Odontogenic Fibroma, Including Amyloid and Ossifying Variants

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Abstract Sixty-five cases of odontogenic fibroma (OdonF) are herein presented having been segregated into peripheral, extra bony tumors ($n = 40$) and tumors arising in bone or centrally ($n = 25$). All cases were characterized microscopically by a fibrous proliferation that varied within and between cases in cellularity and collagen fibril diameter, with intermixed odontogenic epithelial islands and cords. All central lesions presented as well demarcated radiolucencies and resorption of contiguous tooth roots was a common finding. These intraosseous lesions were of the WHO type; the so-called nonWHO type was excluded as all lesions with this diagnosis were devoid of an epithelial component and could be reclassified as other soft tissue fibrogenic tumors. Neither the central tumors nor the peripheral lesions recurred following enucleation/curettage, with a mean follow-up of 4 and 3.4 years respectively. Three distinct microscopic variations were encountered in this series: (1) two cases of OdonF with giant cell reaction, (2) two instances of OdonF with ossifying fibroma; and (3) four instances of OdonF with odontogenic ameloblast-associated protein (ODAM), an amyloid-like protein found deposited adjacent to epithelial cords plus CD1a+/S-100+ Langerhans dendritic cells entwined around the epithelial element. A single instance of the odontogenic fibroma-like hamartoma/enamel hypoplasia syndrome has been included in this series.

Keywords Odontogenic fibroma · Jaw tumors · Langerhans cell · Amyloid · ODA

Introduction

Odontogenic fibroma (OdonF) is classified as a mesenchymal odontogenic tumor. It occurs most often in females, usually located in the anterior aspect of the maxilla, presenting as a well circumscribed radiolucency that may induce root resorption [1, 2]. Microscopically, these tumors are comprised of fibrous connective tissue showing a range of collagen density varying from loose, somewhat myxoid patterns to more mature collagen fibers. Cellularity is also varied, is usually moderate to low. The epithelial elements in OdonF are dispersed throughout the fibrous component, appearing as small clusters, oval nests, and linear cords. The tumor may occur centrally in bone or on the gingiva as a peripheral lesion. OdonF behaves benignly without a tendency for recurrence following enucleation and curettage.

In this case series, 65 instances of OdonF, including three rare variants were identified: OdonF with giant cell lesion, OdonF with ossifications, and OdonF with amyloid-like protein deposition, respectively. Amyloid-like protein is produced by developing tooth germs and by odontogenic epithelium in the calcifying epithelial odontogenic tumor (Pindborg tumor) [3, 4]. This amyloid protein has been termed odontogenic ameloblast-associated protein (ODAM) derived from a locus that encodes a 279-residue polypeptide [5, 6]. The histopathologic features of these variants are detailed along with immunohistochemical profiling and amyloid staining.

Material and Methods

The archives from the Oral Pathology Diagnostic Services of San Diego and the Pacific Oral Pathology Laboratory,

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Fig. 1 Age distribution comparing central and peripheral tumors

University of the Pacific School of Dentistry, were reviewed over a 10 year period (91,248 accessions) from which 65 cases met the World Health Organization (WHO) criteria for the diagnosis of OdonF [7]. OdonF is a histologically defined odontogenic tumor comprised of a moderately cellular fibrogenic proliferation with monomorphic fibroblastic nuclei and thin yet mature collagen admixed with epithelial cords and islands of putative odontogenic origin that resemble dental lamina. Some of these cases ($n = 16$) were included in a large survey of odontogenic tumors by Buchner et al. [8] yet were not discussed in detail. Representative cases (5 cases of central OdonF, 5 cases of peripheral OdonF, 2 cases of OdonF with giant cell reaction, 2 cases of OdonF with ossification and 4 cases of amyloid associated OdonF) were stained for cytokeratins (AE1, AE3, Dako), S100 protein (Dako), CD1a (Dako) utilizing standard peroxidase immunohistochemistry. Congo red staining for assessment of amyloid green birefringence under crossed polars was performed on the 4 instances of amyloid associated OdonF. Immunoperoxidase staining for odontogenic ameloblast-associated protein (ODAM) was

Fig. 3 Comparison of peripheral and central odontogenic fibroma according to site

conducted in Dr. Alan Solomon's laboratory (University of Tennessee Center for Health Sciences, Department of Medicine) employing an antibody against ODA protein, as previously described [3–6].

