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Relative frequency of peripheral odontogenic tumors: a study of 45 new cases and comparison with studies from the literature

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BACKGROUND: Peripheral (extraosseous) odontogenic tumors are rare, and reports in the literature have mainly been single case reports or a small series of cases. The aim of this study was to determine the relative frequency of peripheral (extraosseous) odontogenic tumors relative to one another and relative to their central (intraosseous) counterparts in an oral pathology biopsy service and to compare these data with information available in the literature.

METHODS: The files of the Pacific Oral and Maxillofacial Pathology Laboratory of the University of the Pacific, San Francisco, CA, USA, served as the source of material for this study. Files were systematically searched for all cases of peripheral odontogenic tumors (POTs) during a 20-year-period.

RESULTS: There were 91 178 cases accessed in which central and POTs were identified in 1133 (1.24%), central tumors in 1088 (1.2%), and peripheral tumors in 45 (0.05%). Peripheral tumors accounted for 4% of all 1133 central and POTs. Peripheral odontogenic fibroma (PODF) was the most common of the 45 POTs accounting for 51.1% (23 cases) followed by peripheral ameloblastoma (PA) 28.9% (13 cases) and peripheral calcifying cystic odontogenic tumor (PCCOT) 13.3% (six cases). Peripheral calcifying epithelial odontogenic tumor, peripheral ameloblastic fibroma, and peripheral ameloblastic carcinoma were also identified – each comprised 2.2% (one case each). PODF was more common than its central counterpart by a 1.4:1 ratio. This was the only peripheral tumor that was more common than its central counterpart. PA accounted for 9.3% of all ameloblastomas and PCCOT for 26% of all calcifying cystic odontogenic tumors.

CONCLUSION: There is only scarce information in the literature on the relative frequency of POTs. Additional studies should be conducted to determine the true relative frequency. To ensure accuracy, pathologists with experience in the field of odontogenic tumors should conduct these studies. Intraosseous tumors that perforate through the bone to the gingival tissue, clinically presenting as 'peripheral tumors' should be excluded.
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Keywords: odontogenic tumors; gingival neoplasms; jaw neoplasms; mandibular neoplasms; maxillary neoplasms

Introduction

Peripheral odontogenic tumors (POTs) are tumors that demonstrate the histologic characteristics of their intraosseous counterparts but occur solely in the soft tissue covering the tooth-bearing portion of the mandible and maxilla. These lesions are also known as extraosseous odontogenic tumors, soft tissue odontogenic tumors, or odontogenic tumors of the gingiva (1).

Peripheral odontogenic tumors are rare with mostly single case reports or a small series of cases reports reported in the literature. Odontogenic tumors, described as originating in the gingiva, include ameloblastoma, calcifying epithelial odontogenic tumor, squamous odontogenic tumor, calcifying cystic odontogenic tumor (calcifying odontogenic cyst), adenomatoid odontogenic tumor, ameloblastic fibroma, odontoma, odontogenic fibroma, and odontogenic myxoma, some of which are exceedingly rare.

There is no valid information in the literature regarding the relative frequency of POTs. Several attempts have been carried out by accumulating all case reports of POTs published in the literature and analyzing their frequency (1, 2). However, this method is inaccurate as published case reports tend to describe only very rare or unusual lesions. The best source to obtain information on the relative frequency of POTs is

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from records of a single oral pathology diagnosis service. Information gained from these records is extremely valuable and probably represents the only large data source presently available (3).

The purpose of this study was to determine the relative frequency of POTs relative to one another and relative to their central (intraosseous) counterparts in an oral pathology biopsy service and to compare these data with information available in the English language literature.

Material and methods

The files of the Pacific Oral and Maxillofacial Pathology Laboratory of Arthur A. Dugoni School of Dentistry, University of the Pacific at San Francisco, CA, USA, served as a source of material for this study. This laboratory serves the communities of Northern California with most biopsies received from private oral and maxillofacial surgeons. Files were systematically searched for all cases of central (intraosseous) odontogenic tumors and peripheral (extraosseous) odontogenic tumors during a 20-year period (1984–2004). Cases submitted for consultation from other oral or general pathologists were excluded from the study. Odontogenic tumors were classified according to the criteria in the recent WHO histological classification of odontogenic tumors (4). Clinical information, including patient's age, gender and location, was obtained from the biopsy submission forms.

