Odontogenic Tumors

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Purpose: This study aims to analyze the frequency and distribution of odontogenic tumors in a Greek population and compare the findings with those reported in the recent literature.

Methods: Records of the Department of Oral Medicine and Pathology, Dental School, University of Athens, with histologic diagnosis of odontogenic tumors (based on the World Health Organization 2005 classification) were reviewed retrospectively from January 1970 to December 2011.

Results: A total of 652 cases of odontogenic tumors were reported. Of these, 651 (99.8%) were benign and only 1 (0.2%) was malignant. Keratocystic odontogenic tumor was the most frequent lesion (52.7%), followed by odontoma (18.9%) and ameloblastoma (16.1%). The mean age of patients was 38.0 years with a wide range (2.5–92 years).

Conclusions: Odontogenic tumors are rare lesions and appear to show a definite geographic variation. In Athens, Greece, they are presented mainly by the keratocystic odontogenic tumor, odontoma, and ameloblastoma.

Key Words: Odontogenic tumors, WHO classification, epidemiology, frequency

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Odontogenic tumors (OTs) are unique to the jaws and originate from tissue associated with tooth development.[1] They include entities of a hamartomatous nature, such as odontoma, benign neoplasms, some of which are aggressive as is the case of ameloblastoma and myxoma, and malignant neoplasms capable of metastasis.[2] These heterogeneous tumors are comparatively rare, comprising about 1% of all jaw tumors.[3]

Because there is a diversity of lesions that can arise from the odontogenic tissues, several classification schemes have been published in an attempt to define their diagnostic criteria. Based on the 1971 and 1992 World Health Organization (WHO) histologic classifications,[4,5] there were a number of reports of OTs from various parts of the world, but many controversial issues still needed to be addressed concerning subtypings, terminology, and diagnosis. In 2005, the WHO published the third edition[6] of OT histologic typing that brought some substantial changes; for example, the odontogenic keratocyst (parakeratinized) is now regarded as a new entity of OT and termed as *keratocystic OT*, on account of its clinical behavior and genetic and molecular features. Although this redefinition of the keratocystic OT produced an increase in the frequency and prevalence of OTs, few retrospective studies are published based on the latest updated edition.[2,7–15]

Moreover, the overall and relative frequency of individual OTs is believed to vary in different geographic sites, mainly because of high genetic and cultural diversity.[13] Although this information is helpful to clinicians and oral pathologists, as OTs pose a significant diagnostic and therapeutic challenge, clinicopathologic reports and statistical data are available only in certain countries.[13]

The purpose of the current study was to determine the epidemiology and clinicopathologic presentation of OTs in a Greek population and to compare these data with that from selected large series in other geographic regions and countries.

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MATERIALS AND METHODS

In this study, the histopathology records of the Department of Oral Medicine and Pathology, Dental School, University of Athens, Athens, Greece, were reviewed retrospectively from January 1970 to December 2011. A total of 652 cases of OTs were obtained and reviewed. The final diagnosis in each case was based on the 2005 WHO histopathologic classification, and keratocystic OTs were included in the study to render results comparable with those reported in the recent literature. Basic clinicopathologic features, clinical data regarding patient's age and sex, and tumor location, were retrieved and analyzed. With regard to site distribution, each jaw was divided into 3 anatomical parts as anterior (including incisors and the canine), middle (including premolars), and posterior (including molars, tuberosity and ramus) regions. Any tumor involving 2 areas or more was assigned as occupying an extensive area of the jaw and calculated separately. Also, the relative frequency of mandible tumors involving the ramus was calculated. In addition, lesions of the mandible or the maxilla involving anterior segment of one side crossing the midline to the anterior segment on the opposite side were recorded and calculated.

The relative frequency of OTs in relation to all biopsy specimens and to one another, distribution regarding sex, age, and tumor site were analyzed and compared with selected studies in the literature.

