**Editorial Review**

The Adenomatoid Odontogenic Tumour (AOT): An Update

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The present biological profile of the adenomatoid odontogenic tumour represents an updating of the data published by the authors from 1990 to 1996. Several new facets of this tumour appear from the approximately 250 cases having been published in recent years. Papers on peripheral variants, AOT-CEOT combined lesions, pigmented AOTs, cases exhibiting tubular dentin induction, new immunohistochemical and ultrastructural data are among the findings having increased our understanding of this interesting tumourous growth. However, the present updating did not in any way change our conception of the unique clinical, radiographical and histological features of the AOT but rather totally confirmed it.

**Key words: AOT, odontogenic tumour, jaws**

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**Introduction**

The first case of what today is known as the *adenomatoid odontogenic tumour* (AOT) was probably described by Dreybladt in 1907 (1). A variety of terms have been used to describe this tumour of which the *adenomatoid odontogenic tumour* was in common usage until Philipsen and Birn in 1969 (2) introduced the now generally accepted nomenclature of AOT. A comprehensive study appeared in 1991 (3) reviewing 500 cases of AOT (including 465 cases from the literature for which search was terminated by the end of 1989) followed by a study on AOT variants (4). From the early nineties onwards approximately 20 new case reports and review articles have been published in English (4-23). Although it is not easy to estimate the exact number of newly published cases due to possible overlapping cases in some large series (6, 7, 19), approximately 250 cases were added to the previous 500, from which to produce the present revised biological profile of the AOT.

In the recent WHO Histological Typing of Odontogenic Tumours (24) the AOT has been defined as:

*A tumour of odontogenic epithelium with duct-like structures and with varying degrees of inductive change in the connective tissue. The tumour may be partly cystic, and in some cases the solid lesion may be present only as masses in the wall of a large cyst. It is generally believed that the lesion is not a neoplasm.*

**Clinical features**

**Frequency**

It has been estimated that the AOT accounts for approximately 2.9 to 6.8 per cent of all odontogenic tumours (3). It gives this tumour a ranking of fourth or fifth among the odontogenic tumours only surpassed by odontomas, myxomas, ameloblastomas and/or cemento-osseous tumours/lesions.

**Age**

The age range of patients is between 3 and 82 years at time of diagnosis. Approximately two thirds of the tumours are diagnosed in the second decade of life (Table 1) and more than half of the cases (53.1%) are found within the teens (13-19 years of age)(3). This age

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distribution with a very narrow and tall peak makes the AOT truly unique among the odontogenic tumours.

**Gender**

The female:male ratio for all age groups together is 2:1 (443 females versus 219 males). Table 1 shows sex distribution by age groups. The very high female:male ratios for Mestizo (4:1), Sri Lanka (3:1) and Japanese AOT cases (3:1) appear to reflect possible racial differences, but it is only 1.4 to 1.5:1 among black Africans (6, 7, 11, 13, 19). The increased ratio of males to females previously noted to be peculiar to Nigerians (25) was corrected after analyzing a larger series of patients (6).

**Race**

AOT has been described in all major races. Fig. 1 shows the global distribution of the reported cases.

**Site**

The AOT appears in three clinico-topographic variants: 1) *follicular*, 2) *extrafollicular* and 3) *peripheral* all of which have identical histology (3). The follicular variant is associated with the crown of an embedded tooth most frequently a permanent canine. The extrafollicular variant has neither a pericorneal nor any other relationship to an embedded tooth. The peripheral type is located in the gingival mucosa and appears clinically as a gingival hyperplasia or fibrous epulis. The follicular and the extrafollicular variants are both intrabony or central tumours and account for approximately 98% of all AOTs of which 72.6% are of the follicular type. The follicular variant is for both females and males nearly three times as frequent as the extrafollicular. Compared with the two central variants, both of which are more common in females than in males, the peripheral AOT shows much higher female prevalence. Surprisingly, 10 of the reported 11 cases are from young females from 3 to 21 years. Although the extrafollicular variants are commonly found in the mandible in a black African population (6), the two central variants together are more common in the maxilla than in the mandible with a total ratio of 1.9:1. On the other hand, the peripheral variant is extremely rare in the mandible (13 of the 14 recorded cases occurred in the maxilla). Table 2 shows location of AOT including all variants by age groups. It is also of interest that for the age group 30 years and over, the mandible is the most frequent site of tumour development. Concerning the distribution of embedded permanent teeth in follicular AOT, all four canines account for 60% and the upper canines alone for 42% (3). As concerns the association with the deciduous dentition, two cases of peripheral AOT with involvement of erupted deciduous central incisor and canine were newly reported (9, 20). Previously, a Japanese case of follicular AOT involving an unerupted deciduous canine and a first molar had been only one exceptional case of this category (3, 19).

