CASE STUDY

Adenomatoid Odontogenic Tumour of Mandibular Anterior Region: Review of Literature and Report of a Rare Case

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ABSTRACT

Adenomatoid odontogenic tumour (AOT) is a rare, benign odontogenic tumour, which is often misdiagnosed as an odontogenic cystic lesion. It accounts for about 3% of all the odontogenic tumours. It is predominantly located in the anterior maxilla in the young female patients and in most cases is associated with an un-erupted permanent tooth. It is a hamartomatous, non-invasive lesion with slow but progressive growth. There are three clinicopathologic variants of AOT: intra-osseous follicular, intra-osseous extra-follicular and peripheral type. A rare case of intra-osseous extra-follicular type of AOT in the mandibular anterior region (unusual site of AOT) in a 16-year-old female patient is reported with its detailed clinical and radiographical features.

INTRODUCTION

Adenomatoid odontogenic tumour (AOT) was first described by Dreibladt, in 1907, as a pseudo-adenoameloblastoma.1 In 1948, Stafne considered it as a distinct entity, but others classified it as a variant of ameloblastoma.2 Since then the clinical and histological features of AOT have been well-studied and documented. AOT is the term used for the lesion previously described as adenoameloblastoma, adenoamneloblastic odontoma, epithelial tumour associated with developmental cysts, adenomatoid ameloblastoma, cystic complex composite odontome and ameloblastic adenomatoid tumour.3 Philipsen and Birn in 1969 proposed the name as adenomatoid odontogenic tumour and suggested that it should not be regarded as a variant of ameloblastoma because of the major differences in its clinical and biologic behaviour.4 This term was then accepted and adopted in 1971 in the earlier editions of the World Health Organization’s (WHO) classification of “Histological Typing of Odontogenic Tumors, Jaw Cysts and Allied Lesions”.5 Marx & Stern coined it the name as adenomatoid odontogenic cyst in 2003.6

Based on clinical and radiologic findings, AOT can be mainly divided into two variants:

A. Central (or intra-osseous) variant

1. Follicular (dentigerous) type: In this type the tumour is associated with the crown of an embedded tooth. The preoperative tentative diagnosis of such type is most often a follicular (dentigerous) cyst (accounting for 73% of total cases).4
2. Extra-follicular type: In this type the tumour has no association with the crown of an embedded tooth. The preoperative tentative diagnosis of this type could be that of a residual cyst, a “globulomaxillary” or a lateral periodontal cyst, depending upon the actual intra-osseous localization of the lesion (accounting for 24% of total cases).4

The terminology suggested for the two central tumour variants (follicular and extra-follicular) serves the single purpose of making a distinction between tumours having and those lacking an association with the crown of an embedded tooth. The terms should not be taken to indicate or suggest any pathogenetic principles.5

B. Peripheral (or extra-osseous) variant

This type can be often misdiagnosed as gingival fibroma or fibrous epulis (3% of total cases).

KEYWORDS mandible, anterior region, adenomatoid odontogenic tumour, rare

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CASE REPORT

A 16-year-old female patient reported to the Department of Oral and Maxillofacial Surgery of College of Dental Sciences and Research Centre with the chief complaint of having a progressively increased painless growth in the posterior portion of the lower jaw for the last 6 months. There was no paraesthesia or anaesthesia of the lower lip or chin. There was no history of trauma and also had no complaint of fluid, blood or pus discharge from the swelling. There was no relevant medical history of any disease especially endocrinal disturbances. She was physically and mentally healthy and not under any medication.

On clinical (extra-oral) examination, the swelling existed in the lower third of face extending from right to left parasympyseal region measuring approximately 7 cm × 5 cm in size (Fig. 1a). Superiorly swelling was obliterating the mento-labial sulcus and up to the lower border of the mandible. The overlying skin was normal in colour and texture but was stretched. The margins of the swelling were diffuse. On profile view, there was slight prognathic appearance (Fig. 1b). On palpation, the swelling was firm, non-tender and with normal temperature.

Intra-oral examination revealed an oval, non-tender and firm swelling, measuring 7 cm × 5 cm in size, which was extending from 45 to 33 with the buccal and lingual cortical plates expansion (Fig. 2). Superiorly swelling was above the level of the occlusal plane. Slight elevation of tongue was observed however there was no restriction in tongue movements or difficulty in swallowing. The overlying mucosa was non-adherent and with normal colour and texture. Severe mesial tilting of all four incisors and mild mesial displacement of 33, 34, 44 and 45 was noticed. No caries was detected. All four anterior teeth were non-tender on percussion with grade I mobility. All inspectory findings were confirmed by palpation.

The patient was subjected for radiographic examination. Mandibular occlusal radiograph and orthopantomogram revealed a well circumscribed unilocular radiolucency with radio-opaque border extending from right second molar to left first premolar, measuring 7 cm × 5 cm in size with tilting and displacement of the same teeth without root resorption. Expansion of the buccal and lingual cortical plates were also observed. There was no perforation of the cortical plates (Figs. 3, 4).