RESULTS

During the period of 40 years, a total of 29,088 biopsies were received, and 2.2% of them were OTs. A total of 652 cases comprised the current series of OTs. Of these cases, 651 (99.8%) were benign and

TABLE 1. Frequency of Occurrence and Sex Distribution of 652 Odontogenic Tumors

Diagnosis	Abbreviation	No.	%	Male	%	Female	%	Ratio
Benign tumors, 651 cases, 99.8%								
Keratocystic odontogenic tumor	KCOT	344	52.7	201	58.4	143	41.6	1.4:1
Odontoma	OC	123	18.9	54	43.9	69	56.1	1:1.3
Ameloblastoma	AME	105	16.1	64	61.0	41	39.0	1.6:1
Calcifying cystic odontogenic tumor	CCOT	17	2.6	7	41.2	10	58.8	1:1.4
Odontogenic myxoma	OM	17	2.6	6	35.3	11	64.7	1:2
Odontogenic fibroma	OF	16	2.4	4	25.0	12	75.0	1:3
Calcifying epithelial odontogenic tumor	CEOT	9	1.4	4	44.4	5	55.6	1:1.3
Adenomatoid odontogenic tumor	AOT	8	1.2	3	37.5	5	62.5	1:1.7
Ameloblastic fibroodontoma	AFO	7	1.1	4	57.1	3	42.9	1.3:1
Ameloblastic fibroma	AF	5	0.8	2	40.0	3	60.0	1:1.5
Malignant tumors, 1 case, 0.2%								
Ameloblastic carcinoma	AC	1	0.2	0	0	1	100.0	NA
Total		652	100%	349	53.5	303	46.5	1.2:1

NA indicates not applicable; ratio, male-female ratio.

only 1 (0.2%) was malignant. The most frequent OT was keratocystic OT (52.7%). The second most frequent tumor was odontoma (18.9%). In the current study, odontomas were classified histologically as complex in 73 cases (59.3%) and as compound in 50 cases (40.7%). The third most frequent lesion was ameloblastoma (16.1%). Histologically, ameloblastomas were classified in 1 of the following patterns: follicular (34.1%), mural (23.4%), plexiform (16.0%), acanthomatous (9.6%), peripheral (6.4%), unicystic (6.4%), granular cell (1.0%), basal cell (1.0%), acanthomatous-plexiform (1.0%), and follicullar-plexiform (1.0%). Calcifying cystic OT and odontogenic myxoma comprised each for 2.6% of OTs, followed by odontogenic fibroma (2.4%) and calcifying epithelial OT (1.4%). The frequency of other benign OTs ranged between 1.2% and 0.8%. One case of ameloblastic carcinoma was the only malignant entity, accounting for 0.2% of all tumors.

Regarding sex, 53.5% of all OTs occurred in males and 46.5% in females. The overall male-female ratio was 1.2:1. The relative frequency and sex distribution of all cases are given in Table 1.

The age of the patients was known for 625 of the present cases. It ranged widely from 2.5 to 92 years, with a mean age of 38.0 years. Most of the cases were distributed between age 10 and 39 years with a peak incidence in the second decade (Table 2).

Of the 652 OTs of the current series, the location was known for 598 cases (Table 3). Regarding the anatomical site, the mandible was the mostly affected site for most tumors, and for overall it is 66.7%, with a mandible-maxilla ratio of 2:1. In general, the posterior part of the mandible was clearly the most frequently affected site, whereas the ramus was involved in 32.8% of mandibular OTs. Lesions that extended through the midline of the mandible or the maxilla were less frequently encountered (5.4% of all cases). Extensive tumors, occupying a large segment of 2 or more anatomical areas of the affected jaw, comprised 11.8% of mandibular and 14.6% of maxillary OTs.

Table 4 shows relative data from selective reports from different countries, classified according to the 2005 WHO edition.[2,7–12,14,15] The data of the current study could be compared with those in the previous reports.