**Clinical presentation**

All types of the AOT appear as a slow but progressive growth with few or no subjective symptoms. Cortical expansion is a common finding in central variants and penetration of the cortical plate has only rarely been
reported (8, 14). The lesion, in particular the extrafollicular type may cause some displacement of neighbouring teeth; root resorption is rare. Although unusually large tumours, some of which were regarded as a neoplasm rather than a hamartoma, have been reported (8, 10, 14, 15), the size of the intraosseous lesions generally varies between 1 and 3 cm in diameter.

**Radiological features**

The intraosseous variants both appear as well demarcated radiolucencies. In approximately two thirds of the reported cases the radiolucency contains small particulated radiopaque foci. It has been indicated that intraoral radiographs are essential for diagnosing AOT in the presence of minimal quantities of calcified deposits (26). The follicular type most often mimicks a follicular (dentigerous) cyst. In fact, 77% were primarily diagnosed as a follicular or dentigerous cyst (2). However, careful examination of radiographs discloses that the tumour in most if not all cases does not possess a true follicular cyst/embedded tooth relationship. Rather than surrounding only the tooth crown, the AOT frequently extends laterally from one surface of the unerupted tooth to envelop a considerable portion of the root (27). The extrafollicular type appears as a radiolucency without any pericoronal relationship and is often primarily diagnosed as residual, globulomaxillary or lateral periodontal cyst depending upon the tumour location. The peripheral type may show slight erosion of the alveolar bone cortex but rarely produces radiographically detectable changes.

**Pathogenesis**

The fact that all AOT variants show identical histology strongly points toward a common origin. In order to conceptualise a unified source of origin for the diverse locations of AOT, only the complex system of the dental laminae or its remnants matches the requirement (4). There is continuous debate in the literature whether to regard AOT as a developmental outgrowth, a hamartoma or a neoplasia of odontogenic epithelium (28-31). For a detailed account on the pathogenesis, see Philipsen et al., 1992 (4).

**Pathology**

Macroscopically, the central variants are roughly spherical in shape with a well-defined fibrous capsule. The cut surface may reveal a solid tumour mass or show one large or several small cystic spaces containing yellowish, semisolid material. In the follicular type a crown of a tooth is found embedded in the tumour mass or projecting into a cystic lumen. It was even suggested that the tumour is in reality a follicular cyst with intracystic epithelial tumour proliferation (32) or that follicular cyst epithelium may give rise to the tumour (17).

**Light microscopy**

Irrespective of the tumour variants the histology is as stressed earlier-identical and exhibits a remarkable consistency. At low magnification the most striking pattern is that of varying sized solid nodules of cuboidal or columnar epithelial cells forming nests or rosette-like structures with minimal stromal connective tissue (Fig. 2). Between the epithelial cells of nodules and in the center of the rosette-like configurations droplets of an eosinophilic amorphous material are present. Spindle-shaped or polyhedral, closely opposed epithelial cells with dark, eosinophilic cytoplasm and round or oval hyperchromatic nuclei fill in the spaces between the epithelial nodules. Interlacing strands of epithelium one to two cells in thickness form a trabecular or cribriform configuration often seen at the tumour periphery. These epithelial cells very likely belong to the same cell population that fills in the spaces between epithelial nodules as just described.

Conspicuous within the cellular areas are structures of tubular or duct-like appearance (Fig. 3). The duct-like

![Fig. 2: A tumour nodule composed of cuboidal or columnar epithelial cells forming rosette-like structures. Note anastomosing thin epithelial strands at periphery of the nodule (HE×100).](image)

![Fig. 3: Tubular or duct-like structures lined by a single row of columnar epithelial cells within the cellular area (HE×200).](image)
spaces are lined by a single row of cuboidal or low columnar epithelial cells, the ovoid nuclei of which are polarized away from the luminal surface. The lumen may be empty or contain a variable amount of eosinophilic material or cellular debris. The ducts vary considerably in diameter. The duct-like structures may not always be present in all lesions. Due to the overall distinctive histomorphology of the AOT, the diagnosis can usually be made without the duct-like structures being present. In addition to forming duct-like structures, the cuboidal to columnar cells form convoluted cords or bodies in complicated patterns often showing invaginations.