Results and comments

For the 20-year period, 91 178 cases were accessed. Central (intraosseous) and peripheral (extraosseous) odontogenic tumors were identified in 1133 (1.24%) in which central tumors were identified in 1088 (1.2%) and peripheral tumors in 45 (0.05%). This is the largest series of POTs reported from one source.

Peripheral tumors accounted for 4% of the 1133 central and POTs (Table 1). Among the 45 POTs, peripheral odontogenic fibroma (PODF) was the most common tumor (51.1%, 23 cases) followed by peripheral ameloblastoma (PA) (28.9%, 13 cases) and peripheral calcifying cystic odontogenic tumor (PCCOT) (13.3%, six cases). The peripheral calcifying epithelial odontogenic tumor (PCEOT), peripheral ameloblastic fibroma (PAF), and peripheral ameloblastic carcinoma (PAC) – each comprised 2.2% (one case each).

Because of the paucity of cases reported in the literature as POTs, the individual data of the tumors identified in our files are presented.

Peripheral odontogenic fibroma

The clinical features of 23 cases of PODF are presented in Table 2. The youngest patient was 12 years old, the eldest 84 years old. Mean age at diagnosis was 32.3 years, which is similar to the mean of 34.4 years reported for the intraosseous odontogenic fibroma (5).

Peripheral odontogenic fibroma occurred in 11 (48%) males and 12 (52%) females. A slight female predominance was also noted in a literature review by Daley and Wysocki (6). The intraosseous odontogenic fibroma shows a clear female predominance with a reported male-to-female ratio of 1:2.2 (5).

Table 1 Relative frequency of odontogenic tumors (terminology according to the recent WHO classification (4))

Type of tumor	*Central (C), n (%)*	*Peripheral (P), n (%)*	*C + P, n (%)*
Ameloblastoma	127 (11.2)	13 (1.2)	140 (12.4)
Calcifying epithelial odontogenic tumor	5 (0.4)	1 (0.1)	6 (0.5)
Squamous odontogenic tumor	3 (0.3)	0 (0)	3 (0.3)
Calcifying cystic odontogenic tumor	17 (1.5)	6 (0.5)	23 (2.0)
Adenomatoid odontogenic tumor	19 (1.7)	0 (0)	19 (1.7)
Ameloblastic fibroma	17 (1.5)	1 (0.1)	18 (1.6)
Ameloblastic fibrodentinoma/ fibro-odontoma	19 (1.7)	0 (0)	19 (1.7)
Odontoma	826 (72.9)	0 (0)	826 (72.9)
Odontogenic fibroma	16 (1.4)	23 (2.0)	39 (3.4)
Odontogenic myxoma/ myxofibroma	24 (2.1)	0 (0)	24 (2.1)
Cementoblastoma	10 (0.9)	0 (0)	10 (0.9)
Malignant odontogenic tumors	5 (0.4)	1 (0.1)	6 (0.5)
Total	1088 (96.0)	45 (4.0)	1133 (100.0)

The most common site for PODF was the mandible: 16 (70%) in the mandible and seven (30%) in the maxilla. The mandibular incisor/canine and premolar areas were the most prevalent sites, affecting both the buccal and lingual aspects of the gingiva. The intraosseous odontogenic fibroma also showed predilection for the mandible but most lesions occurred in the molar and premolar areas (5). The histologic spectrum of PODF was wide. Lesions were non-encapsulated and odontogenic epithelium was obviously present in all. In 12 of the 23 cases (52%), the odontogenic epithelium was closely associated with some type of mineralization – dentinoid and/or cementum-like material.

Peripheral ameloblastoma

The clinical features of 13 cases of PA are presented in Table 3. The youngest patient was 41 years old, the eldest 85 years old. Mean age at diagnosis was 60.4 years, which is much higher than for the intraosseous ameloblastoma (37.4 years) (7). Thus, PA occurs at a significantly older age than its central counterpart.

