Clinical and Radiological Profile of Ameloblastic Fibro-Odontoma: an Update on an Uncommon Odontogenic Tumor Based on a Critical Analysis of 114 Cases

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Abstract Ameloblastic fibro-odontoma is an uncommon benign tumor of the jaws that belongs to the group of mixed odontogenic tumors. The descriptions of its clinical and radiological features in the literature are not always accurate and sometimes even contradictory. The aim of the present study was to critically evaluate their clinical and radiological features as reported in the English-language literature. A total of 114 well-documented cases of ameloblastic fibro-odontomas (103 from publications and 11 of our own new cases) were analyzed. The patients' age ranged from 8 months to 26 years (mean 9.6). There were 74 (65 %) males, with a male-to-female ratio of 1.85:1 ($P = 0.001$). The mandible was involved in 74 (65 %) cases, and the mandible-to-maxilla ratio was 1.85:1 ($P < 0.001$). Nearly 80 % of the lesions were located in the posterior region of the jaws, and most (58 %) were in the posterior mandible. Radiographically, most of the lesions were unilocular and only a few (~10 %) were multilocular. Most lesions were mixed radiolucent-radiopaque, and only a few (~5 %) were radiolucent. Almost all lesions (~92 %) were associated with the crown of an unerupted tooth/teeth. This comprehensive analysis of a large number of patients with an uncommon lesion revealed that ameloblastic fibro-odontomas are significantly more common in males and in the mandible, and that multilocular lesions are uncommon. It also revealed that, based on their clinical

and radiological features, some of them are probably true neoplasms while others appear to be developing odontomas (hamartomas).

Keywords Ameloblastic fibro-odontoma · Mixed odontogenic tumors · Ameloblastic fibroma · Developing odontoma · Odontoma

Introduction

Ameloblastic fibro-odontoma (AFO) has been defined by the WHO as a rare odontogenic tumor with the histopathological features of an ameloblastic fibroma (AF) in conjunction with the presence of dentin and enamel [1]. Histopathologically, the tumor is composed of soft and hard tissues. The soft tissue component is composed of epithelial strands and small islands of odontogenic epithelium associated with a primitive-appearing myxoid connective tissue that resembles the dental papilla. The hard tissue component consists of foci of enamel and dentin [2]. According to the scant information on AFO that is provided in the 2005 WHO classification of odontogenic tumors [1], AFO is a “tumor of children with a mean age between 8 and 12 years with no gender or anatomic site predilection. Radiologically, it exhibits a well-circumscribed, unilocular or multilocular radiolucency with varying levels of radiopacity”. The findings of the present study, which is based on a comprehensive analysis of the literature, add new information on the demographic, clinical and radiographic characteristics of AFO.

AFOs had originally been termed ameloblastic odontomas but in 1971 the WHO suggested that this term is inappropriate since it encompasses two types of odontogenic tumors that share a different histology and biologic

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behavior [3]. They suggested that tumors presenting a histopathological combination of AF and a complex odontoma and that is biologically non-invasive be termed AFOs, and those that histopathologically represent a combination of ameloblastoma and complex odontoma and behave in an invasive manner, like the classical ameloblastoma, be termed odontoameloblastoma.

An AFO is a rare tumor and its relative frequency within the group of odontogenic tumors seen in oral pathology biopsy services in various parts of the world reportedly ranges from 0 to 3.4 % [4]. Because of its rarity, there are sparse details in the literature regarding its clinical and radiological features, and some of the existing reports are conflicting. Except for two comprehensive reviews that were published about 30 and 15 years ago [5, 6] most of the papers on AFOs describe single cases and a few report on small series of cases.

The purpose of the present investigation was to critically analyze the clinical and radiological features of AFOs based on case reports and case series published in the literature, and to add 11 cases from our own files, in order to update and improve our knowledge and diagnostic ability of this entity.

