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Adenomatoid Odontogenic Tumour - A Brief Review

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Research Article

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ABSTRACT

Adenomatoid odontogenic tumour a relatively rare neoplasm constitutes about 2-7% of odontogenic cysts and tumours combined. Also known as the tumour of the 2/3rd due to its clinical and radiographic features. The recent research focussed on histiogenesis suggested towards an origin towards content of the gubernaculum cord and its remenants. With the characteristic histopathological features the diagnosis is a very straight one with all the three variants showing prognostically no significant difference. Recent advances have enlightened the understanding of molecular mechanisms involved with the various aspects of this enigmatic entity.

INTRODUCTION

Adenomatoid odontogenic tumour a relatively rare neoplasm constitutes about 2-7% of odontogenic cysts and tumours combined. It holds a distinctive position due to the relatively extended debate regarding the nature of this pathology with few authors considering it as an developmental hamartomatous odontogenic growth against the current position it holds in WHO classification of odontogenic tumours and allied lesion as and odontogenic tumour [1].

In the current classification of WHO AOT is described as “benign tumour being composed of odontogenic epithelium in a variety of histoarchitectural patterns, embedded in mature connective tissue stroma and characterized by slow but progressive growth [2].”

Researches justifying position of AOT as a benign odontogenic lesion attribute the limited size of the lesion due to early detection and removal of the lesion due to frequent association found with unerupted maxillary cuspids [3].

HISTORY BACKGROUND

The debate of the AOT is not limited just to the nature of lesion, but also for the first author being credited for its discovery and recognition as an entity. Philipsen et al. [4] strongly supported the findings of Harbitz in the year 1915 who gave irrefutable evidence for it. However a further rigorous search for the first AOT case reported, Ide et al. [5] reviewed the American, European and Japanese literature dating back to the second half of the 19th century giving a historical timeline from Kolaczek in 1877 to Thomas in 1934, listing of about 16 cases which fulfilled the present criteria for being called as an AOT. An interesting finding by Ide et al review of very early scientific medical and dental Japanese journals gave evidence that, Nakayama reported two cases of AOT with undeniable proof based on both clinical and pathologic (which included microscopic drawings) characteristics. Okuyama described an unequivocal case of AOT, calling it a ‘tooth cyst’. Ide et al. [5] concluded that it is difficult to draw final conclusions about the origin of the first case report of AOT as no histologic drawings of ameloblastoma were published until the late 19th century [5]. Henceforth with all the evidence gathered by Ide et al. [5], it is recognized that Nakayama should by acknowledged for the earliest complete journal descriptions (in Japanese) of AOT [6].

The current terminology used for AOT has had a history of frequent changes with adenoameloblastoma ameloblastic adenomatoid tumour, epithelioma adamantinum, pseudoadenoma adamantinum by Dreybladt and glandular adamantinoma to name a few. The current terminology of “AOT” is used unanimously after its adoption in the first edition of the World Health Organization classification of odontogenic tumors and cysts in 1971 [1].

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HISTIOGENESIS

AOT is traditionally being believed to be derived from the odontogenic apparatus due to its close association with impacted tooth as well as tooth bearing areas of the jaw and it cytological resemblance to the remenants of enamel organ epithelium, reduced enamel epithelium and rests of Malassez have been postulated as possible sources [3,6].

In a recent article by Ferreira et al. [7] described in detail both the gubernacular cord and the gubernacular canal assessd the possible contribution of these structures in the process of tooth eruption. Philpsen et al. [8] in their article further went ahead to state that regarding origin and pathogenesis of the AOT, it would seem that this lesion is derived from odontogenic epithelium of the dental lamina complex or its cellular remnants located in the gubernacular cord.

CLINICAL AND RADIOGRAPHIC FEATURES

AOT is also a unique lesion that presents in a fairly consistent manner, as a result of which it has come to be regarded as a "tumor of two-thirds," i.e., two-thirds occur in female patients, two-thirds occur in the second decade of life, two-thirds develop in the anterior sextant of the maxilla, two-thirds are superimposed on dentigerous cysts, and two-thirds of associated unerupted teeth are permanent canines. In addition, two-thirds of cases show scattered dot-like (snowflake) opacities within the unilocular radiolucency [5].

AOT are largely limited to younger patients, with peak incidence in 2nd decade (10 to 19) and is relatively uncommon in a patient older than 30 years of age. Striking predilection for anterior jaw and is twice as common in the maxilla as in the mandible. Females: Male ratio is standardised at 2:1. Most AOT, are relatively seldom exceed 3 cm in greatest diameter, with exceptions of few large lesions being reported [3,5,6].

Peripheral or the extraosseous form of the tumor though rare, but when encountered usually presents as small, sessile masses on the facial gingiva of the maxilla. Clinically, these lesions cannot be differentiated from the common gingival fibrous lesions. They are frequently asymptomatic and are discovered during routine radiographic examination or to determine the cause for an unerupted tooth mostly commonly being maxillary canine. Larger lesions cause a painless expansion of the bone [3,6,9].

Radiographically, in majority of the cases, the tumor is a well circumscribed, unilocular radiolucency that involves the crown of an unerupted tooth, most often a canine. Follicular type of AOT is impossible to differentiate radiographically from the more common dentigerous cyst, however the radiolucency associated with the follicular type sometimes extends apically along the root past the cementoenamel junction thus serving as an helpful differentiating factor [6,9].

Rarely AOT may present as a well demarcated unilocular radiolucency that is located between the roots of erupted teeth (extrafollicular type). The lesion may appear completely radiolucent; often, however, it contains fine (snowflake) calcifications which serves as an important finding to differentiate from dentigerous cyst or ameloblastoma [3,5,6,9].