Peripheral ameloblastoma occurred in six (46%) males and seven (54%) females. Other studies show a male predominance with a male-to-female ratio of 1.4:1 (8). A slight male predominance has also been reported for the intraosseous ameloblastoma (7).

The mandible was the preferred site: 10 (77%) compared with three (23%) in the maxilla. The mandibular canine/premolar area was the most common, affecting both the lingual and buccal aspects of the gingiva. The intraosseous ameloblastoma also shows marked predilection for the mandible, mostly in the molar-ramus area (7).

Table 2 Clinical data of 23 cases of peripheral odontogenic fibroma

Case	*Age*	*Gender*	*Group*	*Gingival location*	*Size (cm)*	*Clinical diagnosis*
1	56	M	White	Mandible, canine to 1st premolar	1.0	PG
2	39	M	White	Mandibular gingival	1.1	U
3	18	M	White	Mandible, labial, canine to 1st premolar	1.4	U
4	84	M	White	Mandible, alveolar mucosa	0.4	Fibrous overgrowth
5	16	F	White	Mandible, edentulous 3rd molar	0.7	Fibroma
6	46	M	White	Mandible, lingual, central to lateral incisor	0.8	Papilloma; fibroma
7	23	M	White	Mandible, edentulous 3rd molar	1.0	PG
8	36	F	White	Mandible, 2nd premolar to 1st molar	1.0	PG
9	12	F	Black	Maxilla, 1st to 2nd molar	1.5	Fibrous overgrowth
10	42	F	White	Mandible, lateral incisor to canine	0.8	Fibroma
11	15	M	White	Mandible, edentulous 3rd molar	0.5	PG
12	12	F	White	Maxilla, 2nd premolar	1.0	Fibroma
13	24	F	Hispanic	Maxilla, buccal, canine	0.7	PG
14	51	F	White	Maxilla, central incisor	1.2	PG
15	36	M	Black	Mandible, lingual, 1st premolar	0.6	Fibroma
16	22	F	Black	Mandible, buccal, lateral incisor to canine	0.7	Fibroma
17	26	M	White	Maxilla, 1st molar	0.8	Fibroma; PG; PGCG; Papilloma
18	33	F	Asian	Mandible, 1st to 2nd molar	1.2	PG; PGCG; POF
19	37	M	White	Maxilla, central incisor	0.5	POF; Fibroma
20	17	M	White	Mandible, buccal, canine	0.5	Fibroma
21	30	F	White	Maxilla, canine	0.7	Fibrous hyperplasia
22	35	F	White	Mandible, lateral incisor to canine	0.9	Fibroma
23	32	F	White	Mandible, 1st premolar	0.8	PGCG

U, unknown; PG, pyogenic granuloma; PGCG, peripheral giant cell granuloma; POF, peripheral ossifying fibroma.

Table 3 Clinical data on 13 cases of peripheral ameloblastomas

Case	*Age*	*Gender*	*Group*	*Gingival location*	*Size (cm)*	*Clinical diagnosis*
1	76	F	Asian	Mandible, lingual, 2nd premolar to 1st molar	1.2	PG
2	U	F	Asian	Maxilla, edentulous 1st molar	1.2	PG
3	53	M	White	Mandible, buccal, canine to 1st premolar	1.1	U
4	41	F	Hispanic	Mandible, lingual, 1st to 2nd premolar	0.8	Gingival cyst
5	44	F	White	Mandible, buccal, canine to 1st premolar	0.4	Fibroma; gingival cyst
6	72	F	White	Mandible, edentulous 3rd molar	2.0	Fibroma
7	65	F	Hispanic	Mandible, lingual, 2nd premolar	1.6	PG
8	42	M	White	Mandible, lingual, lateral incisor to canine	0.7	U
9	85	F	White	Maxilla, edentulous 2nd molar	1.5	Fibrous hyperplasia
10	43	M	White	Mandible, lingual, 2nd premolar to 1st molar	1.1	Fibroma
11	52	M	White	Mandible, edentulous 1st molar	2.5	Fibroma
12	84	M	White	Maxilla, palatal gingival, canine to 1st molar	2.2	Mixed tumor
13	68	M	White	Mandible, edentulous 3rd molar	0.8	Wart

U, unknown; PG, pyogenic granuloma.

