Case Report

Adenomatoid Odontogenic Tumour: A Case Report and Review of Literature
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Abstract
The adenomatoid odontogenic tumour is uncommon, non-invasive and constitutes about 3% of all odontogenic tumours. It differs from ameloblastoma in clinical, radiographic and histopathologic features. This tumor is best treated by enucleation, as it separates easily from the bony defect and do not recur. The debate of whether adenomatoid odontogenic tumour is an anomalous developmental hamartomatous growth or a true benign tumour has not been settled yet. Modern studies of DNA microarray analysis and other molecular biology techniques may solve mystery regarding histogenesis of this odontogenic tumour. Hence here we report a case of Adenomatoid odontogenic tumour and review on its histogenesis.

Keywords: Adenoameloblastoma; Odontogenic; Hamartoma; Adenomatoid tumor; Microarray.

Introduction
Adenomatoid odontogenic tumor (AOT) accounts for about 3 - 7% of odontogenic tumours, and is fourth most frequent odontogenic tumor.1 Although it has been reported from 3 – 82 years, predilection for young patient is well established. About 90% have occurred in the anterior regions of the jaws, more frequently in maxilla than mandible. It is usually associated with unerupted teeth (73%) or in the walls of dentigerous cysts. The tumor often displaces teeth rather than causing root resorption. Pericoronal AOTs are diagnosed at an early age than non pericoronal forms. It occurs twice as frequently in women. It is interesting and unexplainable that female: male ratio for gingival lesions is 14:1.1,2 They occur more frequently in maxilla than mandible. Infection of tumour, fracture of jaw, nasal obstruction though rare has been reported.

Most are diagnosed on routine dental radiographic examination, however delayed eruption of tooth or slow growing bony expansion with or without displacement of adjacent teeth, commonly leads to discovery of intra-gnathic AOTs. Less frequently it causes tooth mobility3 jaw bone expansion4 and asymmetrical facial swelling. Peripheral lesions present as a gingival coloured mass that ranges from 1 - 1.5cm in diameter. Diffuse swelling is clinically indistinguishable from maxillary or mandibular enlargement that may occur with central odontogenic cyst and tumors as well as benign fibro osseous lesions and benign mesenchymal neoplasms.

Gingival lesions cannot be clinically differentiated from gingival fibromas, peripheral ossifying fibromas, peripheral giant cell granuloma or peripheral odontogenic tumours.1,4 The close resemblance of the tumor cells to ameloblasts and association with the unerupted teeth indicates its origin from dental epithelium. But actual point of origin is still a mystery. We report a case of AOT and review on histogenesis of the same.

Case Report
A 21 year old female patient reported to the dental college with the complaint of small painless swelling over left anterior maxillary gingival region. Clinical examination revealed gingival swelling in relation to 22, 23, 24 region, normal in colour, and firm in consistency (Fig 1a). No tenderness was noticed. Intra oral and panoramic radiograph revealed irregular radiolucent lesion with flecks of opacity in between the roots of 23 and 24 region and the periapical region of 23 (Fig 1b & c).

Excisional biopsy was done and histopathological examination revealed multinodular proliferation of spindle shaped cells in solid and ductal patterns. Areas with varying number of duct like structures with lumina of varying size that are lined by a single layer of cuboidal – columnar epithelial cells, that have nuclei that frequently are

References

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...polared away from the lumen. The duct like or microcyst lumina frequently were lined by the eosinophilic rim of varying thickness,
suggesting adenomatoid odontogenic tumour (Fig 1d, e, f & g).

Figure 1: The clinical intraoral photograph showing a swelling in the region of tooth #22, 23 and 24 (a) and the radiograph revealed radiolucency in the same region under both IOPA (b) & OPG (c). The photomicrograph under hematoxylin and eosin staining shows multinodular proliferation of spindle shaped cells in solid and ductal patterns lined by a single layer of cuboidal-columnar epithelial cells that have nuclei that frequently are polarised away from the lumen. (d, e, f & g)

Discussion
Stafne reported the first review of Adenomatoid odontogenic tumour in 1948 as epithelial tumour associated with developmental cyst of the maxilla. Bernier and Tiecke were the first to publish a case on aden-ameloblastoma. The classification of AOT simply as an epithelial tumour, was
reported in a recent immunohistochemical studies that used bone morphogenetic protein (BMP) to divide odontogenic tumours into those that were purely epithelial negative for BMP and those that formed enamel, dentin, cementum or bone positive for BMP.  

The debate of whether AOT is an anomalous developmental hamartomatous growth or a true benign tumour has not been settled yet. Assumption of AOT as hamartoma is due to the limited size of most cases and to the lack of recurrence. Assumption as a tumor is because of the belief that the limited size of most cases stems from the fact that most are detected early after a routine radiograph and removed before the slow growing tumour reaches a clinically noticeable size. Many reported chronic cases had resulted in facial asymmetry and distortion that rival many ameloblastomas.  

Clinically before age of 30, nearly twice as many maxillary lesions are diagnosed whereas after 30 yrs, almost twice as many lesion are diagnosed in mandible. Radiographically most AOTs have a well demarcated almost always unilocular radiolucency which generally exhibits a smooth corticated and sometimes sclerotic border. Most lesions are pericoronal or juxtaocoral, but the radiolucency may extend apically beyond to cemento enamel junction on at least one side of root and a scalloped border is observed occasionally. Most lesions are between 1-3 mm, but large as much as 12cm is also reported. About 65% of the cases demonstrate faintly detectable radiopaque foci within the radiolucent lesion. Divergence of roots and displacement of teeth occurs more frequently than root resorption.  

