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REVIEW

Critical evaluation of the radiological and clinical features of adenomatoid odontogenic tumour

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Objectives: The aim of this study was to evaluate the radiological and clinical features of adenomatoid odontogenic tumours (AOTs).
Methods: A total of 272 cases (267 from the English-language literature and 5 new cases) were analysed with special emphasis on their radiological features.
Results: The patients' ages at time of diagnosis ranged from 3 years to 82 years (mean 18.4 years). The maxilla-to-mandible ratio was 1.7:1. Mandibular lesions were significantly more frequent among patients older than 16 years ($p = 0.032$). Expansion of the cortex was significantly more prominent among patients older than 16 years ($p = 0.045$). There was a positive correlation between the size of the lesion and the age of the patient at the time of diagnosis ($p = 0.016$). The size was also associated with increased root resorption ($p < 0.001$), ill-defined borders ($p < 0.001$), expansion ($p < 0.001$) and perforation of the cortex ($p < 0.001$). Small opacities were present in 77% of lesions and were associated with expansion of the cortex ($p = 0.043$). The significant radiological features in patients aged 30 years and above were root resorption ($p = 0.013$) and lesions crossing the midline ($p = 0.019$).
Conclusions: The size of an AOT is influenced by the patient's age. It is also associated with root resorption, ill-defined borders, expansion and perforation of the cortex, but it cannot be ruled out that those changes reflect a longer duration of the lesion.
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Keywords: adenomatoid odontogenic tumour; odontogenic tumours; radiology; jaws

Introduction

Adenomatoid odontogenic tumours (AOTs) are unique odontogenic lesions located either centrally within the jaws or peripherally in the soft tissue overlying the tooth-bearing area. Some authors consider AOTs to be true benign, non-aggressive non-invasive neoplasms, whereas others view them as developmental hamartomatous odontogenic growths.[1] AOTs have three clinicopathologic variants: intraosseous follicular (pericoronal), intraosseous extrafollicular (extracoronal) and peripheral (extraosseous). The follicular type is associated with the crown and also often with part of the root of an unerupted tooth, whereas the extrafollicular type is not associated with unerupted teeth. The peripheral variant is associated with gingival structures.[2]

In 1971, the World Health Organization adopted the term "adenomatoid odontogenic tumour" to describe this entity, as had been proposed by Philipsen and Birn.[3] It is estimated that AOTs constitute about 2.2–7.1% of all odontogenic tumours, and the increasing number of reports in the literature on AOT indicates that the tumour develops more frequently than was formerly expected.[3,4] Based on radiographic findings, differentiating AOTs from dentigerous cysts, keratocystic odontogenic tumours, unicystic ameloblastomas, calcifying cystic odontogenic tumours and calcifying epithelial odontogenic tumours may pose diagnostic dilemmas.[1]

Most published papers on AOT have concentrated upon the epidemiological and clinical characteristics of the lesion. The purpose of this study is to analyse in detail the radiological features of AOTs described in the literature, and to add five new cases from our files. We present radiological diagnostic characterizations of this lesion that have not been reported before.

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Table 1 Clinical and radiological data of five new cases of adenomatoid odontogenic tumour[a]

Case	*Age (years)*	*Gender*	*Jaw*	*Variant (teeth involved)*	*Opacities*	*Size (cm)*	*Displacement*	*Resorption*	*Expansion*	*Perforation*	*Borders*	*Midline*
1	17	Male	Mandible	EF (31–44)	+	3.5	+	–	+	-	WD	C
2	24	Female	Mandible	Fol (43)	–	3.5	–	–	–	-	WD	C
3	22	Male	Mandible	EF (36–43)	–	5.5	–	+	+	+	ID	C
4	17	Male	Maxilla	Fol (13)	–	2	+	–	–	-	WD	NC
5	15	Male	Maxilla	Fol (13)	–	2	+	–	–	-	WD	NC

C, crossed; EF, extrafollicular; Fol, follicular; ID, ill-defined; NC, not crossed; WD, well-defined.
[a]All five tumours were unilocular and radiolucent.