There was no radiologic evidence of bone involvement in nine cases; superficial bony depression of the underlying bone, known as cupping or saucerization, was noted at surgery in four cases. Incomplete excision of the lesion was noted in the histopathologic examination in four cases, and all of these lesions were re-excised by the oral surgeons and re-submitted for histopathologic examination. No further follow-up was available.

Peripheral ameloblastoma is considered to derive from two sources. Lesions located entirely within the connective tissue of the gingiva arise from remnants of the dental lamina (rests of Serres). The others probably arise from the surface epithelium (1). The relationship of the tumor to the overlying mucosal epithelium could be determined in nine cases. There was continuity between the tumor and the surface epithelium in six cases, and a band of connective tissue between the tumor and the surface epithelium in three cases.

Peripheral calcifying cystic odontogenic tumor

The clinical features of six cases of PCCOT are presented in Table 4. The youngest patient was 12 years old; the eldest 76 years old (mean 52 years). The mean age reported for the intraosseous central calcifying cystic odontogenic tumor was 30.3 years (9). PCCOT occurs at a significantly older age than its central counterpart.

Peripheral calcifying cystic odontogenic tumor occurred in two (33.3%) males and four (66.6%) females. Other studies have shown only a slight female predilection for PCCOT (10), as well as for the intraosseous calcifying cystic odontogenic tumor (9). The primary site for PCCOT was the mandible: five in the mandible

Table 4 Clinical data on six cases of peripheral calcifying cystic odontogenic tumor

Case	*Age*	*Gender*	*Group*	*Gingival location*	*Size (cm)*	*Clinical diagnosis*
1	61	F	White	Maxilla, buccal, canine to 1st premolar	0.7	Fibroma
2	56	F	U	Mandibular gingival	0.5	U
3	65	M	White	Mandible, lingual, canine	0.6	U
4	42	F	U	Mandible, central incisor	0.6	Gingival cyst
5	12	M	White	Mandible, edentulous 2nd molar	0.6	Gingival cyst
6	76	F	Hispanic	Mandible, canine to 1st premolar	0.7	U

U, unknown.

compared with one in the maxilla. The most common sites were the mandibular incisor/canine and premolar areas. The intraosseous calcifying cystic odontogenic tumor does not have any predilection for either the maxilla or mandible, with most lesions located in the incisor/canine area (9). Histologically, PCCOT may exhibit cystic or solid architecture (known as peripheral dentinogenic ghost cell tumor). All six cases were of the cystic type.

Other peripheral odontogenic tumors

Three other POTs were identified in the files. The first was a PCEOT in the gingiva of a 71-year-old white female. Unfortunately no additional clinical information was available. The second was a PAF in an 8-year-old white male, located in the first molar area of the maxillary gingiva that measured 1.2 cm. The third was a PAC in a 63-year-old white male. The tumor developed in a recurrent PA located in the posterior maxillary tuberosity area.

Discussion

Peripheral odontogenic tumors, as a group, should be considered rare, with only 0.05% of all biopsy specimens submitted to an oral pathology biopsy service. Of all POTs, 51% were PODFs, 29% PAs, and 13% PCCOTs. The remainder of the peripheral tumors was about 2% each.

In the present study, POTs accounted for 4% of all odontogenic tumors. Review of the English language literature revealed only a paucity of information on the relative frequency of POT. Most studies regarding odontogenic tumors relate only to central tumors. It is difficult, if at all possible, to determine whether the authors intentionally reported only central tumors or included peripheral tumors without mentioning it. The few studies found that relate to both central and peripheral tumors are presented in Table 5. The percentage of POT from the total number of odontogenic tumors ranged from 0.1% to 8.9%. In all the studies that revealed a relatively high frequency of POT, the PODF was the sole responsible tumor.