Methods

The English-language literature was searched for adequately documented cases of AFOs published between 1967 and 2010. Medline's PubMed and Google Scholar were searched using the keywords "ameloblastic fibro-odontoma" and "ameloblastic odontoma". References of published papers were also searched for additional cases. Included in the study were only cases that exhibited the histopathological features of AFO, namely the presence of dental papilla-like tissue with epithelial strands and nests, as seen in AF, and induction changes with the formation of dentin and enamel. Additional inclusion criteria were information of the clinical features and an acceptable radiographic image or detailed radiological description for each case. Not all data were available for all cases. Special attention was given to cases that were diagnosed in the past as ameloblastic odontoma since this term was used historically for both ameloblastic fibro-odontoma and odontoameloblastoma [3]. The cases of ameloblastic odontoma in which the histopathology was consistent with odontoameloblastoma were excluded from the study, as were cases that were published under the title of AFO but the histopathology was consistent with ameloblastic fibrodentinoma or odontoma.

We also omitted from our study cases that were diagnosed as ameloblastic fibrodentinoma (AFD) because of the ongoing debate as to whether AFD is a variant of ameloblastic fibroma, a variant of AFO, or a separate entity

altogether. In the 1971 WHO classification [3], AFD was considered to be a separate entity. In the 1992 WHO classification [2], it was considered to be a variant of AFO, and in the latest 2005 WHO classification [1], it was considered to be a variant of ameloblastic fibroma. On the other hand, Reichart and Philipsen [7] and Praetorius [8] have recently suggested that AFD should be considered a separate entity and did not include AFD in their analysis of AFOs. Because of the continuous debate and the lack of agreement among oral pathologists, we decided not to include AFD in our current analysis. Finally, the series of cases by Buchner et al. [4] and Hooker [9] were excluded because there was no individual clinical and radiological information.

A total of 114 cases (103 from publications and 11 new cases from our files) were analyzed [10–84]. The data of 11 new cases are described in Table 1 and Figs. 1 and 2, and they represent the largest detailed series of cases from one biopsy service to have been thus far reported.

The histopathologic features of our 11 cases were basically similar. The lesions were composed of a soft tissue component and calcified elements. The soft tissue resembled ameloblastic fibroma and exhibited mainly strands and cords of odontogenic epithelium that resembled the dental lamina (Fig. 3a). In a few cases, the lesion also contained epithelial islands that consisted of a peripheral layer of columnar palisaded cells, which enclosed loosely arranged cells resembling the enamel organ of a developing tooth (Fig. 3b). The epithelial elements were supported by loose primitive connective tissue containing randomly oriented fibroblasts that resembled the dental papilla of a developing tooth. Mesenchymal tissue dominated in some lesions, while there was an abundance of epithelial elements in others. The calcified elements showed the characteristic structure of an odontoma consisting of irregular dentin, an enamel matrix and enamel in close relationship to the epithelial elements (Fig. 3c). The dentin contained entrapped epithelial and mesenchymal cells. The dentinal structures enclosed clefts or hollow spaces that contained mature enamel that was removed during decalcification. The spaces also contained areas of enamel matrix (Fig. 3d). The soft tissue component dominated in some lesions, while hard tissue was abundant in others.

All the cases were treated by enucleation and curettage, except for case 11 that was treated by segmental resection. Follow-up of the 11 lesions ranged from 5 to 20 years and none had a recurrence.

The clinical and radiological data of the 114 lesions were evaluated according to the criteria proposed by White [85], which include age, gender, location, symptoms, expansion and radiological features of lesion size, content, borders, loculation, tooth relation, tooth impaction, tooth displacement and root resorption. The size was determined

Table 1 Clinical and radiological features of 11 new cases of ameloblastic fibro-odontoma

