

Letter to the Editor

Adenoid Ameloblastoma: An Epithelial or a Mixed Odontogenic Neoplasm?

 Deepak Pandiar,  Reshma Poothakulath Krishnan

Department of Oral Pathology and Microbiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu

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Dear Editor,

Adenoid ameloblastoma (AA) is comparatively a new entity which has been included in the 5th edition of WHO classification of head and neck tumors published in 2024, under the category of benign epithelial tumors.^[1] Sporadic case reports and series have been reported in literature and the lesion has been designated under different terminologies such as ‘dentinoameloblastoma’, ‘atypical plexiform ameloblastoma with dentinoid’, ‘adenoid ameloblastoma with dentinoid’ or merely adenoid ameloblastoma.^[2,3] Conventional classification of benign odontogenic tumors divides the neoplasms into three categories: a) odontogenic epithelium with mature fibrous stroma (odontogenic ectomesenchyme not present), b) odontogenic epithelium with odontogenic ectomesenchyme +/- dental hard tissue formation, and c) mesenchyme and/or odontogenic ectomesenchyme with or without included odontogenic epithelium. Thus, tumors of first category have mature, fibrous connective tissue and formation of mesenchymal component including dentine/dentinoid seems questionable, in the absence of odontogenic ectomesenchyme. The phenomenon of hyalinization is well documented and is commonly seen in ameloblastoma, which has been hypothesized as a failed attempt of mature stromal cells to induce dentinogenesis secondary to inductive effects of peripheral ameloblast like cells.^[4] Literature search revealed cases,

where the formation of true dentinal tubules have been reported and illustrated in so called adenoid ameloblastoma,^[2,3] raising a query regarding differentiation of true odontoblasts and formation of dentin. We hypothesize that the ‘so called adenoid ameloblastoma’ is better categorized under the tumors of mixed origin along side dentinogenic ghost cell tumor (DGCT) with which it share many characteristics as discussed in the following sections.

Previous reports have demonstrated that ‘adenoid ameloblastoma’ bears a striking histomorphological resemblance with conventional solid multicystic ameloblastoma (SMA) and adenomatoid odontogenic tumor (AOT), such as plexiform architecture, ameloblast like cells, stellate reticulum like cells and ductal structures. Additionally, cribriform pattern, morules, dentinoid, clear cells and ghost cells have been shown to be important histological features of AA (Fig. 1). It was postulated that the ductal structures do not truly represent glandular differentiation but instead results from the degeneration of the stromal elements.^[5] Further, analysis demonstrated that AA lacks the signature molecular mutations either of SMA or AOT. No BRAF or KRAS mutations were seen in adenoid ameloblastoma,^[6,7] which are commonest mutations seen in ameloblastoma and AOT respectively, deciphering that AA is not definitely related to SMA or AOT, and represents a separate entity.

Address for correspondence: Deepak Pandiar, MDS, PhD, FHN. Department of Oral Pathology and Microbiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu

Phone: +918894088985 **E-mail:** deepakpandiar1923@yahoo.com

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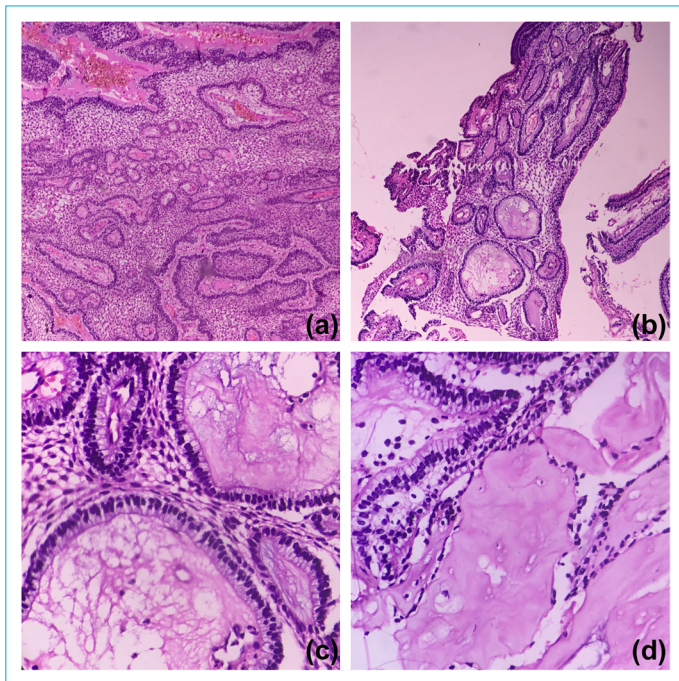


Figure 1. Photomicrographs of H&E stained sections of a case of recurrent AA in a 22 years old male showing cribriform arrangement of ameloblastomatous epithelium (a-b), stromal degeneration yielding ductal elements (c) and dentinoid in the vicinity (d).