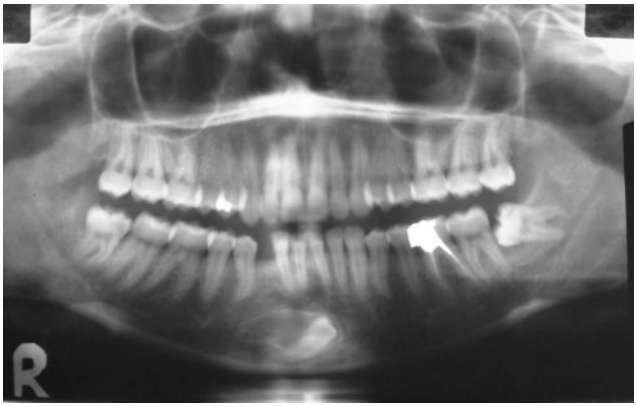

Figure 1 Mandibular adenomatoid odontogenic tumour. The lesion crosses the midline (extending from the right lower first premolar to the left lower lateral teeth). The right mandibular canine is unerupted. The borders are well-defined and sclerotic

Materials and methods

The English-language literature was reviewed for adequately documented cases of AOT published between 1950 and 2010. Medline's PubMed interface and the Google Scholar search engine were searched using the keywords ''adenomatoid odontogenic tumour'' and ''adenoameloblastoma''. Criteria for inclusion were clinical and histopathological diagnoses of AOT, and acceptable radiographic images or detailed radiological descriptions for each case. Not all data were available for all cases.

A total of 272 cases (267 from publications and 5 new cases) were analysed.[5–133] The clinical and radiological data of the five new cases are described in Table 1 and Figures 1 and 2. Clinical data of age at time of diagnosis, gender, location, symptoms and radiological data of density, expansion, borders, locularity, size and impact on adjacent teeth[134] were used to evaluate these cases. In the present study, incisors and canines were regarded as making up the anterior region, while the posterior region comprised premolars and molars. Lesions were considered unilocular when a single discrete radiolucent cavity was present and multilocular when septa divided the lesion into compartments. Lesions were considered as

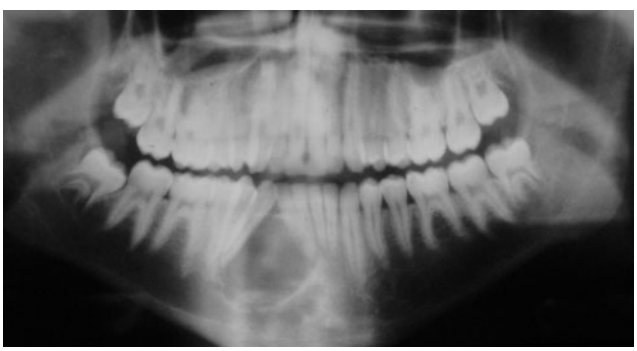

Figure 2 Mandibular adenomatoid odontogenic tumour. The lesion is extending from the right lower first premolar to the left lower central teeth, displacing four teeth. The borders are well-defined and sclerotic

radiolucent when their content was dominantly radiolucent, including cases that contained small radio-opacities inside the radiolucent lesion. Lesions were considered as radio-opaque when their content was dominantly radio-opaque. The borders of the lesions were considered well defined when they were clearly defined or as being ill defined when the margin was not clearly delineated.[135] The size of a lesion was determined by its greatest diameter. Lesions were considered small when the diameter was under 2 cm, medium-sized when it was between 2 cm and 3 cm, and large when it was above 3 cm. Teeth were considered as being involved in the lesion when they were impacted, displaced or resorbed by it. The lesion was referred to as follicular (pericoronal) when the tumour was associated with unerupted teeth, extrafollicular (extracoronal) when it had no association with unerupted teeth and peripheral (extraosseous) when it was attached to gingival structures.[2]

The various parameters of AOTs were analysed for the entire cohort and for specific groups of patients up to 16 years of age (which we found to be the median age of the patients at the time of diagnosis) and those older than 16 years. A separate analysis was performed on a group of patients aged 30 years and above at the time of diagnosis, because an earlier study had shown that it was related to changes in jaw predilection.[136]

Statistical analysis

A descriptive analysis was used to evaluate the frequency of nominal variables. The χ^2 and Fisher's exact tests were used to calculate possible associations between age, gender, presenting symptoms and the various radiographic characterizations. Pearson correlations were used to evaluate the correlation between the age of the patient and the diameter of the lesion. A *t*-test was used to evaluate the association between the diameter of the lesion and various radiographic characterizations (SPSS® v. 10.0; SPSS, Chicago, IL). The level of significance was set at $p < 0.05$.