Case #	Age (years)	Gender	Jaw	Area	Expansion	Size (cm)	Locularity	Content	Border	Unrupted tooth	Displaced tooth
1	6	F	Max	Molars and sinus	Yes	2.5	Uni	RI with scattered opacities	Mostly defined ^a	16	Superior
2	12	M	Max	Incisors	Yes	1.0	Uni	RI with small central opacity	Well defined	No ^b	Distal
3	13	M	Mand	Molar and ramus	Yes	5.0	Uni	RI with large number of opacities	Well defined	47	Inferior
4	3	M	Max	Incisor	No	1.1	Uni	RI with few opacities	Well defined	51	Superior
5	8	F	Mand	Molars	No	1.5	Uni	RI with small opacity	Well defined	46	Inferior
6	3	M	Mand	Cuspid	Yes	0.8	Uni	RI with dense mass	Well defined	83	No
7	10	M	Mand	Molars	Yes	3.0	Uni	RI with few opacities	Well defined	46 ^c	Inferior
8	13	M	Mand	Molars	Minimal	1.5	Uni	RI with few opacities	Mostly defined ^a	47 ^d	Inferior
9	9.5	M	Max	Molars and sinus	No	3.0	Uni	RI with opacities	Well defined	25–27	25–26 superior, 27 posterior
10	8.5	F	Mand	Premolars and molars	Yes	1.5	Multi	RI with few small opacities	Well defined	35	Inferior
11	9	M	Mand	Premolar and molar	Yes	4.0	Multi	RI with few small opacities	Well defined	44–46	Inferior

M male, *F* female, *Max* maxilla, *Mand* mandible, *Uni* unilocular, *Multi* multilocular, *RI* radiolucency

^a Mostly but not entirely defined

^b Between roots of erupted teeth 11,12; ^c Missing tooth 47; ^d Missing tooth 48

according to the greatest dimension. In the present study, incisors and canines were regarded as composing the anterior region. Premolars (or primary molars), molars and ramus (in the mandible) and molars and sinus (in the maxilla) were regarded as composing the posterior region.

Differences in the frequency of the lesions between genders, jaw location (mandible or maxilla) and lesion size (in the mandible versus in the maxilla) were analyzed by the Chi-square test and crosstabs test using the SPSS software (Chicago, IL, USA). Significance was set at $P < 0.05$.

The study was approved by the Research and Ethics Committee of Tel Aviv University.

Results

A total of 114 cases of AFO were analyzed, of which 11 were new and are now being reported for the first time. Data on the age and gender distribution of AFOs were known in all 114 cases and they are shown in Fig. 4. At the time of initial presentation, the patient's age ranged from 8 months to 26 years (mean 9.6, median 9.0). Most of the cases (71 %) were diagnosed in patients between 5 and 14 years of age, and only 4.3 % cases were diagnosed in patients older than 20 years. There were 74 (65 %) males and 40 (35 %) females, with a male-to-female ratio of 1.85:1 ($P = 0.001$).

The distribution of the lesion (mandible or maxilla) was known for all cases. Lesions were located in the mandible in 74 (65 %) cases and in the maxilla in 40 (35 %), with a mandible-to-maxilla ratio of 1.85:1 ($P < 0.001$). Figure 5 shows the specific location within the mandible and maxilla. Nearly 80 % of the lesions were located in the posterior region of the jaws and only 15.8 % in the anterior region, while 4.4 % of the lesions were located in both regions. In patients 7 years and older, the posterior mandible was the most frequently involved region compared to the anterior region of the mandible and anterior and posterior regions of the maxilla ($P < 0.001$).

The clinical presentation of the AFOs was reported in 94 cases. An AFO is characteristically painless and slow growing, and usually expands with time. In 27 (29 %) cases, the lesion was asymptomatic and discovered on radiographs taken because of failure of tooth eruption or during preparation for orthodontic treatment. There was a painless expansion of bone in 44 (47 %) cases and facial asymmetry, sometimes very pronounced, due to severe expansion of bone in 23 (24 %) cases. Only two patients complained of pain [18, 65].

Data on radiographic characteristics of AFOs are shown in Table 2. AFOs usually manifested as unilocular lesions (90.3 %), and multilocular lesions were uncommon (9.7 %).

Fig. 1 Radiographs showing ameloblastic fibro-odontoma. **a** Case 1. **b** Case 3. **c** Case 8. **d** Case 9

Fig. 2 **a** Panoramic radiograph of Case 11 showing a multilocular radiolucency with few small opacities. **b** and **c** Radiographs of the resected specimen of the mandible

Most of the lesions were described as being mixed radiolucent-radiopaque (94.8 %) and only a few were radiolucent (5.2 %). In the latter lesions, the amount of the calcified material was so small that it was not visible on radiographs.

