Case Report

Hybrid odontogenic tumor masquerading as a salivary gland lesion: A diagnostic predicament

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Abstract

Hybrid odontogenic tumors are sporadic, where the distinctive areas of more than one odontogenic tumor tissue type have been reported. The occurrence of adenomatoid odontogenic tumor (AOT) with calcifying epithelial odontogenic tumor (CEOT) like areas histologically simulating salivary gland pathology is an unusual finding that has not been previously reported in the literature. We report the case of a 32-year-old female presenting with slow-growing firm swelling, radiographically as a pear-shaped radiolucent lesion in the interdental region of maxillary incisors. Histologically, the tissue showed nests and anastomosing strands of the bland cuboidal to squamoid epithelial cells showing nuclear pleomorphism, hyperchromatism, and abundant cytoplasm with prominent intercellular bridges focally. Multiple basophilic calcifications, amyloid-like material, duct-like formation, and mucinous spillage are seen. Tumor cells showed immunopositivity for CK 7, CK 19, CK 8/18 and low Ki67, p63, and immunonegativity for S100 suggesting of a hybrid lesion of CEOT with AOT.

Keywords: Adenomatoid odontogenic tumor, calcifying epithelial odontogenic tumor, odontogenic tumours, salivary gland pathology

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INTRODUCTION

Odontogenesis is a complex phenomenon where epithelium and connective tissue both play an equal contributory role. Their sequential and reciprocal interactions in the formation of teeth and their subsequent histologic features are associated with odontogenic tumors.[1] These lesions customarily have been benign, presenting not only as true neoplasms but also as hamartomas.

An imperious ambiance in the domain of oral pathology is generated by a diverse histopathology which is exemplified by the sporadic occurrence of hybrid odontogenic tumors, where the distinctive areas of more than one odontogenic tumor tissue type can be identified. Their biological nature is usually benign and signifies that of the predominant tumor type. However, sometimes, these lesions can be locally invasive. Peripheral odontogenic tumors are the ones that are located in the alveolar structures and gingiva, being similar to their intraosseous counterparts.[2] The objective of this article is to present a case of a benign odontogenic tumor occurring in the maxillary anterior region histologically simulating salivary gland pathology,

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CASE REPORT

A 32-year-old female reported with complaints of pain and swelling in the maxillary anterior region for 3 years. There was no history of trauma and pus discharge with the swelling. Swelling was slow in growth and associated with pain. The patient had taken unknown medications for the same with no reduction in the size of the swelling. Personal history, family history and medical history was noncontributory, and history of tobacco habit was not present. Upon extraoral examination, the overlying skin was found to be normal in color with the smooth surface without any gross facial asymmetry. Intraoral examination revealed the swelling to be round to ovoid, firm to hard in consistency [Figure 1a], nontender, noncompressible and located on the labial gingival margin in the region of right maxillary central and lateral incisors. The overlying mucosa was normal in color. Intraoral periapical radiographs showed a well-defined pear-shaped radiolucent lesion in the interdental region of right maxillary central and lateral incisors, extending from the mid root level to the periapical region [Figure 1b]. On the basis of clinical and radiographic features, differential diagnosis of radicular cyst, lateral periodontal cyst and benign odontogenic tumor such as adenomatoid odontogenic tumor (AOT) were postulated.

The patient was conventionally managed by surgical debridement of the lesion followed by regenerative therapy. The involved tooth was nonvital, and endodontic therapy was carried out. The lesional tissue specimen was sent for the histopathological examination.

Gross examination revealed multiple tissue fragments with the largest measuring 1.0 cm × 0.5 cm × 0.4 cm, being yellowish-white in color and soft in consistency [Figure 1c]. Histopathologically, the sections exhibited stratified squamous surface epithelium at the one end of the section with the lesional tissue in the rest of the area. The lesional tissue was composed of nests, islands and anastomosing strands of varying size and shape consisting of bland cuboidal to squamoid epithelial cells interposed in a mature fibrous stroma. Few of the areas show epithelial islands exhibiting branching pattern and cystic degeneration within them. Polyhedral epithelial cells showing nuclear pleomorphism, hyperchromatism and abundant cytoplasm with prominent intercellular bridges were noted in few areas. Multiple basophilic calcifications in the form of spherules of varying sizes with the adjacent areas of eosinophilic amyloid-like material were also noticed. Few of the epithelial islands also showed duct-like formation within them [Figures 2 and 3]. The areas of mucinous spillage were seen in the isolated areas. Peripheries of the lesional tissue show part of a degenerated fibrous capsule.

