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# Adenomatoid odontogenic tumor: What is the true nature?

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ABSTRACT

The Adenomatoid odontogenic tumor (AOT) is one of the most controversial benign odontogenic tumor, which has been known to the pathologists for the past 100 years. Since then the history, histogenesis and histopathologic designation of AOT remains a matter of debate. Some authors consider it as a true benign neoplasm while others consider it as a hamartoma and still others as an odontogenic cyst. Here we propose that the AOT should not be considered as a cyst because its true cystic nature remains questionable. We hypothesize that when the AOT arises from a change in REE covering of the impacted tooth, then it appears as cystic in nature & certainly not a true cyst by origin. Further studies on the histogenesis are required to change the nomenclature of AOT to adenomatoid odontogenic cyst (AOC).



## Background

The Adenomatoid odontogenic tumor (AOT) has been known to the pathologists for the past 100 years as a benign, slow growing odontogenic tumor [1]. Search for the first identifiable case is challenging, because over the years credit has been given to different authors like Steensland, Dreybladt, James and Forbes, L'Esperance and Stafne for reporting the earliest case of AOT. According to Philipsen and Reichart, Stafne was the first author to consider AOT as a separate entity. Although, Stafne did not propose a specific term for the lesion, he reported a series of three cases under the title "Epithelial tumors associated with developmental cysts of maxilla" [2]. The first case demonstrating irrefutable proof of an AOT, is the one reported from Norway by Harbitz in 1915 as a "cystic adamantoma" [2,3]. Since, then it has been described under various terminologies like "cystic adamantoma", "adenoameloblastoma", "cystic complex composite odontoma', "tumor of enamel organ epithelium", "glandular ameloblastoma" "ameloblastic adenomatoid tumour", "odontogenic adenomatoid tumour", "pseudo-adeno adamantinum" & "pleomorphic adenoma –like tumor" [4,5].

WHO (1971) adopted the term proposed by Philipsen and Birn as "adenomatoid odontogenic tumour" and later (1992) defined the lesion as "A tumor of odontogenic epithelium with duct-like structures and with varying degrees of inductive change in the connective tissue. The tumor 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 [1]. The relative frequency of AOT corresponds to 2.2–7.1%, making it the fourth most common odontogenic tumor. The current understanding of its clinical, radiologic and pathologic attributes is comprehensive. It is well-established that there are three clinical variants of AOT pericoronal [70.8%], extracoronal [26.9%] and peripheral [2.3%]) [2].

Histologically AOT may present as a cystic or solid lesion as stated in the WHO definition, but very few cases with cystic presentation have been reported. Whether AOT is truly cystic, neoplastic in origin or a hamartoma remains a matter of controversy. Here this article focuses on various controversies related to the clinical presentation, behaviour, histogenesis of cystic & solid type AOT.

## Histogenesis

Clinically there are three variants of AOT viz. follicular, extrafollicular and peripheral type. The follicular and extrafollicular variants are intrabony [2,6,7].

Histogenetically the specific stimulus that triggers proliferation of the progenitor cells of AOT is unknown [3]. However, various school of thoughts have been put forward from time to time. Due its exclusive occurrence within the tooth-bearing areas of the jaws (associated closely with an unerupted or impacted tooth), Philipsen et al. have strongly suggested that the AOT arises from rem-

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nants of the successional dental lamina or the accessional dental lamina. According to Hodgson and as elaborated by Reichart and Philipsen, the odontogenic epithelial rests are not distributed haphazardly but are confined to the gubernaculum dentis.

Theoretically, the eruption of a permanent tooth/teeth adjacent to an odontogenic tumor may be halted when the tumor envelopes the crown of the tooth and disrupts the gubernaculum dentis, also where the developing tooth erupts into a hamartomatous or neoplastic mass, the guiding influence of the gubernaculum dentis is lost. Hence, a pericoronal lesion associated with an unerupted tooth is formed. Similarly, if the odontogenic tumor were to arise from epithelial rests outside the eruptive path, eruption of the adjacent tooth/teeth would not be impaired and, following normal eruption, the tumor would be located lateral, or possibly even apical, to the erupted tooth/teeth [5,7,8]. However, Philipsen HP et al. could not answer (1) why the number of AOTs derived from the parent dental lamina were considerably smaller (by a factor 25 or more) than those derived from the successional dental lamina or (2) why the follicular variant and in particular the one associated with unerupted permanent canines was so much more frequent than the other variants? [6]

Bhaskar was of the view that AOT is a follicular cyst with intracystic proliferation derived from outer enamel epithelium [4]. Spouge suggested origin from preameloblast cells found in the cervical region of inner enamel epithelium, prior to induction of odontoblast & before deposition of enamel matrix [9]. This view was substantiated by Tagaki ultrastructurally. Association of the tumor with well-formed embedded teeth would suggest a possible origin from the REE (reduced enamel epithelium) surrounding the crown or from the epithelial lining of the cystic cavity [4]. With the formation of tumor the lining may have encircled the whole tooth within it.