Mixed lesions exhibited several patterns, such as radiolucency with a few scattered opacities, radiolucency with a large number of opacities in various size and shapes, and a single opaque mass (usually in the center) that was

Fig. 3 Photomicrographs of ameloblastic fibro-odontoma. **a** Strands, cords and nests of odontogenic epithelium supported by richly cellular connective tissue (HE, original magnification $\times 200$). **b** Epithelial islands showing a peripheral, tall columnar palisaded layer enclosing stellate reticulum-type cells in a primitive-appearing myxoid connective tissue (HE, original magnification $\times 200$).

c Intermediate zone between the soft tissue component and the hard tissue composed of dentin and enamel (HE, original magnification $\times 200$). **d** Higher magnification of the hard tissue component composed of dentin (*a*), enamel matrix (*b*) and enamel spaces (*c*) (HE, original magnification $\times 400$)

Fig. 4 Age and gender distribution of ameloblastic fibro-odontomas at the time of presentation (n = 114)

surrounded by a narrow or wide area of radiolucency. The borders of the lesion were well-defined in almost all cases (91 %), and only a few lesions were mostly but not entirely defined and locally non-defined (9 %).

The tooth relationship with the lesion was known for 95 cases. Most of the lesions (n = 87, 91.6 %) were associated with a single unerupted tooth or with several unerupted teeth, usually of the permanent dentition but also of the primary dentition. The lesion was usually located

coronally to the crown of the tooth/teeth. Table 3 shows the specific unerupted teeth that are associated with the lesion. Sixty-three cases were associated with one unerupted tooth and 24 cases with several (i.e., 2–5) unerupted teeth. The first and second permanent molars were the most common teeth to be associated with an AFO. The unerupted teeth were usually displaced inferiorly in the mandible and superiorly in the maxilla. In a very few cases, the AFOs had developed between roots of erupted teeth, in the

Fig. 5 Distribution of ameloblastic fibro-odontomas in the mandible and maxilla (n = 114)

Table 2 Radiological features of ameloblastic fibro-odontomas

Locularity (n = 93)	
Unilocular	84 (90.3 %)
Multilocular	9 (9.7 %)
Density (n = 97)	
Radiolucent	5 (5.2 %)
Radiolucent and radiopaque (mixed)	92 (94.8 %)
Few scattered opacities	33
Large number of opacities	8
Single opaque mass	19
Mixed, WS	32
Border (n = 89)	
Well-defined	81 (91 %)
Mostly defined and locally not defined	8 (9 %)
Tooth relationship (n = 95)	
Associated with crown of unerupted tooth	87 (91.6 %)
Not associated with unerupted tooth	8 (8.4 %)

WS without specification

periapical area of erupted teeth, or in place of a tooth [10, 56, 61, 63, 65, 84], Cases 2, 7, and 8 of the present study]. Root resorption caused by AFO was rare, having been reported in only three cases [33, 56, 74]. Perforation of the cortical plates is also uncommon, having been reported in only six cases [23, 30, 43, 45, 71, 75].

The size of the AFO was known in 93 cases. Lesion size ranged from 0.8 to 14 cm (mean 3.3 cm, median 3.0 cm). Although the mean size of the mandibular lesions was 3.1 cm and that of the maxilla 3.6 cm, the differences were not statistically significant ($P > 0.05$). Also, there was no association between the size of the lesions and the age of the patients ($P > 0.05$). It is worthy to note that the sizes of AFOs are relatively large considering the fact that they develop in the small jaws of children.