Approximately 160 cases of PODF have been reported in the English language literature. The two major sources of information are the review of Daley and Wysocki (6) on 109 cases and the study of Siar and Ng (16). The present study adds 23 new cases and is one of the largest series from one source. In this study, PODF was the most common POT, even more common than its central counterpart by a 1.4:1 ratio, which is supported by most studies in the literature (Table 6). PODF is the only POT that is more frequent than its central counterpart.

Table 5 Percentage of peripheral tumors of all odontogenic tumors in various studies

Author	*Year*	*Total*	*Central*	*Peripheral*	*Percentage of peripheral*
Present study		1133	1088	45[a]	4.0
Ladeinde et al. (11)	2005	319	308	11[b]	3.4
Ochsenius et al. (12)	2002	362	360	2[c]	0.5
Santos et al. (13)	2001	127	126	1[d]	0.8
Mosqueda-Taylor et al. (14)	1997	349	338	11[e]	3.1
Daley et al. (3)	1994	392	357	35[f]	8.9
Regezi et al. (15)	1978	706	705	1[g]	0.1

PODF, peripheral odontogenic fibroma; PA, peripheral ameloblastoma; PCCOT, peripheral calcifying cystic odontogenic tumor.
[a]23 PODF, 13 PA, six peripheral calcifying cystic odontogenic tumor, one calcifying epithelial odontogenic tumor, one ameloblastic fibroma, one ameloblastic carcinoma.
[b]Seven PODF, three myxoma, one PA.
[c]Two PA.
[d]One PODF.
[e]11 PODF.
[f]35 PODF.
[g]One amelobastic fibroma.

Approximately 90 cases of PA have been reported in the English language literature, mostly as single case reports and several as a small series of cases (8). The present study adds 13 new cases to the literature. Except for the study of Rick et al. (17), published as an abstract, providing pooled data on 18 cases, this study is the largest from one source, with individual data. An additional 74 cases have been reported in the Japanese

Table 6 Percentage of peripheral odontogenic fibroma of all odontogenic fibromas in various studies

Author	*Year*	*Total*	*Central*	*Peripheral*	*Percentage of peripheral*
Present study		39	16	23	59.0
Ladeinde et al. (11)	2005	17	10	7	41.2
Santos et al. (13)	2001	1	0	1	100
Mosqueda-Taylor et al. (14)	1997	16	5	11	68.7
Daley et al. (3)	1994	54	19	35	65.0

language literature (8). The present study revealed that PA is the second most common POT (28.9%) and accounts for 9.3% of all ameloblastomas. Review of the English language literature shows that 0–10% of all ameloblastomas are PAs (Table 7).

Approximately 80 cases of PCCOTs have been reported in the English language literature, mostly as single case reports or reports of a small series of cases. The major source of information is the review of Buchner et al. (10) on 45 cases and the studies of Hong et al. (21) and Johnson et al. (22). The present study adds six new cases. PCCOT is the third most common POT (13.3%) and accounts for 26% of all calcifying cystic odontogenic tumors. Review of the English language literature shows that PCCOT comprises from 0% to 30% of all calcifying cystic odontogenic tumors with a mean of about 20% (Table 8). It is of interest to note that Regezi et al. (15) clearly states that of their 15 cases of calcifying cystic odontogenic tumor, no lesion was of the peripheral type.

A single case of a PCEOT was identified in our files, which accounted for 2.2% of all POTs and 17% of all calcifying epithelial odontogenic tumors. Philipsen and Reichart (26) reviewed the literature and accumulated 181 cases of calcifying epithelial odontogenic tumors in which 170 (94%) were central tumors and 11 (6%) peripheral.

A single case of a PAF was identified in our files. The histopathologic picture was typical and identical to that of the central ameloblastic fibroma. This tumor accounted for 2.2% of all POTs and 5.5% of all ameloblastic fibromas. PAF is an exceedingly rare tumor. Regezi et al. (15), in a study of 706 odontogenic tumors, identified one case of PAF in the maxillary premolar region of a 5-year-old boy. Takeda (27) reviewed case reports from the literature and found only one acceptable case of PAF that was reported by Kusama et al. (28). However, the diagnosis of this case was recently challenged by other pathologists (29). Two cases of PAF have been reported in the Japanese language literature (30). Because of the rarity of PAF, its relative frequency cannot be determined from the literature.