So, the development of AOT from epithelial remnants present in the gubernaculum dentis can give a unified concept or better explanation as far as histogenesis is concerned in most cases of AOT.

## Cyst, tumor or hamartoma

Whether AOT is a cyst, tumor or a hamartoma is still a matter of debate. Some authors consider it as a true benign, non-aggressive, non-invasive neoplasm while others consider it as a hamartomatous odontogenic growth. In the recent past, certain authors preferred calling it as a cyst because on histopathologic examination they found a cystic lumen, lining and connective tissue capsule. Marx & Stern proposed the term adenomatoid odontogenic cyst and considered it to be a cyst, that has a hamartomatous intraluminal proliferation of epithelial cells derived from Hertwig's epithelial root sheath & these cells fill the lumen & give the impression of a solid tumor [10].

The various possibilities related to the nature of AOT being a tumor, hamartoma or cyst are discussed as follows:

## AOT as hamartoma

Hamartomas represent a dysmorphic proliferation of tissue that is native to the area and does not have the capacity for continuous growth but merely parallels that of the host. The distinction between a hamartoma and a benign neoplasm is often arbitrary [11]. Most author's consider it as a hamartoma due to

a) Limited size in most cases (attributed to its minimal growth potential).
b) The lack of recurrence (even following definitely incomplete removal).
c) Occurence in tooth bearing area & histopathologically resemblance to enamel organ.

## AOT as benign neoplasm

Benign neoplasms also are dysmorphic proliferations of tissues, but they have the capacity for continuous autonomous growth. These neoplasms will continue to proliferate, albeit slowly in most cases, unless completely removed [11]. AOT is also considered as a nonaggressive, noninvasive benign neoplasm because

a) Some authors believe that the limited size of most cases stems from the fact that most cases are detected early and removed before the slow-growing tumor reaches a clinically noticeable size [3].
b) They also point to the considerable size of some reported cases that had gone undetected or untreated for many years and resulted in facial asymmetry and distortion [12–14].
c) Histologically, the lesion shows greater deviation from the arrangement of the normal odontogenic apparatus than should be expected in a developmental anomaly [3].
d) Few cases of recurrence have been reported in the literature [7,15,16].

Further, reviewing the literature revealed that features were both in favour of it being a hamartoma and tumor. Therefore, to regard it either as a hamartoma or a tumor is justifiable.

## AOT as cyst

Regezi et al. described AOT as an intracystic epithelial proliferation composed of polygonal and spindle cells [17]. Marx and Stern proposed that AOT is not a tumor, rather a cystic lesion in which intraluminal proliferation occurs and hence, proposed the term "Adenomatoid odontogenic cyst" (AOC) [18]. In the past, few cases had been reported describing AOT as a cyst. Cystic presentation of AOT was first described by Harbitz in 1915 who reported the lesion as "cystic Adamantoma" [2,19].

The systematic review of literature of AOTs associated with or originating from an odontogenic cyst and reported primarily as cystic AOT, has shown that most of the lesions described in the past lacked the clear description of the lining epithelium and the photographic evidence [12,14,20–22]. Some cases mentioned the cystic appearance on gross examination but didn't describe the histopathology [15].

Few lesions which were described as cystic, were basically hybrid tumors and associated with COC (calcifying odontogenic cyst) & Unicystic ameloblastoma [23–25].

Very few authors in their case reports have histologically described the cystic lining as non-keratinized, stratified squamous of 2–4 cell thickness, but elaborate description was missing. [16,19,26–28].

## Hypothesis

Here we propose that the AOT should not be considered as a cyst because its cystic nature remains questionable. The histogenesis of AOT is still uncertain, with various sources of origin being mentioned in the literature. Depending upon its histogenetic origin, AOT may appear either solid or cystic. We hypothesize that when the AOT arises from a change in REE covering of the impacted tooth, then it appears as cystic. This is certainly not a true cyst at all as the presentation also depends upon the duration of the lesion.