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Adenomatoid odontogenic tumor: A series of four clinico-pathological variants

Namrata N Patil, Abhishek Singh Nayyar, Vijay Wadhwan

ABSTRACT

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Case Series: Herein, we have discussed a case series of four cases of follicular adenomatoid odontogenic tumors in the maxilla, illustrating the diverse clinical, microscopic and biological features of the tumor.
Conclusion: Several updates and data available have grouped adenomatoid odontogenic tumor into different areas of classifications of odontogenic group of tumors. Histological evidences have been put forth by several authors by denoting the histogenesis of each cell type that an inductive influence process does indeed occur in adenomatoid odontogenic tumor. Through this case series we have emphasized the importance of the relation between the dental follicle and the tumor tissue in the origin and histogenesis of this vital odontogenic lesion.

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Keywords: Adenomatoid Odontogenic tumor (AOT), Hamartomatous, Neoplasm, Epithelial origin, Odontogenic, Histogenesis

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Received: 08 July 2013
Accepted: 08 August 2013
Published: 01 January 2014

How to cite this article

Patil NN, Nayyar AS, Wadhwan V. Adenomatoid odontogenic tumor: A series of four clinico-pathological variants. International Journal of Case Reports and Images 2014;(1):1–7.

doi:10.5348/ijcri-2014-01-428-CS-1

INTRODUCTION

The unique hamartomatous benign odontogenic tumor distinctively recognized as adenomatoid odontogenic tumor (AOT) located centrally or peripherally in the jaws is not unknown. A large number of literatures prominently describe this lesion based on its clinical, radiological, histological and epidemiological characteristics [1]. A variety of terms have been used to portray this lesion of which the adenoameloblastoma was in common use for many years since the tumor was considered a histological variant of ameloblastoma. An AOT known today has been first described by Dreybladt in 1907. Philipsen and Birn in 1969 introduced the now generally accepted and very popularly used nomenclature of AOT. Some authors reflect AOTs as being truly benign, non-aggressive non-invasive neoplasms, whereas others see them as a developmental hamartomatous odontogenic growths [2]. Adenomatoid odontogenic tumors constitute about 2.2–7.1% of all odontogenic tumors, and the escalating number of reports in literature on AOT indicates that the tumor develops more often than formerly expected [3, 4]. It has been theorized that the complex system of

the dental laminae or its remnants is the likely origin of the AOT mimicking a peri-apical radiolucent lesion most commonly in the maxillary incisor area [5].

This report presents several unique presentations of AOT with their diversely occurring radiographic and histological connotations and provides an overview about the diagnostic aspects of this tumor including current controversies in its pathogenesis and management.

CASE SERIES

Case 1: A 16-year-old girl was presented with complaints of swelling in the upper right front tooth region of one month duration. Extra-oral examination revealed a diffuse firm non-tender expansion in the right maxillary anterior region. Intra-orally the right maxillary lateral incisor was clinically missing and a hyperemic swelling in the upper labial vestibule was observed. Radiological examination revealed the tumor extending to the close proximity of the right maxillary sinus and the impacted permanent maxillary lateral incisor with a unilocular radiolucent area around the tooth. An occlusal projection radiograph revealed a unilocular cystic lesion measuring 1x1.5 cm near the periapical region of 11 (Figure 1). There was slight erosion of the palatal bone. Vitality test was positive for the teeth in adjoining areas. Based on the clinical and radiographic findings, a provisional diagnosis of dentigerous cyst in relation to impacted maxillary right lateral incisor was given and a differential diagnosis of a benign odontogenic tumor was suspected. Radiographic differential diagnoses included adenomatoid odontogenic tumor and calcifying odontogenic tumor/cyst with impacted maxillary right lateral incisor. Macroscopic findings of the extirpated tumor revealed a variegated, dark-red and grayish-white, roughly granular wall with impacted tooth along with some areas in the lateral side of it appearing like a thin membrane (Figure 2). Microscopic examination revealed the typical pattern of AOT. The odontogenic cells constituted of whorled nests of epithelium together with areas of glandular or ductal pattern (Figure 3). At a few places the cystic cavity was lined by the thin layered stratified squamous epithelium. The solid part of the tumor was composed of sheets of epithelial cells with scanty connective tissue stroma. Characteristic duct like structures comprised a central lumen lined by tall columnar cells in a single layer scattered throughout the tumor (Figure 4). The lumina enclosed fibrillar or homogenous, eosinophilic material attached to the free-margin of the columnar cell in a cuticle-like fashion. In other places, the epithelial cells formed convoluted or whorl-like structures consisting of double strands of columnar cells without central lumen. Other remaining cells were stellate or spindle-shaped, with clear cytoplasm and oval nuclei, forming solid sheets among the structures of columnar cells. The spindle-shaped cells in looser areas gave an appearance resembling stellate reticulum. Eosinophilic, non-calcified, droplets like materials were also recognized within the epithelial sheets. The periphery of the tumor comprised of strands of epithelium one or two cell in thickness forming a trabecular or cribriform configuration.