Clinical demographic data were assessed from submitted clinical histories and postoperative follow-up was obtained. Cases diagnosed as nonWHO type of OdonF because they were devoid of an epithelial element were reclassified as soft tissue fibrogenic tumors, including a nerve sheath tumor (S100+), two myofibromas of bone (smooth muscle actin positive), one solitary fibrous tumor (CD34+) that had eroded bone and one odontogenic myxoma with a mixed fibrous and myxoid pattern.

Fig. 2 Peripheral odontogenic fibromas presenting as exophytic gingival masses

Results

Clinical Features

Sixty-five cases met the criteria for the diagnosis of OdonF, including 25 cases that arose in bone (central) and 40 that arose from the gingival/alveolar mucosa (peripheral). Age distribution among central lesions showed a shallow curve, with all decades represented whereas the peripherally located lesions showed a predilection for the 2nd to 4th decades of life (Fig. 1). Clinically, peripheral odontogenic fibromas arose as exophytic masses, usually from the interdental region, and appeared either inflamed, red and ulcerated or coral pink, firm and fibrous (Fig. 2).

Among central lesions, the mandible ($N = 12$) was affected almost equally with the maxilla ($N = 13$) while peripheral lesions were slightly more common on the mandibular gingiva (23 mandible; 17 maxilla). Furthermore, intraosseous tumors were relatively evenly distributed in the anterior, premolar and molar regions whilst

peripheral lesions tended to arise in the anterior sextants of the jaws (Fig. 3). There is a slight female predilection for central tumors (3F:2M) with a more pronounced female predominance for peripheral tumors (2F:1M).

Imaging Features

None of the peripheral tumors showed any significant lesion-associated crestal alveolar bone resorption, although some patients had accompanying generalized bone loss consistent with chronic periodontitis. All central lesions appeared as well delineated, yet noncorticated, radiolucencies with or without expansion. Interradicular, pericoronal and multilocular patterns were represented and root resorption was noted, especially with interradicular lesions (Fig. 4a, b, d). Interproximal lesions of the palate showed palatal mucosal pit like depressions or dimpling in two cases (Fig. 4c). One case that was left untreated failed to exhibit any significant growth over a 1.5 year period of follow up (Fig. 4e, f). Giant cell tumors accompanying

Fig. 4 a, b Axial cone beam CT cuts demonstrating a well defined radiolucency with expansion and erosion of both buccal and palatal plates. c Palatal dimpling overlying a maxillary tumor. d Maxillary tumor with extensive root resorption. e Odontogenic fibroma with

radiolucency and root resorption, f same tumor as e showing slow growth 1.5 years later. g Periapical radiolucency with central opacities in odontogenic ossifying fibroma. h, i Odontogenic fibroma with giant cell tumor

Fig. 5 Bilateral pericoronal radiolucencies in the mandible with defective enamel formation in the enamel hypoplasia/odontogenic fibroma-like hamartoma syndrome

odontogenic fibroma caused root resorption and one was expansile and multilocular (Fig. 4h, i). The enamel hypoplasia/odontogenic fibroma-like hamartoma is detailed later (Fig. 5). The variant cases were not included in the demographic summary data.

Microscopic Features

Microscopically, both intraosseous and peripheral lesions share common features. A fibrous tumor is seen, comprised of mildly cellular monomorphic appearing fibroblasts in a

patternless arrangement with mature and thin collagen fibers and small caliber vascular channels. Dispersed throughout are oval and linear epithelial islands teleologically assumed to be odontogenic in their differentiation, and resembling strands of dental lamina remnants from tooth germs (Fig. 6). The odontogenic epithelial cytoplasm often stains pale, whereas in some cases it is brightly eosinophilic. In many of the peripheral lesions, extremely elongated and slender rete pegs penetrate deeply into the connective tissue; in cross and tangential sections, these contribute to the epithelial nests and cords encountered in the deeper extent of these tumors. As expected, the fibrous element is strongly positive for vimentin and the epithelial elements are cytokeratin cocktail (AE1/AE3) positive (Fig. 6b, d). Most of the epithelial components consist of clusters and aggregates or islands, however, numerous, single, cytokeratin positive cells can be seen embedded throughout the fibrous proliferation. No delineated capsule can be seen.

