observed in the posterior region of the mandible, whereas the anterior region of the maxilla was the predominant site for involvement of MixOTs, in accordance with the literature (7,8,10–14,20,21). In general, there was a predilection for mandibular lesions, except for compound odontomas. The maxilla to mandible ratio (1:1.2) was similar to that in series from Mexico, Turkey, Brazil, and Libya (10,13,15,16,20) but higher percentages of mandibular OTs were observed in China and Egypt (7,8,14). AME showed a significantly high occurrence in the posterior region of the mandible, and, notably, OD-Cd occurred in the anterior region of the maxilla. The maxilla to mandible ratio was 3:1 for OD-Cd, 1:2 for KCOTs, and 1:4.5 for AMEs, in agreement with results from the recent literature (7,8,13,15,16,20). Table 5 shows a comparison of the most frequent OTs and the distribution of sex and location in selected series from various countries around the world.

This study provides epidemiological information on OTs in a Turkish population. OTs were rare lesions in the studied population and were composed mainly of ODs, KCOTs, and ameloblastoma. KCOTs became one of the most prevalent OTs after the introduction of the WHO 2005 classification system. It was very difficult to make a valid comparison between frequencies and types of OTs from various parts of the world because of the changes that occurred over the years in the definition and classification systems.

In conclusion, a marked geographic variation was apparent in the relative incidences of various OTs, which may be attributed to socioeconomic and genetic factors. Moreover, the use of old terminology and definition systems made older studies contradictory; therefore, further studies should be conducted to determine the real frequency of OTs. Furthermore, research on databases from large data sets should be supported by international agencies and government authorities with technical assistance.

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