Discussion

An AFO belongs to the group of mixed odontogenic tumors that histopathologically represent odontogenic epithelium

with odontogenic ectomesenchyme, with or without hard tissue formation [2]. In general, this group of lesions is composed of AFs, ameloblastic fibro-dentinomas and AFOs. There is ongoing debate and disagreement among oral pathologists as to the relation of these lesions to the complex odontoma lesion. Some believe in the “maturation theory”, which suggests that an AF will develop through a continuum of differentiation and maturation into an AFO and eventually to a complex odontoma, which is a hamartoma [86]. Other authors claim that while an AF is probably a true neoplasm, an AFO should be regarded as an immature complex odontoma, thereby indicating that AFO is a hamartoma [5, 6]. On the other hand, there are oral pathologists who believe that AFs and AFOs are separate and distinct pathological entities that represent a neoplasm [1, 2, 8, 87]. They claim that an AFO differs significantly from the hamartomatous odontoma by having a greater potential for growth and causing considerable deformity and bone destruction [88, 89]. Furthermore, there is a malignant counterpart for AFO, the ameloblastic fibro-odontosarcoma [90, 91]. Trodahl [92] suggested that the truth may lie somewhere between these two poles of opinion. He pointed out that odontomas must have gone through a development stage and that a non-calcified stage of development must have occurred. This stage would mimic the histopathological appearance of an AF. As such, he concluded that there are two lesions that have the same histopathological appearance of an AF: one is the early stage of a developing odontoma and the other is the actual neoplasm. According to Gardner [93], the same also holds true for an AFO, i.e., some lesions with the histopathological appearance of an AFO are probably developing odontomas and some are the actual neoplasms. The problem is that the histopathological appearance of AFO in its neoplastic form is indistinguishable from a developing odontoma, whereupon clinical and radiological features may be of assistance in making the distinction. There is no question that large, expansile lesions that exhibit extensive bone destruction, cortical perforation and loosening of teeth are neoplasms. Some typical example are huge maxillary tumors, like the one reported by Miller et al. [18 Case 4], in which the extensive maxillary enlargement caused disfigurement and interfered with nasal respiration, feeding and speech, as well as the maxillary aggressive tumor reported by Piette et al. [40] that caused destruction of the maxillary sinus and extended to the orbital floor and pterygoid region. Other examples are the massive aggressive tumor of the maxilla reported by Hegde and Hemavathy [75] that caused facial disfigurement, perforated the buccal plate and presented as a soft tissue mass, and the case described by Ozer et al. [47] in which the tumor occupied the maxillary sinus with expansion of its walls causing proptosis. There are several other reports of large

Table 3 Unerupted teeth associated with ameloblastic fibro-odontomas (n = 87)

Mandible				Maxilla			
Permanent		Primary		Permanent		Primary	
Tooth #	No. of cases	Tooth #	No. of cases	Tooth #	No. of cases	Tooth #	No. of cases
<i>Single tooth</i>				<i>Single tooth</i>			
1	1	1	–	1	3	1	1
2	–	2	–	2	–	2	–
3	1	3	3	3	1	3	–
4	1	4	–	4	–	4	–
5	1	5	2	5	–	5	1
6	16			6	9		
7	15			7	2		
8	5			8	1		
<i>Total</i>				<i>Total</i>			
	40		5		16		2
<i>Multiple teeth</i>				<i>Multiple teeth</i>			
3–5	1	2–3	1	2–6	1	1–2	1
4–6	1	4–5	1	4–7	1	1–3	1
4–7	2			5–7	2		
5–6	3			6–7	3		
5–7	1			7–8	1		
6–7	3						
6–8	1						
<i>Total</i>				<i>Total</i>			
	12		2		8		2

aggressive maxillary tumors in the literature [29, 54, 67, 68, 74]. Examples of large destructive mandibular lesions where the tumor extended from the premolar or molar area to the sigmoid notch, coronoid notch or neck of the condyle were reported by several authors [17, 19, 46, 50]. On the other hand, asymptomatic small lesions directly overlying the crown of an unerupted tooth in young subjects, with no or minimal expansion of bone, are likely to be developing odontomas (immature odontomas) rather than neoplasms [2, 54, 93]. Examples of these are probably the cases reported by Olech and Alvares [10], Miller et al. [18, Case 3], and Warnock et al. [38].