In this series, variants of OdonF were encountered (Table 1). The first of these variants is OdonF with giant cell reaction (odontogenic fibroma/giant cell granuloma) (Fig. 7). Two cases presented with mandibular radiolucent lesions of OdonF associated with a giant cell-rich lesion identical to central giant cell granuloma of the jaws. In these two cases, the two histologic components were not intimately admixed; rather, they were arranged in a

Fig. 6 a Microscopic features of peripheral odontogenic fibroma showing a moderately cellular fibrous element with linear and oval epithelial foci scattered throughout. **b** Same tumor showing cytokeratins (AE1,AE3) in epithelial element. **c** The same features are seen in central intraosseous tumors. **d** Cytokeratins in a central lesion

Table 1 Odontogenic fibroma variants and associations

Association/variant	Age	Sex	Location
Granular cell odontogenic fibroma			See Ref [34]
Odontogenic fibroma/ giant cell granuloma	42	F	Mandible, body
	27	F	Mandible, ramus, impaction
Ossifying odontogenic fibroma	40	F	Maxilla, anterior
	35	F	Mandible
Amyloid/dendritic cell associated odontogenic fibroma	77	F	Maxilla, premolar region
	39	F	Maxilla, premolar region
	38	F	Maxilla, premolar region
	27	M	Maxilla, molar region
Enamel hypoplasia/ odontogenic fibroma hamartoma syndrome	<10	F	Both jaws, bilateral

juxtaposed yet separate dimorphic pattern. A larger series would need to be investigated in order to ascertain the consistency of this dimorphism.

Two other cases presented with mixed radiolucent/radiopaque lesions—one in the maxilla and one in the mandible—that showed the typical fibroosseous microscopic features of ossifying fibroma (Fig. 8). This variant was characterized by nonsegregated, dispersed epithelial odontogenic islands intimately admixed with tumor trabeculae. The stroma was cellular with monomorphic fibroblastic nuclei and the trabeculae were found to be irregular in shape and often ovoid.

Four central lesions were characterized by amyloid production and Langerhans cell intercalation into the epithelial elements, consistent with the so-called “amyloid/dendritic cell associated odontogenic fibroma” (Fig. 9). This variant showed the typical aforementioned histologic appearance of OdonF with the addition of amyloid deposits. These deposits were ovoid or globular acellular hyalinized structures in three of the cases and in the fourth case, periepithelial amyloid deposition (cuffing) was

observed. These deposits were positive for Congo red and demonstrated green birefringence under crossed polars. The positive immunohistochemical reaction pattern employing antibodies to ODAM confirmed that this protein is, in fact, odontogenic amyloid, as found in developing tooth germs. The epithelial element showed a core of cytokeratin positive cells surrounded by a network of dendritic cells that stained positively for CD1a and faintly with antibody to S100 protein.

The last variant recognized here is characterized by multiple unerupted posterior teeth with significantly enlarged pericoronal/peridental radiolucent follicular zones in association with generalized enamel defects (Fig. 5). This variant has been termed the odontogenic fibroma-like hamartoma/enamel hypoplasia (or amelogenesis imperfecta) syndrome. Previously reported cases were identified in a black African family. In the single case reported here, the patient was a 10-year-old Middle Eastern female immigrant to the United States. She presented with generalized enamel hypoplasia involving both deciduous and adult teeth. Unerupted teeth, particularly molars, show pericoronal radiolucencies with well defined borders that lack cortication. Histologically, these pericoronal lesions appeared identical to central OdonF.

Outcome

All cases of peripheral OdonF were treated with simple excision, many with additional root planning. Central lesions were treated by enucleation curettage with extraction of contiguous teeth when root resorption was present. Among peripheral lesions, none recurred with a mean follow-up of 4 years (24 patients followed over 4 years). Likewise, none of the intraosseous tumors recurred with a mean follow-up of 3.4 years (10 patients followed over 4 years). As alluded to earlier, one case was found to persist virtually 1.5 years without appreciable enlargement radiographically.