Case 2: A 13-year-old boy was presented with pain and swelling in upper left back tooth region of the jaw since 15 days. The pain was continuous and dull in nature. Intra-orally buccal and palatal extension of swelling was seen extending from left central incisor to first premolar area. Deciduous lateral incisor and canine in the region were retained. A provisional diagnosis of dentigerous cyst was suggested which was followed by differential diagnoses of AOT, infected radicular cyst with the anterior teeth, central giant cell granuloma and ameloblastoma. Radiographic examination revealed a unicystic radiolucent lesion encroaching the left maxillary sinus with impacted maxillary left lateral incisor and canine. A panoramic radiograph revealed a large, well circumscribed radiolucency extending throughout the anterior maxilla from the left canine to first premolar region (Figure 5). The lesion produced an expansion extending into the alveolar processes, disrupting the usual orientation of the anterior teeth. Pathology test results were in accordance with the clinical diagnosis of lesion compatible with AOT. Surgical removal by complete enucleation of the lesion and associated unerupted teeth and associated lining was achieved in toto under general anesthesia. Postoperative endodontic therapy and prosthetic rehabilitation were planned further. The excised specimen revealed crown of tooth enclosed within tumor mass and suggested the tumor in reality a follicular cyst with intra-cystic epithelial tumor proliferation or follicular cyst epithelium which may give rise to the tumor (Figure 6). The canine was also extirpated and thin fragmented tissue was seen attached to the cervical portion of the crown. Histopathology indicated typical findings of follicular AOT derived from odontogenic epithelium, which establishes itself around the corona of unerupted, anterior teeth in young patients and constituted of whorled nests of epithelium with areas of glandular or ductal patterns intermixed with occasional spherical calcifications.

Case 3: A 17-year-old boy without any clinical history observed slow growing firm painless mass in the right upper front tooth region extending from the right maxillary lateral incisor to the mesial aspect of right first premolar since three months (Figure 7). Intra-orally retained deciduous canine was observed with normal eruption of the lateral incisor and premolars. Intra-oral periapical radiograph found an impacted permanent canine within a single unilocular radiolucent lesion. A provisional diagnosis of a dentigerous cyst in relation to impacted maxillary canine was arrived at. On local excision, the mass revealed the tumor enclosing the tooth. Microscopy indicated a distinctive histomorphology of AOT in addition to ductular or glandular patterns. The cuboidal or columnar cells formed convoluted cords or bodies in complicated patterns showing invaginations.