A single case of PAC arising in a recurrent PA was identified in our files. PAC has been reported to arise *de novo* and as dedifferentiated carcinoma from a preexisting benign PA. PAC is exceedingly rare and only about six cases have been reported in the English language literature (8, 31).

The peripheral adenomatoid odontogenic tumor, peripheral squamous odontogenic tumor, peripheral myxoma and peripheral odontoma (PO) were not identified in our files. Except for the peripheral adenomatoid odontogenic tumor, the others are exceedingly rare.

Philipsen and Reichart (32) surveyed the literature of adenomatoid odontogenic tumors and identified 412 cases in which 394 (95.6%) were central and 18 (4.4%) peripheral.

Squamous odontogenic tumor is rare and the peripheral type is exceedingly rare. In a study of 39 cases from the literature (33), 36 were central tumors and three (7.7%) considered peripheral (34–36). However, the diagnosis of one of these peripheral tumors (34) was challenged by other pathologists (35), and it appears to us that another case (36) probably represents a PA and not a squamous odontogenic tumor.

Peripheral odontogenic myxoma (POM) is considered an extremely rare tumor. Surprisingly, Ladeinde et al. (11) in a study of 319 odontogenic tumors identified three POMs. As no clinical and radiological details were provided, it is difficult to determine whether they represent true peripheral tumors or central odontogenic myxoma that perforated the alveolar bone and extended to the gingiva. There are several case reports of POM in the English language literature (37–39), in which the tumor caused bone destruction or appeared to infiltrate bone. Thus, it is difficult to determine whether these tumors represent true peripheral tumors. It is also possible that some so-called POMs are actually oral focal mucinosis, which may resemble POM (40).

Odontoma is the most common central odontogenic tumor. However, PO is extremely rare. A case of erupted complex odontoma in the mandibular posterior alveolar ridge in an 83-year-old male has been identified in our files. Nevertheless, erupted odontoma is not considered to be a true peripheral tumor. There are only four acceptable case reports of PO in the English language literature (41–43) which shows the rarity of this peripheral tumor.

Table 7 Percentage of peripheral ameloblastoma of all ameloblastomas in various studies

Author	*Year*	*Total*	*Central*	*Peripheral*	*Percentage of peripheral*
Present study		140	127	13	9.3
Ladeinde et al. (11)	2005	201	200	1	0.5
Ochsenius et al. (12)	2002	74	72	2	2.7
Gurol and Burkes (18)	1995	213	205	8	3.8
Reichart et al.[a] (7)	1995	3677	3604	73	2.0
Daley et al. (3)	1994	53	53	0	0
Waldron and El-Mofty (19)	1987	116	110	6	5.2
Ueno et al. (20)	1986	104	102	2	1.9
Rick et al. (17)	1985	180	162	18	10.0
Regezi et al. (15)	1978	78	78	0	0

[a]Review of world literature.

Table 8 Percentage of peripheral calcifying cystic odontogenic tumor of all calcifying cystic odontogenic tumors in various studies

Author	*Year*	*Total*	*Central*	*Peripheral*	*Percentage of peripheral*
Present study		23	17	6	26.0
Johnson et al. (22)	1997	57	40	17	29.8
Hong et al. (21)	1991	79	69	10	12.7
Buchner et al. (23)	1990	21	17	4	19.0
Shamaskin et al. (24)	1989	20	15	5	25.0
Praetorius et al. (25)	1981	16	12	4	25.0
Regezi et al. (15)	1978	15	15	0	0

Summary

The present study attempts to determine the relative frequency of POT. However, to accurately determine the true relative frequency of POT, further studies should be conducted by pathologists, experienced in the field of odontogenic tumors. Detailed clinical and radiological history should be obtained from the clinician to exclude intraosseous tumors that perforated through the bone to the gingival tissue, clinically presenting as 'peripheral tumors'.

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