Fig. 7 a Odontogenic fibroma (left side of figure) with associated central giant cell lesion (GC—giant cell component, OE—odontogenic epithelium, low magnification). **b** Same lesion, high magnification

Fig. 8 Ossifying variant of central odontogenic fibroma. **a, b** Fibroosseous pattern with odontogenic epithelium interposed among ovoid densely pink to purple calcifications. **c** Cytokeratins (AE1,AE3) are evident in the epithelium (EPI); OS—ossifications

Fig. 9 Amyloid variant of central odontogenic fibroma, **a, b** ovoid hyalinized globules are found adjacent to epithelial linear strands showing prominent cytoplasmic eosinophilia. **c** Congo red stains hyalinized globules. **d** Congo red under crossed polars demonstrates

green birefringence. **e** Immunostain for ODAM protein localizes to hyalinized foci (courtesy of Dr. Alan Solomon). **f** CD1a immunohistochemistry shows dendritic cells intertwined around linear epithelial strands

Discussion

The odontogenic fibroma has been subclassified by the WHO into two subtypes: (1) the WHO variant, a designation made with the issuance of the initial multiauthored

WHO fascicle on Odontogenic tumors and recently revised in 2005; and (2) the non-WHO variant [7]. The WHO variant, considered a mesenchymal odontogenic tumor (i.e.; derived from the mesodermal component of the tooth germ) is comprised of two distinct cell types, a fibrous

element and an epithelial element that resembles the dental lamina or the rests that are seen in normal dental follicles. The epithelial component of OdonF has been considered a quiescent, non-neoplastic accompaniment. In contrast, the so-called non-WHO variant lacks an epithelial component, being a monomorphic fibroblastic tumor purported to be of odontogenic mesenchymal origin ostensibly derived from pulpal or follicular fibroblasts. In this study, five cases were originally classified as such, but upon review and application of IHC markers, all were relegated to other subtypes of fibrogenic tumors, including two cases of intraosseous myofibromas (smooth muscle actin +), and one case each of solitary fibrous tumor (CD34+), myxoma, and nerve sheath tumor (S100 protein +). Therefore, these cases were excluded with the caveat that they may have been derived from odontogenic mesenchyme, yet failed to show any features or markers that would substantiate such a claim. In this paper, additional variants were described.

Peripheral lesions of OdonF were more common than central ones, and occurred twice as often in females, showed with a predilection for the second to fourth decades, and were found to arise more often in the anterior regions of the gingiva. No recurrences were noted although mean follow-up was only 4 years. This study mirrors the findings in previous reports of peripheral OdonF [9–17].

Central lesions of OdonF showed a less robust female prevalence. No age peak was noted, as the tumors were relatively similar in their age of occurrence throughout the decades. They were also evenly distributed in anterior, middle, and posterior regions of the jaws [18–26]. Recurrence was not encountered following thorough curettage and selective tooth extraction was undertaken when dental root erosion was attributed to tumor extension. It might be argued that some tumors designated OdonF represented enlarged dental follicles around impacted third molars. The two cases with follicular localization (i.e.; pericoronal) showed follicular spaces that measured in excess of 5 mm and histologically showed diffusely distributed epithelial rests, features that do not support simple hyperplastic dental follicles. The syndrome associated case is an exception (vide infra).

Another odontogenic tumor with features similar to OdonF is the *Central Granular Cell Odontogenic Tumor*, a neoplasm that was originally designated *granular cell ameloblastic fibroma*, later referred to as *Granular Cell Odontogenic Fibroma* and ultimately *Granular Cell Odontogenic Tumor* [27–36]. This lesion was not included here because a previous case series of this entity was coauthored by the current author and it is now recognized as a distinct entity rather than a variant of odontogenic fibroma [34]. It is a central lesion that appears radiolucent and expansile with cellular fibrosis, odontogenic epithelial nests and islands and granular cells located in the fibrous

regions, epithelial component or both. A peripheral counterpart has been observed for this tumor [28, 36].

The concomitant occurrence of odontogenic fibroma and central giant cell lesion, while rare, is well documented [37–40]. The congeniality of these two entities growing side by side is a special and significant event. If the giant cell lesion simply represents a reactive phenomenon to the existence of a tumor, then why isn't this association seen with other odontogenic tumors? There must be some sort of signaling process to stimulate an endosteal giant cell proliferative response in OdonF. Growth factors, chemokines and cytokines may play some role in this regard. Alternatively, perhaps it is the giant cell lesion that in some way influences the genesis of an OdonF.