The study was approved by the ethical committee of Tel Aviv University.

Results

A total of 272 cases of AOTs were reviewed, of which 5 were new and had not been reported until now. The age of the patients was known for 267 cases: it ranged from 3 years to 82 years, with a mean of 18.4 years and a median of 16 years (Table 2). The highest incidence of AOTs (67%) was in patients aged 10–20 years (Table 3), and most of those cases involved patients in the age range 12–16 years. The gender was known for 239 cases: 141 (59%) were females and 98 (41%) were males, with a female-to-male ratio of 1.4:1. Distribution of the lesions in the maxilla and mandible was known for 241 cases: 152 (63%) were in the maxilla and 89 (37%) were in the mandible, with a maxilla-to-mandible ratio of 1.7:1. Mandibular lesions constituted 45% of all lesions among patients older than 16 years of age, compared with 31% among patients younger than 16 years of age ($p = 0.032$). Specific locations within the jaws that enabled applying the criteria of "anterior" and "posterior" were known for 211 cases (Table 4): the lesions were located anteriorly in 58% of the cases. Symptomatology was known for 157 cases: 136 (87%) patients were asymptomatic and 21 (13%) complained of pain.

Table 2 Age and gender distribution of the patients with adenomatoid odontogenic tumours

Results	*Males*	*Females*	*Total*
Total	98 (41)	141 (59)	239
Mean (years)	20	17.6	18.4
Median (years)	16	16	16
Age range (years)	8–75	3–82	3–82

Data are number (percentage) unless otherwise indicated.

The radiological features of AOTs are summarized in Table 4. The most common variant was the follicular (pericoronal). Follicular lesions accounted for 137 (69%) of the cases, and 85 of them (76%) were in the group of patients younger than 16 years of age. The extrafollicular (extracoronal) variant was reported in 54 (27%) of all cases, with 35 (42%) of them in the group of patients older than 16 years of age. The peripheral (extraosseous) variant was present in 9 (5%) of the cases, of which 8 were in the group of patients younger than 16 years of age. The follicular variant was significantly more prominent in the maxilla, whereas the extrafollicular variant was significantly more prominent in the mandible ($p = 0.018$).

Canines were the most common unerupted teeth associated with AOTs (74% of all unerupted teeth), and maxillary canines were the most common among them. Lesions were unilocular in 112 (91%) cases and multilocular in 11 (9%). They were classified as predominantly radiolucent in 163 (98%) of the cases, and radio-opaque in only 3 (2%). In 92 predominantly radiolucent lesions, a definite determination could be made as to the presence or absence of calcifications in the lesion; opacities (dominant and non-dominant) were present in 71 (77%) of those lesions. The opacities were described as flecks or snowflakes, patchy areas of calcification, spicules of calcification, scattered radio-opacities, irregular radio-opacities, amorphous radio-opacities, fine

Table 3 Distribution of adenomatoid odontogenic tumours by decade of life

Decade (range, years)	*Reported cases (n)*	*%*
First (0–9)	15	5.6
Second (10–19)	180	67.4
Third (20–29)	52	19.5
Fourth (30–39)	10	3.7
Fifth (40–49)	3	1.1
Sixth (50–59)	2	0.7
Seventh (60–69)	3	1.1
Eighth (70–79)	1	0.37
Ninth (80–89)	1	0.37
Total (%)	267	100

Table 4 Location and radiological features of adenomatoid odontogenic tumours[a]