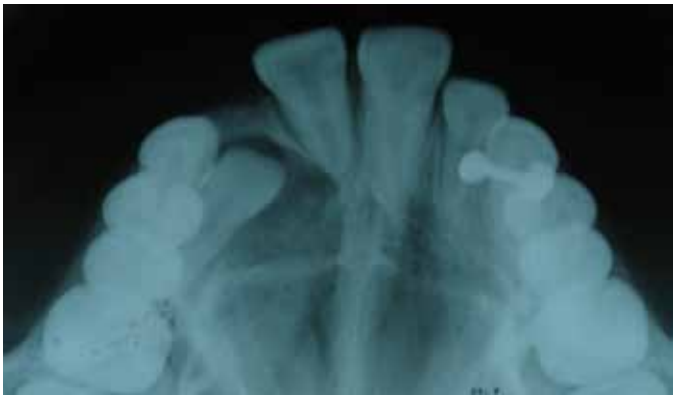

Figure 1: An occlusal projection radiograph showing a unilocular cystic lesion measuring 1 x 1.5cms near the peri-apical region of 11.

Figure 2: Macroscopic findings of the extirpated tumor showing a variegated, dark-red and grayish-white, roughly granular wall with impacted tooth along with some areas in the lateral side of it appearing like a thin membrane.

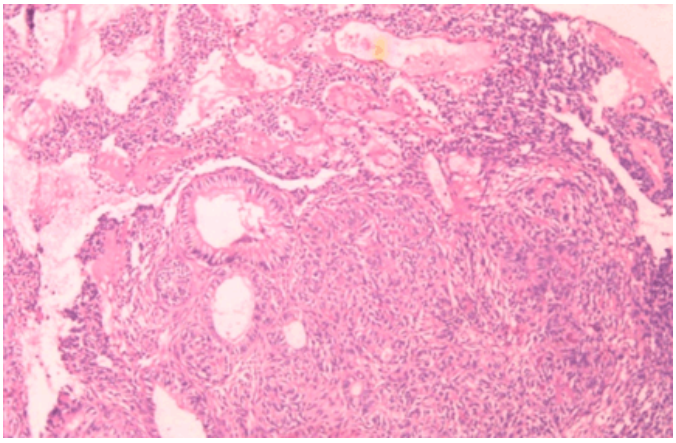

Figure 3: The odontogenic cells constituted of whorled nests of epithelium together with areas of glandular or ductal pattern (H&E stain, x100)

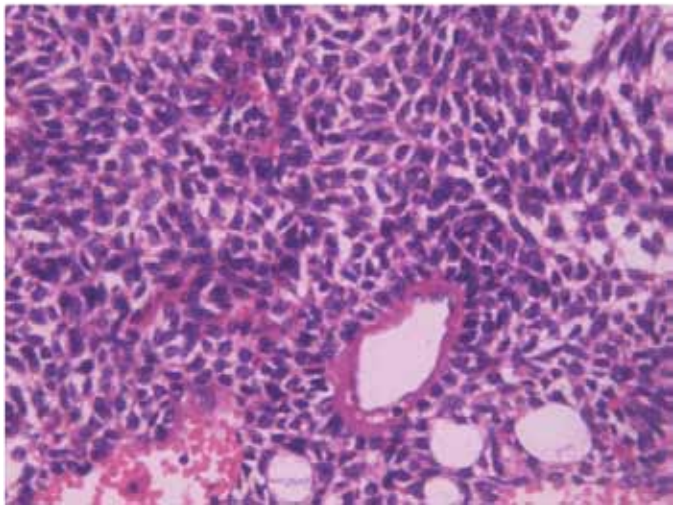

Figure 4: Characteristic duct like structures comprised a central lumen lined by tall columnar cells in a single layer scattered throughout the tumor (H&E stain, x400).

Figure 5: Panoramic radiograph revealing a large, well circumscribed radiolucency extending throughout the anterior maxilla from the left canine to first premolar region.

Case 4: A 12-year-old boy was diagnosed with gradually increasing extra-oral painless swelling on left facial region since two months. Intra-orally extension on the palate was seen extending from the central incisor

Figure 6: The excised specimen revealing crown of tooth enclosed within tumor mass.