The coexistence of ossifying fibroma and OdonF is singularly unique and rare [41]. This variant differs from the giant cell lesion/OdonF chimera in that two individual tumor entities do not become juxtaposed, but, rather, are fully integrated. The fibrous component is hypercellular with monomorphic spindle shaped fibroblasts that lack any mitotic activity. Randomly dispersed throughout are oval odontogenic epithelial islands that appear similar to embryonic rests encountered in dental follicles intermixed with irregular trabeculae, many of which are ovoid. One could argue that this represents an ossifying fibroma with odontogenic epithelium; alternatively, the term odontogenic fibroma with ossifications would be equally acceptable. Ossifying odontogenic fibroma is proposed to be the preferred term.

The presence of an amyloid-like protein deposit adjacent to epithelial elements in developing tooth germs is well documented by Congo red staining and demonstration of green birefringence under polarized light [3–6]. Biochemical analysis has been undertaken and this protein is referred to as ODAM (odontogenic ameloblast-associated protein). The calcifying epithelial odontogenic tumor (Pindborg tumor) synthesizes homogeneous sheets as well as hyalinized eosinophilic globules in which ovoid concentric calcifications are encountered, the so-called Leisegang rings. Recently, a noncalcifying variant of Pindborg tumor has been described in which amyloid globules are deposited within the connective tissues and CD1a+ dendritic cells are intercalated with linear strands of odontogenic epithelium [42]. Herein are described four more cases of this amyloid producing, dendritic cell odontogenic tumor that is considered to be a variant of odontogenic fibroma.

Arguments in favor of a kinship with calcifying epithelial odontogenic tumor include (1) amyloid deposition, and (2) the presence of epithelial cells exhibiting cytoplasmic eosinophilia. Countering this argument are the following features that support reclassification as a variant of odontogenic fibroma: (1) these cases show a growth

pattern akin to that of OdonF with fibroplasia and diffusely dispersed linear odontogenic cords, as opposed to sheets of contiguous epithelial cells enmeshed in or surrounding more diffuse amyloid deposits; (2) in this report, two cases demonstrated significant cytoplasmic eosinophilia, while two others did not; (3) no ring structure calcifications were noted; and (4) unlike Pindborg tumors, this variant behaved nonaggressively and failed to recur after curettage. More recently, some authors have demonstrated a lesser degree of aggressiveness after treatment of Pindborg tumors; however, some of these reports probably included the so-called noncalcifying variant that is herein considered to be an odontogenic fibroma [43]. In this series, all four cases were located interradiographically in the anterior aspect of the jaws. It is argued that this lesion has features more in common with odontogenic fibroma and has been designated the amyloid/CD1a associated variant.

Lastly, OdonF-like lesions may be multifocal, appearing as hyperplastic dental follicles radiographically with histology identical to OdonF. Hypoplastic enamel defects similar to amelogenesis imperfecta are also extant in this syndrome that was first described in an African family [44, 45].

Summary

Odontogenic fibroma is a benign odontogenic tumor that may arise centrally in the jawbones or peripherally on the gingiva, the latter being more common. Central lesions may cause bony expansion, erosion, and root resorption; however, in this series, none recurred after thorough enucleation and selective extraction of contiguous teeth with root resorption. Five cases diagnosed as nonWHO type odontogenic fibroma were reevaluated and could be reclassified as other benign fibrogenic neoplasms on the basis of combined histomorphology and immunohistochemistry. It is concluded that the nonWHO type should be eliminated from the classification of odontogenic tumors. Three variants are reported here, including odontogenic fibroma with giant cell reaction, odontogenic fibroma with ossification, and amyloid/CD1a associated odontogenic fibroma, respectively. Multiple central pericoronal lesions with concomitant enamel defects constitute a rare variant, the enamel hypoplasia/odontogenic fibroma like hamartoma syndrome.