Based on history, clinical features and radiographic examination, a provisional diagnosis of benign neoplasm of odontogenic origin was postulated. Fine needle aspiration cytology (FNAC) was measured. About 10 ml clean straw coloured fluid was aspirated (Fig. 5). On chemical analysis, the aspirated fluid measured 5.8 mg/dl protein, it was insignificant. Excisional biopsy was performed under general anaesthesia. Intra-oral approach was preferred. With an appropriate incision, the buccal mucoperiosteal flap was raised to visualise the tumour (Fig. 6). The tumour was completely enucleated along with the involved and adherent teeth (Fig. 7). Mental neurovascular bundle on both the sides were identified, separated and preserved. Chemical cauterisation was performed with Carnoy’s solution. Watertight suturing was done (Fig. 8). Healing was uneventful.

On gross examination, the specimen presented an oval and well en-capsulated mass of 5 × 4 cm in size (Fig. 9). Histological examination of haematoxylin-eosin stain, revealed cystic lining with smooth solid nodular area. The solid type appearing masses revealed typical findings of AOT with peripheral narrow strands of smaller cells that formed net-like proliferations and cribriform

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**Fig. 1** Pre-operative extra-oral view. (a) Worm’s eye view showing posterior extension of the lesion extra-orally. (b) Right lateral view showing absence of mento-labial sulcus.
Fig. 2 Pre-operative clinical intra-oral view showing lesion.

Fig. 3 Pre-operative occlusal radiograph showing expansion of cortical plates.

Fig. 4 Pre-operative orthopentomogram showing the lesion in anterior region of mandible.

Fig. 5 Fine needle aspiration cytology reveals 10 ml of straw coloured fluid.

Fig. 6 Lesion after reflection of mucoperiosteal flap with needle in the lesion for fluid aspiration.

Fig. 7 Lesion with embedded teeth (31, 32, 33, 34, 41, 42, 43).

Fig. 8 Water tight suturing after complete enucleation of the lesion.

Fig. 9 Lesion with aspirated straw coloured fluid.
structures, both at the base of nodules and between them. The tumour was composed of nodules of various sizes, consisting of cuboidal or columnar epithelial cells that formed the nests, whorls and rosette like structures (Fig. 10). Foci of cosinophilic hyaline droplet material were also observed. The connective tissue stroma was loosely arranged and contained thin-walled congested vessels. Duct like structures were located in many of epithelial nodules and these structures were lined by similar columnar cells (Fig. 11). Hence overall features were diagnostic for AOT.

Subsequently after 4 months of surgery, with no clinical and radiographical signs of recurrence, removable partial denture was given to the patient (Figs. 12, 13). Post-operative follow-up period is 14 months and it shows no clinical and radiological signs of recurrence (Figs. 14, 15). A cast partial denture has given good dental and aesthetic results (Fig. 16). Lower lip fullness was lost after surgery (Fig. 17a). Following prosthesis, restoration of lower lip fullness was the significant appreciable aesthetic feature (Fig. 17b).
DISCUSSION

AOT is a rare, benign, slow-growing, non-invasive epithelial odontogenic tumour which manifests as a painless intra-oral mass. It has a predilection for maxilla (ratio of cases 2:1 relative to the mandible). These are generally diagnosed in the second and third decade of life and more predominantly in teenage. The female to male ratio for all age groups and all variants is close to 2:1. These lesions are typically asymptomatic, but the growth of the central type of lesions results by cortical expansion, as reported here.

AOT, accounts for approximately 3% of all odontogenic tumours, are less frequent than odontome, cementoma, myxoma and ameloblastoma. It has been suggested that AOT is hamartoma rather than true neoplasm and currently there is no evidence to this dispute. AOT generally does not exceed 1–3 cm in diameter. Most cases of large AOTs described as in the literature have been observed in the maxilla. In a recent analysis of AOTs, the large size of the lesion has been attributed to a higher growth rate in younger patients and delay in seeking treatment.

The involved teeth are commonly impacted which are generally canine or lateral incisors. But in the reported case, there were no impacted or un-erupted teeth. Adjacent teeth are generally displaced, as reported in this case also. It is painless, firm to hard swelling in consistency and can be found on routine radiographic examination. The lesion usually appears radiologically unilocular, although a few multilocular cases have been reported. Irregular root resorption is seldom reported. Minute variable shaped radio-opacities are frequently found within the lesion. These calcified deposits are seen in 78% of AOTs. However, these deposits were absent in the reported case.

The origin of AOT is controversial. It is believed to originate from the odontogenic epithelium of dentigerous cyst. In addition to anterior maxilla, the tumour has also been reported in other areas of the jaw such as the angle of the mandible. Therefore, dental lamina remnants are likely to represent the progenitor cells for this benign odontogenic tumour. According to the “envelopment theory”, the lesion grows (sometimes while forming the cystic space) next to or nearby dental follicle. The reported case though cystic, has all the features of AOT, confirming the “envelopment theory”.