DISCUSSION

Odontogenic tumors constitute a small but very diverse group of lesions that originate from the tissues of tooth formation.[15] The different degrees of intertissue interactions and the various growth patterns that characterize the pathologic pathways that lead to the genesis and growth of these tumors have been extensively studied

TABLE 2. Age Distribution of 652 Odontogenic Tumors

Tumor	Age Group, y											Total Cases	Mean Age
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90–99	NS		
KCOT	5	65	46	50	39	45	49	24	3	—	18	344	40.5
OC	18	42	20	16	6	7	8	1	1	—	4	123	25.6
AME	1	14	11	14	8	17	19	13	5	—	3	105	47.0
CCOT	—	—	3	5	1	1	2	3	1	1	—	17	50.6
OM	—	2	7	3	4	1	—	—	—	—	—	17	30.2
OF	—	2	3	3	4	2	1	—	—	—	1	16	35.2
CEOT	—	—	1	3	—	1	1	2	—	—	1	9	50.9
AOT	—	4	—	2	1	1	—	—	—	—	—	8	28.0
AFO	3	3	1	—	—	—	—	—	—	—	—	7	12.1
AF	1	4	—	—	—	—	—	—	—	—	—	5	11.4
AC	—	—	—	—	—	—	—	1	—	—	—	1	70.0
Total	28	136	92	96	63	75	80	44	10	1	27	652	38.0

Abbreviations as in Table 1.
NS indicates not specified.

TABLE 3. Site Distribution of 652 OTs

	Mandible						Maxilla								Midline		Ramus	
Tumor	**Anterior**	**Middle**	**Posterior**	**EA**	**Total**	**%**	**Anterior**	**Middle**	**Posterior**	**EA**	**Total**	**%**	**NS**	**Ratio**	**No.**	**%**	**No.**	**%**
KCOT	16	29	139	40	224	70.9	20	12	31	29	92	29.1	28	2.4:1	25	7.9	115	51.3
OC	23	10	23	2	58	50.4	38	5	14	—	57	49.6	8	1:1	2	1.7	—	—
AME	14	9	47	4	74	76.3	2	2	19	—	23	23.7	8	3.2:1	3	3.1	16	21.6
CCOT	5	1	1	—	7	50.0	1	2	4	—	7	50.0	3	1:1	—	—	—	—
OM	—	1	7	—	8	47.1	3	1	5	—	9	52.9	—	1:1.1	—	—	—	—
OF	3	1	6	—	10	62.5	4	1	1	—	6	37.5	—	1.7:1	2	12.5	—	—
CEOT	1	—	3	—	4	80.0	1	—	—	—	1	20.0	4	4:1	—	—	—	—
AOT	2	2	—	—	4	57.1	2	1	—	—	3	42.9	1	1.3:1	—	—	—	—
AFO	1	1	3	—	5	83.3	—	—	1	—	1	16.7	1	5:1	—	—	—	—
AF	—	—	4	—	4	100.0	—	—	—	—	—	—	1	NA	—	—	—	—
AC	—	—	—	1	1	100.0	—	—	—	—	—	—	—	NA	—	—	—	—
Total	65	54	233	47	399	66.7	71	24	75	29	199	33.3	54	2:1	32	5.4	131	32.8

Abbreviations as in Table 1.

NS indicates not specified; NA, not applicable; EA, lesions occupying an extensive area; ratio, mandible-maxilla ratio; midline, lesions exceeding midline of jaws; ramus, ramus involved in mandibular tumors.

for many years and still are the subject of contemporary scientific research.[16–18] Although genetic and molecular studies have led to an increasing amount of knowledge and understanding of their complex physiopathologic pathways, the epidemiology of OTs remains unclear. Avelar et al[13] in 2011 conducted a research in epidemiologic studies involving OTs in an attempt to verify the incidence of these lesions worldwide. The authors concluded, in agreement with many retrospective studies from countries of Asia,[7,11,12,15,19–23] America,[8–10,14,24–29] Africa,[2,30–33] and Europe,[34,35] that the relative frequency of different kinds of OTs, the age, and the sex distribution express a marked geographic variation in incidence. The discrepancies in the prevalence of these lesions can be attributed to high genetic and cultural diversity. Moreover, in several less developed countries, many cases of OTs are undiagnosed because of hospital management problems and poor screening of tumors that grow self-limited and may be asymptomatic for long periods, such as odontomas.[13]