References

- Dunlap CL. Odontogenic fibroma. *Semin Diagn Pathol*. 1999;16:293–6.
- Brannon RB. Central odontogenic fibroma, myxoma (odontogenic myxoma, fibromyxoma), and central odontogenic granular cell tumor. *Oral Maxillofac Surg Clin North Am*. 2004;16:359–74.
- Solomon A, Murphy CL, Weaver K, Weiss DT, Hrnica R, Eulitz M, Donnell RL, Sletten K, Westermarck G, Westermarck P. Calcifying epithelial odontogenic (Pindborg) tumor-associated amyloid consists of a novel human protein. *J Lab Clin Med*. 2003;142:348–55.
- Murphy CL, Kestler DP, Foster JS, Wang S, Macy SD, Kennel SJ, Carlson ER, Hudson J, Weiss DT, Solomon A. Odontogenic ameloblast-associated protein nature of the amyloid found in calcifying epithelial odontogenic tumors and unerupted tooth follicles. *Amyloid*. 2008;15:89–95.
- Kestler DP, Foster JS, Macy SD, Murphy CL, Weiss DT, Solomon A. Expression of odontogenic ameloblast-associated protein (ODAM) in dental and other epithelial neoplasms. *Mol Med*. 2008;14:318–26.
- Moffatt P, Smith CE, St-Arnaud R, Nanci A. Expression of odontogenic ameloblast-associated protein (ODAM) in dental and other epithelial neoplasms. *J Cell Biochem*. 2008;103:941–56.
- Barnes L, Eveson JW, Reichart P, Sidransky D. Pathology and genetics of head and neck tumours. WHO classification of tumours, vol. 9. Geneva: WHO Press; 2005.
- Buchner A, Merrell PW, Carpenter WM. Relative frequency of central odontogenic tumors: a study of 1,088 cases from Northern California and comparison to studies from other parts of the world. *J Oral Maxillofac Surg*. 2006;64:1343–52.
- Farman AG. The peripheral odontogenic fibroma. *Oral Surg Oral Med Oral Pathol*. 1975;40:82–92.
- Gardner DG. The peripheral odontogenic fibroma: an attempt at clarification. *Oral Surg Oral Med Oral Pathol*. 1982;54:40–8.
- Buchner A. Peripheral odontogenic fibroma. Report of 5 cases. *J Craniomaxillofac Surg*. 1989;17:134–8.
- Ficarra G, Sapp JP, Eversole LR. Multiple peripheral odontogenic fibroma, World Health Organization type, and central giant cell granuloma: a case report of an unusual association. *J Oral Maxillofac Surg*. 1993;51:325–8.
- Daley TD, Wysocki GP. Peripheral odontogenic fibroma. *Oral Surg Oral Med Oral Pathol*. 1994;78:329–36.
- Siar CH, Ng KH. Peripheral odontogenic fibroma with clear cell odontogenic epithelium. *J N Z Soc Periodontol*. 1995;79:21–4.
- Ide F, Obara K, Mishima K, Saito I, Horie N, Shimoyama T, Kusama K. Peripheral odontogenic tumor: a clinicopathologic study of 30 cases. General features and hamartomatous lesions. *J Oral Pathol Med*. 2005;34:552–7.
- Garcia BG, Johann AC, da Silveira-Júnior JB, Aguiar MC, Mesquita RA. Retrospective analysis of peripheral odontogenic fibroma (WHO-type) in Brazilians. *Minerva Stomatol*. 2007;56:115–9.
- Lin CT, Chuang FH, Chen JH, Chen CM, Chen YK. Peripheral odontogenic fibroma in a Taiwan Chinese population: a retrospective analysis. *Kaohsiung J Med Sci*. 2008;24:415–21.
- Wesley RK, Wysocki GP, Mintz SM. The central odontogenic fibroma. Clinical and morphologic studies. *Oral Surg Oral Med Oral Pathol*. 1975;40:235–45.
- Dahl EC, Wolfson SH, Haugen JC. Central odontogenic fibroma: review of literature and report of cases. *J Oral Surg*. 1981;39:120–4.
- Svirsky JA, Abbey LM, Kaugars GE. A clinical review of central odontogenic fibroma: with the addition of three new cases. *J Oral Med*. 1986;41:51–4.
- Handlers JP, Abrams AM, Melrose RJ, Danforth R. Central odontogenic fibroma: clinicopathologic features of 19 cases and review of the literature. *J Oral Maxillofac Surg*. 1991;49:46–54.
- Kaffe I, Buchner A. Radiologic features of central odontogenic fibroma. *Oral Surg Oral Med Oral Pathol*. 1994;78:811–8.