In light of these collected data, we can assume that some cases that have been reported in the literature under the diagnosis of AFO are, in fact, examples of developing odontoma. However, at the present time, there is no unequivocal way of distinguishing between a neoplastic AFO and a developing odontoma [7, 8, 37, 89, 93].

The clinical and radiological profiles of AFOs that are described in many papers and textbooks of oral pathology are not always accurate because the authors rely on data from small series of cases. There is no argument in the literature that an AFO is an uncommon lesion of children and adolescence. In our current study, the mean age of the

patient was 9.6 years, in the review by Philipsen et al. [6] it was 9.0 years, and in the 2005 WHO classification of odontogenic tumors it was between 8 and 12 years [1]. There is, however, disagreement between our findings on gender differences and some of those reported in the literature. In the 2005 WHO classification [1] as well as in the textbook of Neville et al. [89], it is claimed that there is no gender predilection. Our study revealed that the AFO is significantly more common in males (F:M = 1:1.85, $P = 0.001$). There is also disagreement between our study results and some of those in the literature regarding the site of an AFO lesion. Some authors claim that there is slight predilection for the maxilla [94], others claim that AFO is evenly divided between the mandible and maxilla. The 2005 WHO classification [1] also states that there is no site predilection. Our findings revealed that an AFO is more common in the mandible (maxilla-to-mandible ratio of 1:1.85) and that the difference is of statistical significance ($P < 0.001$).

As for the radiological features of an AFO, most authors state that it presents as a “unilocular or multilocular lesion” [1, 7, 95]. Although this statement generally holds true, our study revealed that about 90 % of the lesions are unilocular and that 10 % are multilocular. Thus, it would

be more correct to state that an AFO is usually a unilocular lesion and that multilocular lesions are uncommon.

The treatment of an AFO, which in most cases is a well-defined, circumscribed, non-aggressive, noninvasive lesion, is by conservative surgical enucleation [7]. However, the larger, more extensive and destructive lesions may require surgical resection of either partial maxillectomy [40, 68] or partial mandibulectomy [33, 66, and Case 11 of the present study].

Recurrence of AFO is uncommon and our search yielded only 4 cases [50, 57, 66]. The histopathology of the recurrent lesions was AFO in two cases [50, 57] and complex odontoma in the other two [66]. The latter two cases may lend support to the theory that some AFOs are indeed immature odontomas. Some authors suggest that recurrence occurs due to a residual lesion resulting from inadequate surgical removal at the time of initial treatment [66], but others refute that possibility [57].

Only a small number of AFOs have been submitted to molecular and genetic studies but no significant findings have been found thus far that can contribute to our knowledge of the biological behavior of this lesion [96, 97].

It is important not to confuse AFOs with odontoameloblastomas that are extremely rare tumors and that, like AFOs, occur in young age groups. Odontoameloblastomas consist histopathologically of a combination of ameloblastomas and odontomas. The odontogenic epithelium proliferates in a follicular or plexiform pattern in a mature connective tissue stroma, like a conventional ameloblastoma. Intermingled with this tissue are dental hard structures similar to a compound or a complex odontoma. Unlike AFOs, odontoameloblastomas have an aggressive biological behavior such as that seen in conventional ameloblastomas and they are treated in the same manner [98].

In summary, an AFO is an uncommon lesion that belongs to the group of mixed odontogenic tumors. There is ongoing debate in the literature as to whether it should be regarded as a true neoplasm or as a developing odontoma (hamartoma). The problem is that both lesions share the same histopathological appearance. Our analysis of the literature revealed that some lesions that exhibit aggressive growth, causing considerable facial deformity and bone destruction, probably represent true neoplasms, while others that are small, asymptomatic and have no bony expansion probably represent developing odontomas (hamartomas). Since the literature relies on single case reports and small series of cases, there are many inaccuracies and conflicting data on the lesion's clinical and radiographic features. Our current analysis revealed that an AFO is not equal between genders but rather significantly more common in males, that it is not equally distributed between the mandible and the maxilla but significantly

more common in the mandible, and that it does not present as a unilocular or multilocular lesion but mostly unilocular and that multilocular AFO lesions are uncommon.

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