Figure 7: A 17-year-male with a slow growing firm painless mass in the right maxillary anterior region.

area towards the first permanent molar. Panoramic view revealed impacted permanent canine with a unilocular radiolucency and well demarcated distinct sclerotic margin. Root resorption with premolars and second molar was distinctively visible. Local excision of the mass in toto revealed tumor enclosing the tooth within with gritty and fragile lining of the cystic cavity. Hematoxylin and eosin stained sections indicated cystic lumen lined by highly proliferative odontogenic epithelium arranged in the form of whorls, solid nests, rosettes and ductal patterns with scanty intervening stromal tissue (Figure 8). The epithelial cells in nest and rosette pattern were polyhedral in shape with round prominent nuclei with two to three layers of spindle shaped cells forming stream like pattern, center of nodules showed eosinophilic amorphous or flocculent material within the lumen. The ducts like structures were lined by tall columnar epithelial cells with elongated oval nuclei which were seen polarized away from luminal surface. Calcified masses scattered among the cellular pattern were significantly observed.

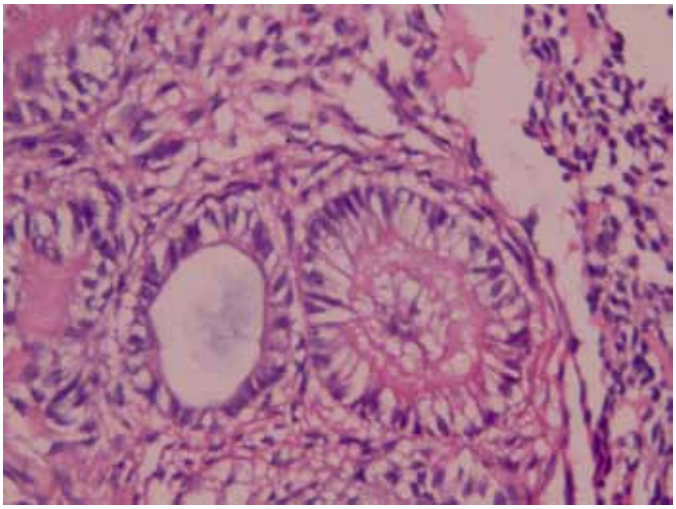

Figure 8: Hematoxylin and eosin stained section indicating cystic lumen lined by highly proliferative odontogenic epithelium arranged in the form of whorls, solid nests, rosettes and ductal patterns with scanty intervening stromal tissue (H&E stain, x400).

DISCUSSION

This case series illustrates the clinico-pathological variants of the follicular variety of AOT which is often pre-operatively interpreted as a follicular odontogenic cyst with the association of an unerupted or impacted tooth. AOT is frequently misdiagnosed as other odontogenic cysts and tumors on radiographic examination [5, 6]. Seventy-seven percent of follicular type AOT's are initially diagnosed as dentigerous cysts [7]. This entity is most commonly encountered in young patients, especially in the second decade of life and is exceptional in the older age groups [8]. Its common occurrence in the maxilla, presentation as a slow growing asymptomatic lesion and its frequent discovery during routine radiography makes it amongst the preferred presumptions in the differential diagnosis of anterior maxillary tumors. Radiographically, the intra-bony variants comprise follicular and extra-follicular types. The most common and widely accepted clinico-topographic variants include (i) follicular (ii) extra-follicular and (iii) peripheral; all of which possess analogous histological findings [9]. The follicular type shows a well-defined unilocular round or ovoid radiolucency associated with the crown and often part of the root of an unerupted tooth thus mimicking a