In 2005, the third edition of the WHO histologic typing for OTs was published in which definitions of some pathologic entities have been changed and some new ones have been introduced.[6] The most important change was the addition of the parakeratinized odontogenic keratocysts under the name of "keratocystic OT." Already from 2002, Shear[36–38] in a series of 3 articles, had indicated that the odontogenic keratocyst "… was an aggressive lesion with a predilection for recurrence unlike the majority of other jaw cysts. This led to the tentative suggestion that the OKC might be a benign neoplasm...". This new classification with the addition of keratocystic OT to OTs had an impact on the epidemiologic profile of these lesions and rendered very difficult or even impossible the comparison between retrospective studies of OTs conducted before and after the last WHO classification.[13]

Literature search revealed that only 9 large series of OTs based on the 2005 WHO classification have been published until now. These are series from Brazil,[8–10] Mexico,[14] China,[7,15] Sri Lanka,[12] India,[11] and Egypt.[2] The current report is the first retrospective study of OTs in a Greek, hence in a European population based on the latest WHO classification.

The relative frequency of OTs in the current study was 2.2% of a total of 29,088 biopsies. From Table 4, it can be seen that this incidence is lower than the prevailing frequency in most of the recent series.[7–9,11,12,14] Only da-Costa et al[10] from Brazil reported a lower frequency (1.3%).

This study confirms that benign tumors (99.2%) are the most frequently seen OTs, in agreement with most other series.[2,8,9,11,12,14,15] Malignant OTs are rare, and there was only 1 in the current study. The incidence of malignant OTs was significantly higher in a Brazilian (5.5%)[10] and a Chinese (6.0%)[7] population.

In the current series, male patients were affected slightly more frequently than female patients, in support of recent studies from

TABLE 4. Data from Recent Reports and the Current Study, Based on the 2005 WHO Classification

Continent	Author	Country	No. Biopsies	OT Cases	OT More Common	% Malignant OTs	Male-Female Ratio	Mandible-Maxilla Ratio
Asia	Jing et al[15]	China	NS	1642 (NS)	AME (40.3%)	3.0	1.4:1	4.0:1
	Luo and Li[7]	China	33354	1309 (3.9%)	KCOT (38.7%)	6.0	1.4:1	3.5:1
	Varkhede et al[11]	India	2075	120 (5.8%)	AME (40.8%)	No cases	1.4:1	2.8:1
	Siriwardena et al[12]	Sri Lanka	44458	1677 (3.8%)	AME (48.7%)	1.4	1:1	2.8:1
South America	Avelar et al[8]	Brazil	NS	238 (4.76%)	KCOT (30.0%)	No cases	1:1.3	2.1:1
	Gaitán-Cepeda et al[14]	Mexico	2706	136 (5.0%)	KCOT (38.9%)	No cases	1:1.6	NS
	Osterne et al[9]	Brazil	6231	185 (2.97%)	AME (29.2%)	No cases	1:1.6	2.1:1
	Da-Costa et al[10]	Brazil	15758	201 (1.3%)	KCOT (32.3%)	5.5	1.3:1	2.7:1
Africa	Tawfik and Zyada[2]	Egypt	NS	82 (NS)	AME (41.5%)	3.7	1.2:1	4.9:1
Europe	Current Study	Greece	29088	652 (2.2%)	KCOT (52.1%)	0.2	1.2:1	2:1

Abbreviations as in Table 1.

NS indicates not specified.

Egypt,[2] Brazil,[10] India,[11] and China.[7,15] However, female preponderance was reported in most studies from South America,[8,9,14] and an equal sex distribution was reported in Sri Lanka.[12]

In general, OTs in this series occurred more commonly in the mandible than in the maxilla, in keeping with the recent reports based on the 2005 WHO classification.[2,7–12,16,17] The marked preference for the mandible in reports from China[15] and Egypt[2] could be explained by the prevalence of ameloblastoma.