Feature	*Maxilla,* n (%)	*Mandible,* n (%)	*Total (%)*
Location			
Anterior	77 (58)	46 (58)	123 (58)
Posterior	55 (42)	33 (42)	88 (42)
Variant			
Pericoronal	89 (74)	48 (60)	137 (68.5)
Extracoronal	24 (20)	30 (37.5)	54 (27)
Extraosseous	7 (6)	2 (2.5)	9 (4.5)
Locularity			
Unilocular	59 (92)	53 (89)	112 (91)
Multilocular	5 (8)	6 (11)	11 (9)
Displacement			
Present	48 (86)	35 (73)	83 (80)
Absent	8 (14)	13 (27)	21 (20)
Resorption			
Present	12 (25.5)	6 (13)	18 (19)
Absent	35 (74.5)	40 (87)	75 (81)
Expansion			
Present	43 (69)	37 (66)	80 (68)
Absent	19 (31)	19 (34)	38 (32)
Radiolucent	97 (99)	66 (97)	163 (98)
Radio-opaque	1 (1)	2 (3)	3 (2)
Opacities[b]			
Present	33 (73)	38 (81)	71 (77)
Absent	12 (27)	9 (19)	21 (23)
Perforation			
Present	7 (8)	6 (9)	13 (9)
Absent	77 (92)	58 (91)	135 (91)
Midline			
Not crossed	87 (96)	52 (78)	139 (88)
Crossed	4 (4)	15 (22)	19 (12)
Borders			
Well defined	58 (87)	48 (84)	105 (85)
Ill defined	9 (13)	9 (16)	18 (15)

[a]The percentage given represents the proportion of cases in which accurate interpretation could be made.
[b]Referring to predominantly radiolucent lesions.

radio-opacities and faint radio-opacities. The size of the lesions ranged from 0.4 cm to 12 cm, with a mean of 2.9 cm. 28% of the lesions were considered small (under 2 cm), 32% were medium-sized (2–3 cm) and 40% were large lesions (above 3 cm).

Expansion of the cortex was present in 80 (68%) cases and it was significantly more prominent among patients who were older than 16 years of age ($p = 0.045$). Borders were well defined in 105 (85%) cases and ill defined in 19 (15%). Tooth displacement was noted in 83 (80%) cases, and root resorption was described in 18 (19%). There was perforation of the cortex in 13 (9%) cases. The lesion crossed the midline in 19 (12%) cases and involved the mandible in 15 (79%) of them ($p < 0.001$).

Small opacities were significantly associated with expansion of the cortex ($p = 0.043$). There was no significant association between lesion size and opacities, but there was a significant correlation between lesion size and the age of the patient at the time of diagnosis ($p = 0.016$). Lesion size was also associated with increased root resorption ($p < 0.001$), ill-defined borders ($p < 0.001$), expansion ($p < 0.001$), perforation of the cortex ($p < 0.001$) and whether or not the lesion crossed the midline ($p < 0.001$).

There were particularly interesting findings in patients aged 30 years and above at the time of diagnosis. These patients have shown significant predilection towards lesions in the mandible ($p = 0.011$, *vs* the entire cohort), root resorption ($p = 0.013$) and crossing the midline ($p = 0.019$).

Discussion

It had been generally accepted that the relative frequency of AOT corresponds to 2.2–7.1% of all odontogenic tumours. However, a comprehensive worldwide literature survey by Philipsen et al[1] disclosed a much wider range, *i.e.* from 0.6% to 38.5 %. The histological findings of AOTs are remarkably similar in the literature. An AOT has been described as a tumour of odontogenic epithelium with duct-like structures and with varying degrees of inductive changes in the connective tissue. The tumour may be solid or partly cystic and may contain globular masses of calcified material.[2]

Some clinical findings of the present study are in general agreement with other studies published in the English-language literature. We and others have found that an AOT is usually a symptom-free lesion[33,136,137] and that patients with follicular AOTs are significantly younger than those with the extrafollicular variant. This is probably due to the fact that follicular AOT is associated with the lack of tooth eruption, which leads the patient to seek dental consultation and results in early diagnosis.[137,138]

The mean age of the patients at the time of diagnosis was 18.4 years in the current study. Although there is a general agreement regarding the peak incidence of the tumour in the second decade of life,[136–142] the mean age varied between 16 years[33] and 21 years[143] in the different reviews.