Like in other odontogenic tumours, the specific stimulus that triggers proliferation of the progenitor cells is unknown in AOT also. But because of its exclusive occurrence within the tooth bearing areas of jaws and its histological resemblance to the dental lamina and reduced enamel epithelium, there is an agreement that AOT is of odontogenic origin.

According to Philipsen, the development of extrafollicular AOT may proceed when the epithelial rests, tenderness which give rise to the tumours, are located at the periphery of the path of tooth eruption. The tooth...
would, therefore, not be impeded in its eruption by the developing tumour and the AOT would not be associated with the tooth. The lesion presents radiographically as a residual, developmental, lateral, periodontal or radicular cysts depending on the location of the rests.\textsuperscript{15}

WHO has described the histological features of AOT as follows: “A tumor of odontogenic epithelium with duct like structures and with varying degree of inductive changes 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.” The histological appearance of all variants is identical and exhibits remarkable consistency. At low magnification, the most striking pattern is that of various sizes of solid nodules of columnar or cuboidal epithelial cells forming nests or rosette-like structures with minimal stromal connective tissue. Between the epithelial cells of the nodules and in the centre of the rosette-like configuration eosinophilic amorphous material is found which is often described as tumour deposits. Conspicuously, within the cellular areas are tubular or duct-like structure appearance. A third characteristic cellular pattern consists of nodules of polyhedral, eosinophilic epithelial cells with squamous appearance and exhibiting well-defined cell boundaries and prominent intracellular bridges. These islands may contain pools of amorphous amyloid-like material and globular masses of calcified material (thus the suggestion of a combination of calcifying epithelial odontogenic tumour and AOT). Another epithelial pattern has a trabecular or cribriform configuration. Occasional foci of mitotic activity can be traced. Induction of hyaline, dysplastic dentinoid material or calcified osteodentin has been described. Ultrastructurally, the tumour having epithelial cell types have been recognised, corresponding to the types that are evident on light microscopy. The connective tissue stroma is very loosely structured and contains thin-walled congested vessels characteristically showing marked degenerative (fibrinoid) changes of the endothelial lining, vessel wall and perivascular connective tissue. It has been suggested recently that the tumour droplets represent some form of enamel matrix.\textsuperscript{16}

Common neoplastic cases, such as ameloblastoma, calcifying epithelial odontogenic tumour (CEOT), ameloblastic fibroma, ameloblastic fibro-odontoma and dentigerous cyst are also taken into consideration in the differential diagnosis of AOT. But these are easily differentiated histologically. CEOT shows larger and more numerous calcifying spherules within eosinophilic cytoplasm of large cells along with smaller cells with hyperchromatic nuclei. Amyloid like eosinophilic material is also present in CEOT. Ameloblastoma has characteristic lining and arrangement of stellate reticulum besides its usual location in mandible and posterior maxilla in contrast to AOT.\textsuperscript{17}

During the last few years, several studies have been published dealing with the immunhistological properties of AOT. Immunohistochemicaly, the classical AOT phenotype is characterised by a cytokeratin (CK) profile similar to follicular cyst and/or oral or gingival epithelium based on positive staining with CK5, CK17 and CK19. On the other hand, the classical AOT is negative for CK4, 10, 13 and 18. Recently, Crivelini et al. detected the expression of CK14 in AOT and concluded that this probably indicate its origin from the reduced dental epithelium which is also positive for staining with CK14 antibodies.\textsuperscript{19} Positive reactions for amelogenin in limited areas in AOT are also reported as well as in ameloblasts and in the immature enamel matrix.\textsuperscript{20}

Interestingly, Takahashi et al. observed a positive staining for iron-binding proteins (transferrin, ferritin) and proteinase inhibitor (alpha-one-antitrypsin) in various cells of AOT indicating their role to the pathogenesis of AOT.\textsuperscript{21} Gao et al. studied the expression of bone morphogenetic protein (BMP). Cimentifying fibromas, dentinomas and compound odontomas demonstrated a positive reaction to BMP whereas all AOTs, as well as ameloblastomas and calcifying CEOTs were negative.\textsuperscript{22}

**SUMMARY**

The reported case is rare because of the tumour’s size, location and tumour having cystic cavity filled with straw coloured fluid. Also, the tumour was not involving any impacted or un-erupted tooth and histologically was without any calcification. The above mentioned features make this case a unique entity.

**CONCLUSION**

It is concluded that AOT is a rare, benign, asymptomatic slow growing, non-invasive and epithelial odontogenic tumour preferentially arising in the jaws. Extra-follicular variant of AOT is very rare. It is also referred as “two-thirds tumour” because of two-third of its cases in the maxilla, most commonly found in 2nd and 3rd decade of life, two-third occur in young females, two-third of the cases are associated with un-erupted teeth and two-third of the affected teeth are maxillary canines. Although its incidence is very low it should be considered in the differential diagnosis of mandibular lesions. Only careful diagnosis and adequate interpretation of clinical and radiographic findings may help in arriving at the correct diagnosis. Extensive surgery could be avoided unless it is misdiagnosed as unicystic ameloblastoma. All variants are en-capsulated and can be managed conservatively by surgical enucleation with very low rate of recurrence.

**REFERENCES**