In the current study, OTs showed a peak incidence in the second decade of life, which seems to be related to the marked prevalence of keratocystic OT and ameloblastoma in this age range in this sample. This is in accordance with the results of Brazilian studies, such as that by Osterne et al[9] and Avelar et al,[8] whereas many other recent reports demonstrate an overall peak incidence in the third decade of life.[2,7,10–12,15]

Keratocystic OT was the most frequent tumor in this study, in agreement with reports by other authors that followed the 2005 WHO classification.[7,8,10,14] It has to be pointed out that the incidence of keratocystic OTs observed in this study is significantly higher compared with that in these reports. In our sample, a total of 344 cases were verified, accounting for 52.7% of all the OTs. They occurred in 201 males and 143 females with a male-female ratio of 1.4:1. Only 2 South American studies reported a female predominance.[8,9] In this study, keratocystic OTs were mainly distributed in the second, third, fourth, sixth, and seventh decades of life, with the second decade being the most affected (65 cases), in contrast to most of the recent reports that showed a peak incidence in the third decade.[2,7,9,10,12,15] Only Osterne et al[9] reported a peak incidence in the second decade in a Brazilian population, whereas Titinchi and Nortje[39] analyzing 145 keratocystic OTs reported an equal peak incidence in the second and third decades of life. In this sample, the youngest patient was 8 years of age and the oldest 89 years (mean age, 40.5 years). Most keratocystic OTs occurred in the mandible (70.9%) in agreement with all recent studies. The posterior mandible was the most frequently affected area (139 cases) with the ramus being involved in 51.3% of mandibular keratocystic OTs (115 cases).

Odontomas were encountered in 123 cases in this study (18.9%). This incidence is comparable to those reported in Brazilian[8–10] populations. Only Gaitán-Cepeda et al[14] in Mexico have reported a higher incidence (30.8%). Findings in Asian studies have shown that the incidence of odontomas seems to be very low in Chinese populations.[7,15] In this sample, females were affected in 56.1% of cases with male-female ratio of 1:1.3. Like keratocystic OTs, odontomas affected mainly the second decade of life in the current series (42 cases). Most recent studies report also a peak incidence of odontomas in the second decade.[2,7–9,11,12,15] In this sample, the youngest patient was 2.5 years of age and the oldest 82 years (mean age, 25.6 years). Odontomas were equally distributed in the mandible and the maxilla, with most cases being located in the anterior maxilla (38 cases), which is similar to the study of Varkhede et al[11] from India.

One hundred five cases of ameloblastoma (16.1%) were identified. In contrast to the findings of this study, ameloblastoma was the most frequent OT in many reports that used the 2005 WHO classification.[9,11,12,15] In this sample, ameloblastoma occurred in 64 males and 41 females with a male-female ratio of 1.6:1. A male predominance was also found in most of the reviewed studies.[2,7–9,15] In this study, ameloblastoma was encountered in almost all age groups with a peak incidence in the sixth and seventh decades (17 and 19 cases, respectively). This is in contrast with most of the recent studies that show a peak incidence in the third decade.[2,8–10,12,15] In this sample, the youngest patient was 6 years of age and the oldest 86 years (mean age, 47.0 years). As expected, most tumors occurred in the mandible (76.3%). The posterior region of the mandible and the maxilla were most frequently affected (47 and 19 cases, respectively), whereas the ramus was involved in 21.6% of the mandibular lesions.

Seventeen cases were diagnosed as calcifying cystic OT, accounting for 2.6% of all OTs, an incidence comparable to those reported by Jing et al,[15] Luo and Li,[7] and da-Costa et al.[10] The male-female ratio was 1:1.4, with a mean age of 50.6 years. In the present cases, calcifying cystic OT affected all age groups in adults, but no lesion was found in the first and second decades. The youngest patient was 22 years of age and the oldest 92 years. Most tumors (5 cases) were found in the fourth decade of life. There was no jaw predilection, while the anterior mandible and the posterior maxilla were the most commonly affected sites.