VARIANTS OF AOT

The three variants of AOT are characteristic—a follicular variant (73%) associated with an impacted and displaced tooth, an extrafollicular variant (24%) mimicking a radicular cyst around the apex of a tooth and a peripheral (epulis-like) variant (3%) exhibiting a periodontal bone defect or ectopic growth. All the variants of AOT exhibit identical histologic features [9].

Follicular Type

This variant of the AOT is thought to originate from the reduced enamel epithelium of the dental follicle. The follicular variant is three times as frequent as the extra-follicular variant resulting in its early earlier diagnosis (mean age, 17 years) compared to the extra-follicular variant (mean age, 24 years), Follicular AOT is associated with one embedded tooth in 93.2% of cases with permanent maxillary canine being the most frequent (60%) cases [10].

Extrafollicular Type

The origin of this variant still remains unclear with few literature suggesting that the origin of some extra follicular AOTs as a secondary phenomenon within pre-existing odontogenic cysts or cystic tumors. The possibility to originate from the epithelial lining of an odontogenic cyst or unicystic ameloblastoma [11,12]. A rare subvariant of the extrafollicular type of AOT with only 12 reported cases were found mimicking radiographically as an periapical pathology [13].

Peripheral Type

The peripheral variant of AOT occurs at a far distant from tooth germ structures is rarely encountered with only about 14 cases reported in literature till date. A marked predilection for female gender and maxilla with approximately 90% of the peripheral AOTs in the anterior maxilla, primarily manifesting in the incisor and can involve the maxillary antrum [14].

HISTOPATHOLOGICAL FEATURES

Macroscopically the central AOT usually presents as a well-defined round-oval mass which is usually surrounded by a thick,

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fibrous capsule. On grossing the surface may appear tan white, solid or may show presence of multiple cystic areas of variable sizes with presence of yellowish brown fluid like material. Presence of calcified masses can also be encountered giving characteristic gritty consistency wile grossing [3,4,6].

Microscopically, the histopathologic features of this lesion are very distinctive to be separated from any other odontogenic tumor. The tumor exhibits population of spindle-shaped epithelial cells that form sheets, strands or whorled masses of cells in a scant fibrous stroma. The epithelial cells show a variety of patterns in form rosettes which appear to be formed around a central space or lumen, which may be empty or contain small amounts of eosinophilic material showing positive staining for amyloid like material [9].

The tubular or duct-like structures may be predominant, scanty, or even absent in a given section. These tubular structures consist of a central space surrounded by a layer of columnar or cuboidal epithelial cell with their nuclei polarized away from the central lumen [6] **(Figure 1).** The lumina are frequently lined by eosinophillic rim of varying thickness popularly known as hyaline ring [3].The mechanism of formation of these tubular structures is not entirely clear but is likely the result of the secretory activity of the tumor cells, which appear to be preameloblasts in nature [6]. In any event, these structures are not true ducts, and no glandular elements are present in the tumour. Small foci of calcification may also be scattered throughout the tumor [9]. These have been interpreted as abortive enamel formation. Some adenomatoid odontogenic tumors contain larger areas of matrix material or calcification which has been traditionally interpreted as dysplastic dentin, dentinoid, osteodentin or cementum like material. Irregular to round concentric layered calcified bodies exhibiting a Leisegang ring pattern may also be evident [3]. At the periphery few of the tumors may show narrow, often anastomosing cords of epithelium in an eosinophilic, loosely arranged matrix adjacent to the capsular area [15]. The supporting stroma is loose hypocellular and fibrovascular and may show presence of prominent vascular component [3,15].

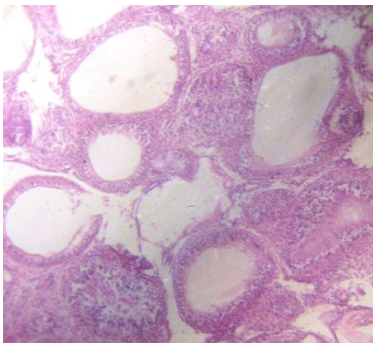

Figure 1. Structure having layer of columnar or cuboidal epithelial cell.

TREATMENT AND PROGNOSIS

The adenomatoid odontogenic tumor is completely benign; because of its capsule, it enucleates easily from the bone. Aggressive behavior and recurrence after enucleation is exceedingly rare thus supporting its questionable hamarmatous nature [3,4,6,9].

MOLECULAR MECHANISM AND RECENT ADVANCES

The mean values for Ki-67 when compared in solid ameloblastomas and AOTs are 4% and 1%, respectively. These values for B-cell lymphoma 2 (BCL-2) in solid ameloblastomas and AOTs are 63% and 26%, respectively. These findings support the harmatomatous behavior of AOT.16 A similar level of PCNA was found for both AOT and ameloblastoma, however solid multicystic ameloblastomas exhibited weaker expressions of p53 and MDM2 thus implying the lesser aggressive behaviour of AOT than ameloblastomas [17,18]. Enamel proteins including amelogenin, ameloblastin, and amelotin, as well as TGF- β/SMADs, are more intensely intensely expressed in AOTs than in ameloblastomas. Thus resulting in lesser aggressive biological behaviour and increased cytodifferentiation and apoptosis in AOT than ameloblastomas [19,20]. Philipsen et al. [4] in their study have suggested continuing reporting of unusual or rare histomorphological features, immunohistochemical findings and applications of molecular biological techniques for better understanding of this unusual odontogenic tumour [4].

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