The histological differential diagnosis of calcifying epithelial odontogenic tumor (CEOT), AOT, squamous odontogenic tumor (SOT) and adenoid cystic carcinoma were considered. The presence of islands of bland looking squamoid cells without any evidence of peripheral columnar cells, palisading nuclei, or stellate reticulum-like cells could also hint toward the presence of a SOT.[3] Areas with probable ductal structures and mucinous spillage areas are also noticed. The appearance of squamous cells could well mimic as epidermoid group of cells as seen in the salivary gland lesion. It is probably one of the very few cases where a histopathological picture of an odontogenic tumor simulated that of a salivary gland lesion. Thus, the sections were exposed to immunohistochemical analysis for CK 7, CK 19, CK 8/18, S100 and proliferation index markers ki-67 and p63. Low intensity staining with Ki 67 and p63 (only <30 cells per high-power field showing p63 positivity) along with the morphological features suggested benign nature of the lesion. Focal weak positivity with CK 19 and strong positivity with CK 7 along with minimal

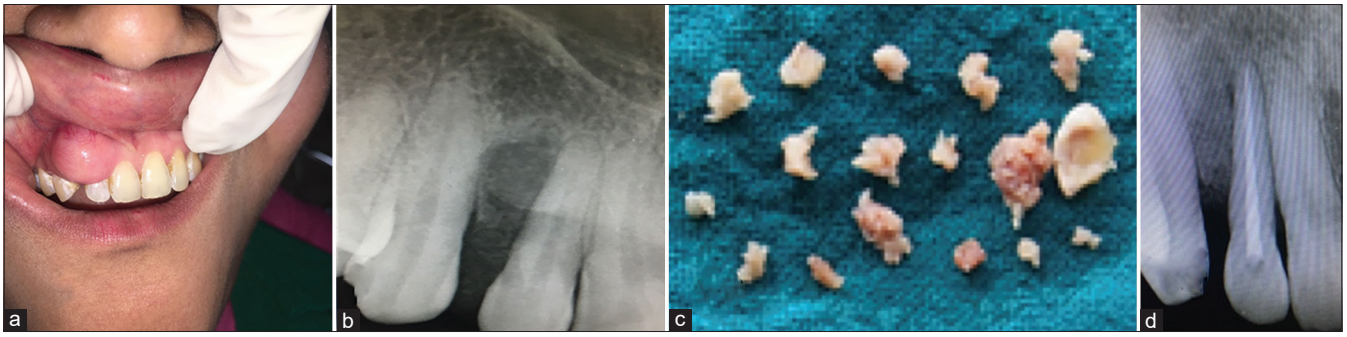

Figure 1: (a) Intra-oral swelling was firm to hard in consistency and nontender, noncompressible. (b) Well-defined pear-shaped radiolucent lesion in the interdental region of 11 and 12. (c) Multiple tissue fragments yellowish white in color and soft in consistency. (d) Surgical site had healed well with good bony regeneration and obvious reduction in the radiolucency

staining with S100 were observed as well [Figure 4]. Thus, considering clinical, radiological, and histopathogical features, the present case was diagnosed with hybrid lesion of CEOT with AOT. The patient was symptom free post operatively at the follow up after 9 months. The surgical site had healed with good bony regeneration and obvious reduction in the radiolucency [Figure 1d].

DISCUSSION

The odontogenic tumors are derived from the tooth-forming apparatus with few tumors arising from the tissues of the enamel organ and others from remnants of the dental lamina. Recent 2017 WHO classification classifies the odontogenic tumors into two categories, i.e., benign and malignant. Odontogenic tumors may be further identified as: Epithelial, mesenchymal, and mixed tumors. Most odontogenic tumors are intra-osseous lesions; however, few occur on the gingiva or in other peripheral locations without involving the underlying bone. In the present case, the lesion was located on the labial alveolar process with bony changes in the right maxillary central and lateral incisor region.