Noteworthy, AA has been shown to harbour β -catenin mutations. Bastos VC et al., showed seven out of eight included cases had β -catenin immunoexpression and four cases showed CTNNB1 exon 3 mutations, namely, p.Ser33Cys, p.Gly34Arg, and p.Ser37Phe,^[7] and lacked BRAF or KRAS mutations. Interestingly, the similar mutations are seen in DGCT and more lately, different studies have shown that AA shows molecular features similar to DGCT.^[5,8] Nuclear β -catenin was demonstrated in all cases of AA and DGCT in both studies. Additionally, AA displayed loss of function mutations in the genes involved in WNT pathways, including APC, SMURF1 and NEDD4L.^[8] The same group of researchers demonstrated same mutations in another ghost cell lesion with ameloblastomatous epithelium, calcifying odontogenic cyst (COC),^[9] supporting the fact that these ghost cell forming lesions which also have ameloblastomatous epithelium and lead to formation of dentinoid show similar mutations in the tumor suppressor genes of WNT pathways. It is worth mentioning here that, COC which shares molecular signature with AA, was also classified under the category of mixed odontogenic tumors, as calcifying cystic odontogenic tumor (CCOT) in 2005 WHO classification. Schematic illustration of the proposed hypothesis is shown in Figure 2.

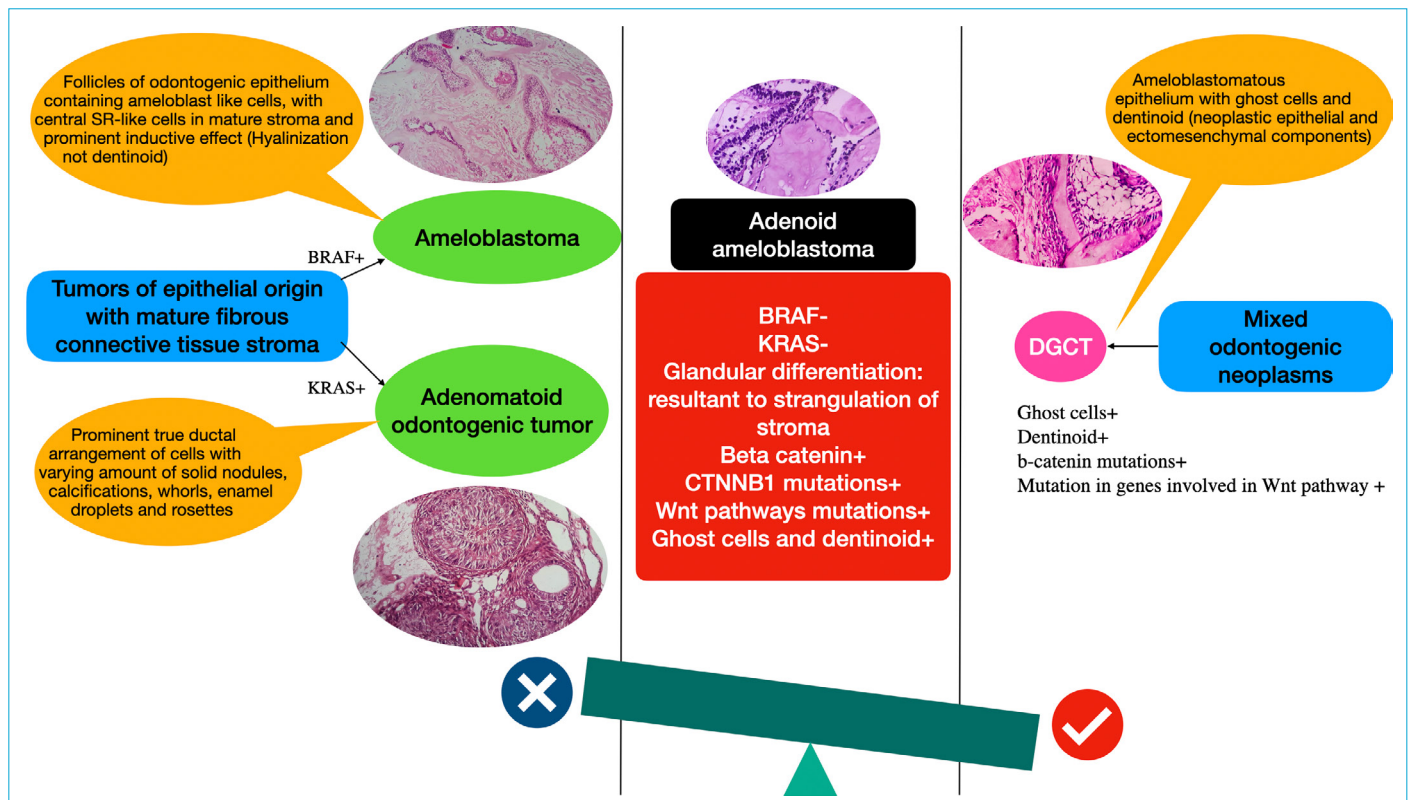


Figure 2. Diagrammatic representation of the hypothesis to support that adenoid ameloblastoma is more closely related to mixed odontogenic tumors.

Thus, in purview of the evidences generated from literature, we support the study results of Xue J et al., and Oh KY et al., that AA is closely related to DGCT and COC rather than the epithelial neoplasms and deserve re-consideration to be classified under mixed odontogenic neoplasms. If the tumor were categorized alongside DGCT, the term 'adenoid ameloblastoma' appear misleading, for which 'adenoid ameloblastomatous odontogenic tumor' is proposed.

Disclosures

Conflict of Interest: None declared.

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