dentigerous or follicular cyst [3]. The follicular variants are significantly more prominent in the maxilla, whereas the extra-follicular variants are more prominently seen in relation to the mandible. The peripheral type is located in the gingival mucosa and appears clinically as a fibrous epulis or a gingival hyperplasia [10]. Panoramic radiography is often incapable to demonstrate radio-opacities when the calcification is minimal, whereupon intra-oral radiographs may be crucial for correct radiographic interpretation of an AOT in the presence of nominal quantities of calcifications [11]. A Kerato cystic odontogenic tumor (KCOT) and a unicystic ameloblastoma (UA) can also mimic a follicular AOT when in a pericoronal location. Both of these lesions are diagnosed in the second and third decade of life similar to an AOT, but they are more common in the posterior regions of the mandible. The calcifying cystic odontogenic tumor (CCOT) also mimics an AOT since it is observed in the anterior region of jaws which may be associated with an unerupted tooth and presence of radio-opacities and diagnosed in the second decade [12]. Permanent canines are the most common unerupted teeth associated and are etiological in around 74% of all cases reported and maxillary canines are the most common amongst them. Opacities are described as flecks, snow-flakes, and patchy areas of calcification, scattered radio-opacities, irregular radio-opacities, amorphous radio-opacities, fine radio-opacities and faint radio-opacities [10]. The extra-follicular variant of AOT is also differentially diagnosed from lateral periodontal cysts (LPCs) which is located between the roots of erupted teeth in the anterior region of the mandible, but diagnosed in age groups older than those with AOTs [13].The clinical findings are in general agreement with supplementary published studies and have found that an AOT is associated with lack of tooth eruption which leads the patient to seek consultation and results in an early diagnosis [14]. A unilocular radiolucency with opacities and tooth displacement in the anterior region of the jaws are the radiological features most characteristic of AOTs.

It is not unknown of AOT being derived from the complex system of dental laminae or its remnants [5]. Odontogenic tumors recapitulate dental ontogeny and portray histologic evidence of reciprocal induction. The dentinal matrix is related to odontogenic epithelium and characterized by tall columnar cells resembling ameloblasts or odontoblasts. The epithelial remains are seen in the form of small nests or clusters intermingled with dental matrix in a lace-like pattern. The circular secretory units consist of rows of tall columnar secretory cells with eosinophilic cytoplasm and with basal nuclei arranged in circular or duct like fashion depositing dental matrix material and resembling odontoblasts and ameloblasts. There is also another group of cells seen with shorter cuboidal or low columnar cells surrounding the ductular units with basophilic cytoplasm and not associated with dental matrix deposition. Very few reports describe tall columnar cells actively secreting dental matrix which indicate evidence of inductive process which is partially accepted [15, 16]. Numerous studies explain the histogenesis of the pseudo-ductular structures which represented invaginations of odontogenic epithelium. It is believed that the epithelium carries ecto-mesenchymal stroma much of which is cut-off from its blood supply and induces atrophy or necrosis while the surviving stroma at the periphery of the pseudo-ductular structures retains its inductive capacity and induces the columnar cells to lay down pre-dentine matrix [16]. In support of this hypothesis, reticulin fibres are demonstrated with toludiene blue metachromasia on the inner aspect of duct-like structures and contains basal lamina like material and granular deposit which has been postulated as pre-dentin layer by Shear. Substantial amount of amyloid-like material was also confirmed in our reports. Amyloid-like material was present in variable amounts intermingled with dental matrix material with characteristic apple green birefringence with congo red stained sections when viewed in polarized light.

CONCLUSION

Odontogenic tumors including the so-called adenomatoid odontogenic tumors (AOTs) comprise a heterogeneous group of lesions that ranges from hamartomas to benign and malignant neoplasms of variable aggressiveness. This case series shows how the lack of uniform criteria employed for their proper identification as well as the histomorphologic similitude found among some of them which behaves in different way, and the scantiness of proper methods to determine their precise origin makes necessary to recognize that at present, in spite of having more or less strict diagnostic criteria which have been internationally accepted, there is a need to continue developing research in the epidemiological, clinico-pathological, morpho-physiological and therapeutical fields in this area of oral and maxillofacial pathology and medicine.

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Acknowledgements
We express our appreciation to all the people who have devoted their life towards this field.

We would to like to take a special mention of H.P. Philipsen and P.A. Reichart who have been the pioneers of odontogenic tumors and have framed this group of lesions into gleam and sheen.

Author Contributions
Namrata N Patil – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Abhishek Singh Nayyar – Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Vijay Wadhwan – Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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Article citation: Patil NN, Nayyar AS, Wadhwan V. Adenomatoid odontogenic tumor: A series of four clinico-pathological variants. International Journal of Case Reports and Images 2014;5(1):1–7

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