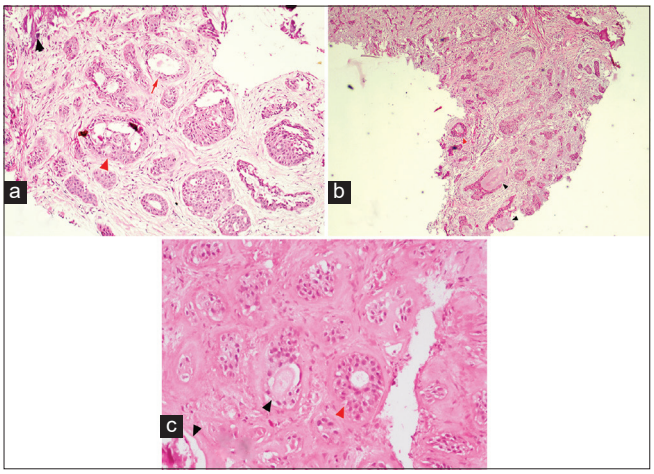

Figure 2: (a) Photomicrographs showing ductal pattern (long red arrow), cribriform pattern (red arrowhead) of Adenomatoid odontogenic tumor and calcifications of CEOT (black arrowhead). (b) Few areas displayed ductal structures (red arrowhead) like salivary gland lesions and sheets and strands of epithelial cells showing bordering eosinophilic amyloid (black arrowhead) characteristic of CEOT. (c) Higher magnification showing amyloid, calcifications (black arrowhead) and ductal arrangement (red arrowhead)

The term "hybrid tumor" has been first used with regard to salivary gland tumors.[4] Hybrid odontogenic tumors comprise of histopathological characteristics of two or more previously recognized odontogenic tumors and or cysts of different categories.[5] They must be differentiated from "collision tumors" in which two tumors of different histogenetic source or different topographical area develop simultaneously and then meet in the border zone. The exact etiology of hybrid odontogenic tumors is hitherto unknown; however, it is stipulated that the pluripotent odontogenic epithelium can give rise to divergent histological patterns within the same tumor.[5] The CEOT or Pindborg tumor is another commonly occurring tumor composed principally of polyhedral epithelial cells with homogeneous eosinophilic material probably amyloid.[6] In addition, calcification is a regular phenomenon in this group of lesion, and the same was evident in the present case. Few of the polyhedral squamous-shaped cells exhibited hyperchromatism, another feature suggestive of a CEOT. The peripheral variant of CEOT appears as gingival fibroma or epulis. Various morphological features are reported in CEOT which includes peripheral variants, multifocal presentation, clear cell differentiation, presence of Langerhans cells, calcified material, rare malignant variant, and recently microcystic variant which may mimic metastatic adenocarcinoma or other odontogenic tumors.[7-9] Ductal, cribriform and rosette pattern seen in the present case also created a diagnostic perplexity to rule out salivary gland lesion especially adenoid cystic carcinoma (AdCC). However, absence of increased mitoses, presence of abundant pink cytoplasm, prominent intercellular bridges, amyloid like material and calcifications and low Ki-67 proliferative index ruled out AdCC. Though immunohistochemistry is of limited importance in differentiating these lesions, our results (positive CK 7, low ki-67 and limited CK 19, S100, p63 positivity) are consistent with previous studies.[7,8,10] Hybrid tumors can

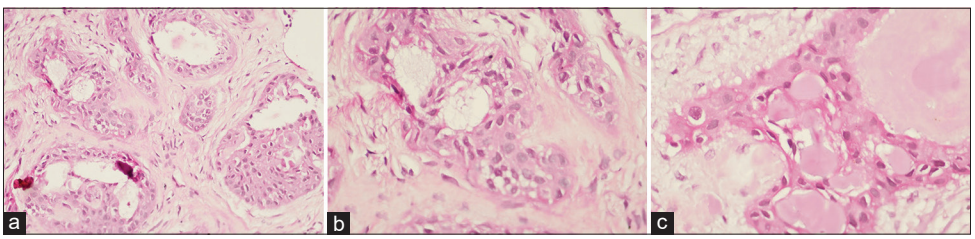

Figure 3: (a) Nests, islands, and anastomosing strands of varying size and shape with few epithelial islands showing duct-like formation or cystic degeneration within them. (b) Epithelial islands comprising of bland cuboidal to squamoid epithelial cells showing duct-like formation. These polyhedral epithelial cells displayed nuclear pleomorphism, hyperchromatism, and abundant cytoplasm. (c) Epithelial cells show adjacent areas of eosinophilic amyloid like material