In this series of OTs, odontogenic myxoma presented with the same incidence with calcifying cystic OT (2.6%), in keeping with the findings of Luo and Li.[7] In the current study, the male-female ratio was 1:2. A female predominance was also reported by Tawfik and Zyada,[2] Luo and Li,[7] and da-Costa et al.[10] In this sample, the mean age of patients with myxoma was 30.2 years. These tumors showed a peak occurrence in the third decade with the youngest patient being 12 years of age and the oldest 54 years. Eight cases were found in the mandible (47.1%) and 9 cases were located in the maxilla (52.9%), with the posterior mandible being the most frequently affected location (41.2% of all odontogenic myxomas).

Sixteen cases of odontogenic fibroma were diagnosed (2.4%), with a male-female ratio of 1:3. A female predominance was also reported by Luo and Li,[7] Osterne et al,[9] and Siriwardena et al.[12] Regarding age, the patients with odontogenic fibroma in this study were widely distributed from the second to the seventh decade, with the youngest patient being 11 years of age and the oldest 61 years (mean age, 35.2 years). Most cases (62.5%) affected the mandible, whereas the location in 2 cases (12.5%) exceeded the midline of the mandible. A marked predilection of odontogenic fibroma for the mandible was also observed in most recent studies.[7–10,15]

Nine cases of calcifying epithelial OT were found among the 652 OTs (1.4%), in keeping with the findings of Gaitán-Cepeda et al.[14] In the current sample, the male-female ratio was 1:1.3. The youngest patient was 27 years of age and the oldest 78 years (mean age, 50.9 years). In 4 cases, the location was not known; 3 cases affected the posterior mandible, 1 the anterior mandible, and 1 the anterior maxilla.

Eight cases of adenomatoid OT were diagnosed corresponding to 1.2% of all the tumors. The lesions affected 3 males and 5 females. The youngest patient was 13 years of age and the oldest 53 years (mean age, 28.0 years) and the highest incidence (4 cases) was observed in the second decade, in accordance with most of the recent studies.[9] Regarding the location, 4 lesions affected the mandible (57.1%) and no tumor was found in the posterior region of the jaws.

Seven cases of ameloblastic fibroodontoma (1.1%) were identified in this study. This incidence is close to the findings of Luo and Li[7] (0.9%). These tumors affected 4 males and 3 females in the current sample. The mean age was 12.1 years with the youngest patient being 5 years of age and the oldest 25 years. Most of these tumors (5 cases) were located in the mandible, and the posterior area was the most frequently affected (3 cases). Siriwardena et al[12] identified only 8 cases in a sample of 1677 OTs (0.5%) with an equal jaw distribution, whereas other recent reports documented no cases of ameloblastic fibroodontoma in their sample.[2,9]

In the current series, 5 cases of ameloblastic fibroma were found comprising 0.8% of all OTs. Other recent studies reported similar findings.[7,12,15] The lesions occurred in 2 male and 3 female young patients with the youngest being 9 years of age and the oldest 13 years. In 1 case, the location was not known, whereas the remaining 4 cases affected the posterior mandible.

One case of ameloblastic carcinoma (0.2%) was found, corresponding to the only malignant lesion of this study. This incidence is in accordance with the findings of Siriwardena et al.[12] Luo and Li[7] and Jing et al[15] reported higher incidence of ameloblastic carcinoma

in Chinese populations (1.3% and 1.6%, respectively), whereas da-Costa et al[10] reported the highest incidence (3.5%) in a Brazilian population. In the current sample, this malignant tumor was diagnosed in a 70-year-old female patient, occupying an extended area of the body of the right mandible.

In conclusion, the current study shows that OTs are rare lesions in Greece and are presented mainly by the keratocystic OT, odontoma, and ameloblastoma. In the studied population, OTs exhibit a male preponderance with a peak incidence in the second decade of life, whereas the mandible is the most common affected site. As many studies are outdated and inappropriate for valid comparison because of the latest WHO reclassification of OTs in 2005, data from more retrospective studies are needed to improve the existing knowledge about the epidemiology and behavior of these lesions.

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