Gingival lesions rarely are detected in radiographs, but there may be slight erosions of the underlying alveolar bone cortex. Dentigerous cyst, odontogenic keratocyst, calcifying epithelial odontogenic cyst, unicystic ameloblastoma, ameloblastic fibroma, calcifying epithelial odontogenic cyst are considered in the differential diagnosis. Macroscopically the tumor is soft, roughly spherical with fibrous capsule. Gross sectioning reveals white- tan solid to crumbly tissue with more cystic spaces of varying size; with minimal yellow brown fluid to semi solid material, fine, hard gritty granular material; and one to several larger calcified masses. The specific stimulus causing proliferation of the progenitor cells of AOT is unknown. Many investigators have debated the histogenesis of AOT and the nature of the acellular materials with in the tumour. Because of the exclusive occurrence within the tooth bearing areas of the jaws most often associated closely with an unerupted or impacted tooth and its cytological resemblance to the dental lamina and components of enamel organ, the AOT is odontogenic in origin. The presence of hemidesmosomes and basal lamina at the luminal pole of the cells that form the duct like structures exclusively rules out Thomas’s notion of a dual salivary and odontogenic origin for AOT.  

The duct forming cells exhibit secretory granules and coated vesicles near the luminal pole which renders them highly reminiscent of preameloblasts; these structures were also reported in the non-duct forming columnar cells in various patterns. Immunohistochemical studies revealed differences between the duct and non-duct forming cells: the non-duct forming columnar cells expressed amelogenin activity, whereas the duct forming cells showed no reactivity to amelogenin or other enamel matrix protein enamelin and sheathlin antibodies. Additionally the eosinophilic material that lines the periluminal surface the so called hyaline ring resembled basal lamina by way of TEM and co expressed basement membrane extracellular matrix proteins laminin, type IV collagen, heparan sulphate, proteoglycan, fibronectin enamel matrix protein amelogenin, enamelin. The accumulation and eventual enamelysin degradation of the secretory products are responsible for the development of duct like structures.  

The spindle shaped cells between the cell rich nodules resembles ultrastructurally the stellate reticulum and those that are immediately adjacent to the nodules resemble the stratum intermedium of the enamel organ. The ultrastructural suggestion that the small, irregular calcification may be partially composed of atypical enamel is supported by the positive reactivity of this material to amelogenin, enamelin or enamelysin although it is sheathlin negative.  

Histological feature of the tumour consists of a cellular multinodular proliferation of
spindle, cuboidal and columnar cells in a variety of patterns; usually scattered duct like structures, eosinophilic material and calcification in several forms and a fibrous capsule of variable thickness. At higher magnification some of the cells are seen arranged in clusters, frequently around small foci of eosinophilic material so called hyaline droplets or tumour droplets.\textsuperscript{8,14}

A varying number of duct like structures with lumina of varying size that are lined by a single layer of cuboidal – columnar epithelial cells, that have nuclei that frequently are polarised away from the lumen. The duct like or microcyst lumina frequently are lined by the eosinophilic rim of varying thickness and they may be empty or contain finely fibrillar or flocculent material of variable staining quality. Tall columnar cells with intensely eosinophilic cytoplasm and markedly polarised nuclei are seen occasionally around the solid mass of usually partially calcified eosinophilic material. The columnar cells may demonstrate clear cytoplasm and form rosettes as well as linear, curved, convoluted, invaginated and occasionally branching rows of opposing cells.\textsuperscript{1,3,4,14}

Between the cell rich nodules, swirling streams of variably stellate reticulum like spindle cells to normal polygonal epithelial cells with zones of intense basophils are noticed. Small amounts of eosinophilic material or calcification also may be seen between the cells. The spindle shaped cells adjacent to the cell rich nodules are frequently arranged with their long axis parallel to the periphery of the nodule which results in a vague layered appearance.

Variably sized areas composed of 1-2 cell wide anastomosing strands of cuboidal epithelial cells arranged in a plexiform trabeculae, cribriform or lattice- work configuration are present in the peripheral subcapsular areas. These small round cuboidal cells with small round dark nuclei, and often clear cytoplasm, resemble cells or rests of the dental lamina.

Many AOTs may have a few cluster of well-defined eosinophilic polyhedral squamous epithelial cells with prominent intercellular bridges and occasionally mild nuclear pleomorphism usually pools of amorphous amyloid like material and globular masses of calcified substances also are present that bear histopathologic resemblance to calcifying epithelial odontogenic cyst.\textsuperscript{8,11,12}

Cystic components of AOT may be due to pooling of the mucoid stroma due to the rupture of the thin lattice- work pattern or of the tumour developed within or adjacent to a pre-existing cyst. Some tumour exhibit pools of finely fibrillar eosinophilic material at the epithelial connective tissue interface. This was immunoreactive for the basement membrane component laminin.\textsuperscript{6} Because of the benign behaviour of all AOTs, conservative surgical excision, by enucleation and curettage is the treatment of choice.\textsuperscript{1,4,14} Recurrence rate is very low.

**Conclusion**

Adenomatoid odontogenic tumor is one of the most profiled odontogenic tumor. The remaining mysteries regarding the origin of tumor, dysplastic dentin or dentinoid, reduplicated basement membrane, calcified bodies/ Liesegang rings, occasional cellular atypia in this tumor may be resolved with modern studies of DNA microarray analysis, in situ hybridization, genetic analysis and other molecular biology techniques.

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