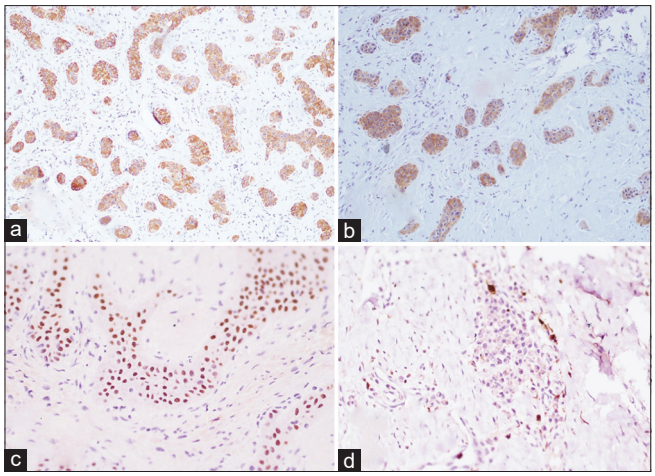

Figure 4: Immunohistochemical staining reveals that tumor cells show immunopositivity for CK7 under ×10 (a) and CK-19 under × 0 (b). Tumor cells showed weak immunopositivity for p63 under ×10 (c) and immunonegativity for S100 under ×20 (d)

show immunohistochemical expression of cytokeratins like AE1/AE3, CK5, CK14, CK19 in most of the cases and CK-7, CK8, Ck18 in few cases. Nevertheless, the morphological features along with immunohistochemical results in the present case indicated towards benign hybrid tumor of CEOT with AOT. CEOT-like epithelial nests are also described in dental follicles with unidentified significance.[10] The presence of a well-delineated fibrous peripheral capsule with ducts and rosette-like structures indicate toward the presence of a concurrent AOT.[6] Similar features were observed in the present case with few areas displaying fragmented peripherally placed fibrous capsule with few ductal structures further indicating toward a coexisting AOT. Minute dystrophic calcific deposits may be noted in 58% of AOTs. Histologically, AOT characteristically presents with a glandular or ductal pattern of preameloblast like cells in a multinodular arrangement of the stroma. The presence of eosinophilic amyloid-like material with few calcific droplets is seen within the stroma of AOT. The present case showed an interesting finding of CEOT like areas. Although numerous authors have reported it as a "Hybrid tumor;" WHO (2017) has suggested that CEOT-like areas in AOT are the normal constituent of AOT[6] and are specific to those areas where inductive changes are taking place.[11] Sah has further elaborated that these areas are not representative of true CEOT as they lack predominance over AOT along with absence of typical pleomorphism seen in CEOT.[11]

The presence of "CEOT-like areas" within AOT was first reported by Damm *et al*. and such lesions were named these as "combined epithelial odontogenic tumor."[12] The WHO (2017) has reported that such "hybrid tumors" behave biologically like AOTs, i.e., having limited growth potential. This is congruent with a case reported as hybrid tumor of CEOT and ameloblastoma,[13] where the tumor behaved in a gentle manner, similar to the present case where the lesion is perhaps a mixed tumor of CEOT and AOT and the patient was symptom-free postoperatively for a period of 6–9 months. The postoperative surgical site had healed well with good bony regeneration and observable reduction in the radiolucency [Figure 4].

Considering the complicated nature of odontogenic tumors and a very rare case of this combination we met, we presented this hybrid tumor "a mixed odontogenic tumor" to remind us that the term "mixed" sometimes can be used to express a degree of confusion. These ambiguous tumors should not generally be considered true hybrids; rather, they should be identified simply as anomalous histodifferentiation process.[14]

The overlapping features between AOT and CEOT seen in a few cases can raise problems. In addition, no immunohistochemical marker has been reported with reliability that distinguishes hamartomas from neoplasms. Similar diagnostic difficulties have been encountered in differentiating AOT from adenoid ameloblastoma with dentinoid in small biopsies[6] and immunohistochemical markers to distinguish these entities would be welcome. AOT has been reported to have areas imitating CEOT, odontomas, hamartomas, calcifying odontogenic cyst, dentigerous cyst and other odontogenic tumors. Mosqueda-Taylor *et al*. emphasised that CEOT-like areas in AOTs do not present as solid, infiltrative nests and characteristic pleomorphism as in true CEOT. Moreover, their presence does not affect the biologic behavior and growth potential of AOTs suggesting that CEOT-like areas should be considered within the histomorphological spectrum of AOT.[12,15]

Many authors have reiterated the fact that such lesions should be given lawful connotation, should and must be included in the WHO classification of odontogenic tumors with distinctive criteria of diagnosis as they show varied histomorphology with their biological nature still abstruse and their propensity to exclusively occur in the maxillary region.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/ have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will

not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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