A third characteristic cellular pattern is nodules composed of polyhedral, eosinophilic, epithelial cells of squamous appearance exhibiting well-defined cell boundaries and prominent intercellular bridges (Fig. 4). Their nuclei may occasionally show very mild (degenerative) pleomorphism. These islands may contain pools of amorphous amyloid-like material and globular masses of almost translucent calcified substances. Occurrence of one or more nodules of this cellular arrangement has led to a number of authors (12, 16, 33-35) to suggest the existence of a so-called combined AOT/calcifying epithelial odontogenic tumour (CEOT) lesion. The presence of CEOT-like foci does not seem to influence the biological behaviour and growth potential of AOT. In a recent paper (13) reporting on 12 AOT cases, CEOT-mimicking nodules of varying size were found within all tumours. Therefore, such CEOT-like areas are not unusual findings of AOT and may be considered as a normal feature within the continuous histomorphological spectrum of AOT rather than reflect a true combination of two distinct or separate entities (13). In fact, there are no reported cases of the combined epithelial odontogenic tumour in which CEOT predominates over AOT.

Mitotic activity among tumour cells is generally minimal and epithelial atypia has never been reported. In rare instances melanin pigmentation of tumour tissue and stroma cells and presence of melanocytes may be found in AOT (5, 22, 36).

Whereas induction of hyaline, dysplastic dentinoid material or calcified osteodentin, rarely with concomitant abortive enamel, has been described in this tumour (14, 17, 18), true dental hard tissues have not been detected. However, one of the present authors (HN) has experienced a case of AOT in which dentin with dentinal tubules was formed between the tumour epithelium and odontoblast-like stromal cells (Fig. 5) (37). Calcified material is on the other hand quite commonly found. Calcified bodies most likely representing dystrophic calcification may be found in the loose connective tissue stroma. Scattered throughout the tumour tissue are small foci and infrequently larger masses of calcified bodies or globules, often found adjacent to rows of tall columnar cells resembling ameloblasts.

The connective tissue stroma is generally very loosely structured containing thin-walled congested vessels often showing marked degenerative changes of endothelial lining, vessel walls and perivascular connective tissue (3). Cellular elements are few.

**Histochemistry and immunohistochemistry**

Histochemical studies have mainly focused on the nature of the hyaline or eosinophilic deposits and calcified structures (38-40). The fact that some investigators consider the eosinophilic material to be an abortive form of preenamel while others are equally convinced that it presents some type of mesenchymal product clearly expresses the inadequacy of previous "conventional" histochemical techniques. The same arguments may apply to the question about the nature of amyloid, amyloid-like or pseudoamyloid substance disclosed in AOT. An immunohistochemical study (41) has demonstrated co-expression of keratin and vimentin in the tumour cells at the periphery of the ductal, tubular or whorled structures. In contrast, the spindle or columnar
cells showed slight or no staining reaction. Whereas tumour cells were positive for keratin stains, mineralized and hyaline materials were negative. Sakur et al. (42) described positive staining reaction for amelogenin and enamelin in small mineralized foci, the tumour cells surrounding them and in the hyaline droplets in AOT. Amelogenin was also revealed by Mori et al. (43) in the tumour cells of AOT.

**Electron microscopy**

Almost all ultrastructural studies have been performed on tissues taken from the follicular type of AOT. The epithelial nature of the tumour has been confirmed through the finding of well-developed gap junctions, desmosomes and desmosome-like junctions, whereas tight junctions have not been observed. Tonofilaments are present in varying amounts. Three morphologically different types of epithelial tumour cells corresponding to the three cell populations seen in light microscopy have been described (12, 44-47). The material found in the duct-like spaces has a granulo-fibrillar appearance. This material is separated from the adjacent tumour cells by a basal lamina-like zone, a finding lending support to earlier theories suggesting the duct-like spaces to be the result of degeneration of the stromal tissue. Hemidesmosomes are formed between the cells and this matrix. Tumour cells demonstrating squamous metaplasia (representing CEOT-like areas) are polygonal, contain an abundance of tonofilaments and possess well-formed desmosomes. The ultrastructure of the eosinophilic amorphous masses is heterogeneous and according to El-Labban (48) they consist of three types of fibrils: thin collagen fibrils, electron-dense fibrils, and amyloid filaments. A recent study (49) has revealed that the most conspicuous feature of the amorphous eosinophilic material is concentrically arranged tubular structures (Fig. 6), the surface of which may be coated with a fine granular material. Amyloid filaments or collagen fibrils were not encountered in this study.

**Treatment**

Since all variants of AOT show an identical benign biological behaviour and since they in almost all cases are well encapsulated lesions, conservative surgical enucleation or curettage has proven the treatment modality of choice. In only three Japanese cases among 750 cases has recurrence of this tumour occurred (19, 50), and in only one instance extension of recurrent tumour into the intracranial space was recorded (50).

**References**


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**Fig. 6. Tumour droplet (TD) ("eosinophilic amorphous mass") of homogeneous type with concentrically arranged tubular elements. (×50,000).**
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