In the current study, the predilection for females was shown as a female-to-male ratio of 1.4:1. This finding was in agreement with the findings among African[138] and non-Asian populations.[137] However, the female-to-male ratio among Asian populations was reported as high as 2.3:1, and up to 3:1 among Japanese populations.[137]

The predilection for the maxilla and anterior region of the jaws was shown in the current study with a maxilla-to-mandible ratio of 1.7:1. Other studies reported maxilla-to-mandible ratios of 1.4:1,[140] 1.8:1,[33,138] 1.9:1[137] and 2:1.[136]

The present study is, to our best knowledge, the first one to demonstrate the continuing influence of age on the radiological characterizations of AOTs through the analysis of multiple radiological features below and above the ages of 16 years as well as above the age of 30 years. The size of the lesion is correlated with increasing age and is significantly associated with features such as increased root resorption, ill-defined borders, expansion, perforation of the cortex and lesions crossing the midline. These changes may reflect a longer duration of the lesion due to a late diagnosis.

Our results showed that patients older than 16 years of age are more likely to present with a lesion in the mandible, the extrafollicular variant and expansion of the cortex. Patients older than 30 years are more likely to present with a lesion that displays root resorption and lesions crossing the midline.

An AOT requires a radiological differential diagnosis from a variety of odontogenic lesions. Differentiating it from a dentigerous cyst is difficult when the AOT is completely radiolucent and has a follicular relationship with an unerupted tooth.[144] The follicular type of AOT, however, sometimes extends apically along the root beyond the cementoenamel junction, while dentigerous cysts are attached to the tooth at the cervical region: this feature can help to distinguish between the two types of lesions. In addition, an AOT often contains fine radio-opacities, which may also be helpful. In this regard, it is of interest to note that panoramic radiography is often unable to demonstrate radio-opacities when the calcification is minimal, whereupon intraoral radiographs may be essential for correct radiographic interpretation of an AOT in the presence of minimal quantities of calcified deposits.[139] A keratocystic odontogenic tumour (KCOT) and a unicystic ameloblastoma (UA) can also mimic a follicular AOT when they are in a pericoronal location. Both of those lesions are diagnosed in the second and third decades of life (similar to an AOT), but they are more common in the posterior area of the mandible,[144] as opposed to an AOT, which is more common in the anterior region of the jaws. Another lesion that needs to be distinguished from a follicular AOT is a calcifying cystic odontogenic tumour (CCOT). This lesion is similar to an AOT because it is also found in the anterior region of the jaws; it may also be associated with an unerupted tooth, may also contain radio-opacities, and is also diagnosed in the second decade of life. Because of so many close similarities, it is often impossible to differentiate between CCOTs and AOTs.[145]

The extrafollicular variant of AOT also needs to be differentially diagnosed from several odontogenic and non-odontogenic lesions. Among the radiolucent odontogenic lesions it has to be differentiated not only from KCOTs and UAs that are not associated with unerupted teeth but also from lateral periodontal cysts (LPCs). An LPC is located between the roots of erupted teeth in the anterior region of the mandible, but is diagnosed in patients older than those with AOTs.[146] When the extrafollicular variant of an AOT contains foci of radio-opacities, it resembles not only a CCOT that is not associated with unerupted teeth but also ameloblastic fibro-odontomas (AFOs) and calcifying epithelial odontogenic tumours (CEOTs). However, these last two lesions are located mainly in the posterior area of the mandible, and, while AFO is diagnosed mainly in young children (mean age of 10 years), CEOT is diagnosed in patients older than those with AOTs.[146]

In conclusion, a unilocular radiolucency with opacities and tooth displacement in the anterior region of the jaws are the radiological features most characteristic of the majority of AOTs. The present analysis reveals that other features of the lesion are more variable and that they are influenced mainly by the age of the patient and by the size of the lesion. Patients older than 16 years of age are more likely to present with a lesion in the mandible, a lesion of the extrafollicular variant and expansion of the cortex. Patients older than 30 years of age are more likely to present with a lesion that displays root resorption and one that crosses the midline. These findings could be explained by the correlation between the age of the patient at the time of diagnosis and the size of the lesion. It cannot, however, be ruled out that these changes reflect a longer duration of the lesion.

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