23. Gardner DG. Central odontogenic fibroma current concepts. *J Oral Pathol Med.* 1996;25:556–61.
24. Bueno S, Berini L, Gay C. Central odontogenic fibroma: a review of the literature and report of a new case. *Med Oral.* 1999;4: 422–34.
25. Ramer M, Buonocore P, Krost B. Central odontogenic fibroma-report of a case and review of the literature. *Periodontal Clin Investig.* 2002;24:27–30.
26. Daniels JS. Central odontogenic fibroma of mandible: a case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2004;98:295–300.
27. Waldron CA, Thompson CW, Conner WA. Granular-cell ameloblastic fibroma. Report of two cases. *Oral Surg Oral Med Oral Pathol.* 1963;16:1202–13.
28. Lownie JF, Altini M, Shear M. Granular cell peripheral odontogenic fibroma. *J Oral Pathol.* 1976;5:295–304.
29. White DK, Chen SY, Hartman KS, Miller AS, Gomez LF. Central granular-cell tumor of the jaws (the so-call granular-cell ameloblastic fibroma). *Oral Surg Oral Med Oral Pathol.* 1978;45: 396–405.
30. Vincent SD, Hammond HL, Ellis GL, Juhlin JP. Central granular cell odontogenic fibroma. *Oral Surg Oral Med Oral Pathol.* 1987; 63:715–21.
31. Shiro BC, Jacoway JR, Mirmiran SA, McGuirt WF Jr, Siegal GP. Central odontogenic fibroma, granular cell variant. A case report with S-100 immunohistochemistry and a review of the literature. *Oral Surg Oral Med Oral Pathol.* 1989;67:725–30.
32. Ardekian L, Manor R, Gaspar R, Laufer D. Central granular cell odontogenic tumor: case report and review of literature. *J Oral Maxillofac Surg.* 1998;56:1343–5.
33. Calvo N, Alonso D, Prieto M, Junquera L. Central odontogenic fibroma granular cell variant: a case report and review of the literature. *J Oral Maxillofac Surg.* 2002;60:1192–4.
34. Brannon RB, Goode RK, Eversole LR, Carr RF. The central granular cell odontogenic tumor: report of 5 new cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;94:614–21.
35. Meer S, Altini M, Coleman H, Daya N. Central granular cell odontogenic tumor: immunohistochemistry and ultrastructure. *Am J Otolaryngol.* 2004;25:73–8.
36. Rinaggio J, Cleveland D, Koshy R, Gallante A, Mirani N. Peripheral granular cell odontogenic fibroma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007;104:676–9.
37. Allen CM, Hammond HL, Stimson PG. Central odontogenic fibroma, WHO type. A report of three cases with an unusual associated giant cell reaction. *Oral Surg Oral Med Oral Pathol.* 1992;73:62–6.
38. Odell EW, Lombardi T, Barrett AW, Morgan PR, Speight PM. Hybrid central giant cell granuloma and central odontogenic fibroma-like lesions of the jaws. *Histopathology.* 1997;30: 165–71.
39. Mosqueda Taylor A, Bermúdez Flores V, Díaz Franco MA. Combined central odontogenic fibroma and giant cell granuloma-like lesion of the mandible: report of a case and review of the literature. *J Oral Maxillofac Surg.* 1999;57:1258–62.
40. de Lima Mde D, de Aquino Xavier FC, Vanti LA, de Lima PS, de Sousa SC. Hybrid central giant cell granuloma and central odontogenic fibroma-like lesion of the mandible. *Otolaryngol Head Neck Surg.* 2008;139:867–8.
41. Günhan O, Gürbüz B, Gardner DG, Demiriz M, Finci R. A central odontogenic fibroma exhibiting pleomorphic fibroblasts and numerous calcifications. *Br J Oral Maxillofac Surg.* 1991; 29:42–3.
42. Wang YP, Lee JJ, Wang JT, Liu BY, Yu CH, Kuo RC, Chiang CP. Non-calcifying variant of calcifying epithelial odontogenic tumor with Langerhans cells. *J Oral Pathol Med.* 2007;36:436–9.
43. Philipsen HP, Reichart PA. Calcifying epithelial odontogenic tumour: biological profile based on 181 cases from the literature. *Oral Oncol.* 2000;36:17–26.
44. Raubenheimer EJ, Noffke CE. Central odontogenic fibroma-like tumors, hypodontia, and enamel dysplasia: review of the literature and report of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;94:74–7.
45. Feller L, Jadwat Y, Bouckaert M, Buskin A, Raubenheimer EJ. Enamel dysplasia with odontogenic fibroma-like hamartomas: review of the literature and report of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;101:620–4.