Adenoid ameloblastoma with dentinoid and cellular atypia: a rare case report

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ABSTRACT

Adenomatoid odontogenic tumor (AOT) is always a benign tumor with rare incidence of recurrence while ameloblastoma is the commonest gnathic tumor, which is always aggressive. Although co-occurrence of these lesions has been reported, this paper describes a homogenous combination of *atypical* AOT and ameloblastomatous proliferation with some malignant microscopic features. To date, a dozen cases or slightly more of this uncommon composite odontogenic tumor have been, quite correctly, reported in the literature under the designation of *adenoid ameloblastoma*. Of these, neither cellular atypia nor pleomorphism has been revealed. This extremely rare ameloblastomatous variant can pose a significant diagnostic challenge. Moreover, we report new findings of severe nuclear vacuolization, mitotic figures, cellular pleomorphism and nuclear hyperchromatism and chromatin peripheralization. However, the scattered occurrence of these was not sufficient for claiming a malignancy. To confirm, two immunohistochemical markers - calretinin and p53 - were recruited. Rendering itself to be suspicious, a rapt attention should be paid toward well interrogating this lesion histologically and immunohistochemically.

Introduction

Ameloblastoma is a slowly growing, yet destructive, odontogenic epithelial tumor of the gnathion, which accounts for approximately 1% of all oral tumors and about 18% of odontogenic tumors.[1] Adenomatoid odontogenic tumor (AOT), in nature and in designation, is now questioned. Based on clinical and on immunohistochemical findings, scholars suggested that the nature of AOT is hamartomatous with histogenesis from the reduced enamel epithelium.[2] Conversely, testing the immunoreactivity for TGF-β1, Smad-2/-3, Smad-1/-5/-8, and Smad-4 signaling factors suggested a shared pathway in ameloblastomas, adenomatoid odontogenic tumors, and calcifying cystic odontogenic tumors with diverse neoplastic dynamics.[3] Recently, several scholars have depicted the so-called *adenoid ameloblastoma*.[4-7] All in all, about sixteen cases of this variant were roughly reported hitherto.

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Key words: Adenoid ameloblastoma; adenomatoid odontogenic tumor; calretinin.

Acknowledgments: our sincere and deep gratitude is expressed to Professor Dr. Suk Keun Lee, Professor Dr. Adriano Loyola, and Professor Dr. Hedley G. Coleman for their expert opinions and for their valuable suggestions.

Conflict of interest: the authors declare no potential conflict of interest.

Received for publication: 24 August 2015.
Revision received: 10 January 2016.
Accepted for publication: 1 February 2016.

Italian Journal of Medicine 2016; 10:238-240
doi:10.4081/itjm.2016.639

Consent

Written informed consent was obtained from the patient for publication of this case report and for any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Case Report

A 40-year-old male manifested a right mandibular swelling causing numbness and paresthesia. The radiological depicted a lesion, approximately 5×4×3 cm, which embraced the angle of the mandible and entirely destroyed the bone cortex. The lesion was excised by hemimandibulectomy 14 months ago. To date, neither metastatic potential nor recurrence is evident. Following the patient up, the sonographic assessment of the cervical and submandibular lymph nodes showed benign features with the largest lymph node measuring 1.4×1.2 cm in size.

Histologically, the general pattern was that of solid/multicystic ameloblastoma of which a mixture of follicular and plexiform subtypes dominated. Both revealed differentiated stratum-intermedium-like con-

densed cells near focal occurrence of atypical AOT-like areas with duct-like structures (Figure 1). Although the AOT-like arrangements showed no conspicuous eosinophilic materials, which are considered pathognomonic, the lesion exhibited, moreover, dystrophic calcification, intervening dentinoid materials and some sporadic ghost cell transformation. Aside from the nuclear vacuolization, sporadic nuclear atypia, some mitotic figures, and hyperchromatic tumor cells were evident; yet not abundant. Neither collision nor association of calcifying epithelial odontogenic tumor/AOT was seen (Figure 2).

Given the paucity of ghost cells, dentinoid material, as well as the confined mitotic activity, ghost cell carcinoma and dentinogenic ghost cell tumor were signed out. Still, unusual ameloblastic tumor was meant to be confirmed by running confirmatory immunohistochemical tests. Accordingly, the lesion was stained for calretinin and for p53 to probe the nature of the AOT-like occurrence (Figure 3) as well as the lesional malignant microscopic features. All stains revealed strong positive expression; adding up to a platform of *atypical* adenoid ameloblastoma.

Discussion

On the one hand, there are four histological types of ameloblastomas: solid/multicystic ameloblastoma (SAM), peripheral ameloblastoma, unicystic ameloblastoma and desmoplastic ameloblastoma. The most frequent type is SAM with its numerous histological subtypes: follicular, plexiform, acanthomatous, granular, clear cell, keratoameloblastomatous and basal cell (basaloid) subtypes.[1] On the other hand, AOT is classically a multi-nodular proliferation of spindle, cuboidal, and columnar cells in a variety of patterns comprising of scattered duct-like structures. All variants of AOT reveal odontogenic epithelium with duct-like structures and with varying degree of inductive change in the connective tissue. Characteristically, eosinophilic materials are observed along with dystrophic calcifications in several forms; delimited by a fibrous capsule of varying thickness.[8] Pertinently, the epithelial cells of the nodules and the center of the rosette-like configuration may display pools of amorphous amyloid-like material, hyaline, dysplastic ones, and even, in very rare cases, dentin-like material in both lesional and stroma cells of AOT.[9] Given the rare incidence of unequivocal recurrent adenomatoid odontogenic tumor,[10] a malignant AOT is unlikely to be, even, expected.

Nevertheless, a hybridization of ameloblastoma and AOT were reported, with fibrous separation, where numerous criteria of both lesions existed. However, this added up to a fierce controversy since myriad cases of ameloblastoma have evinced to produce duct-like structures which, most likely, represent no more than cystic changes especially when subnuclear vacuoles are, therein, evident. Accordingly, the designation of *ade-*

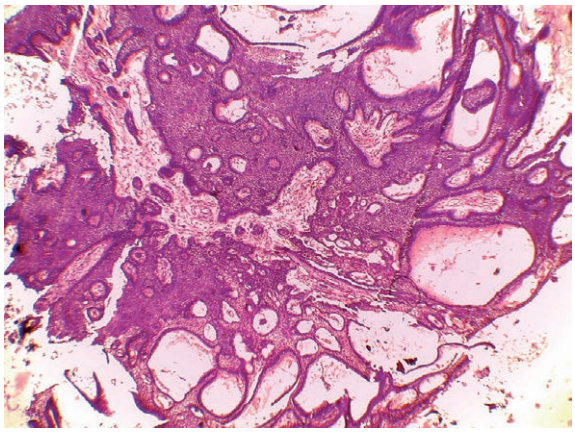

Figure 1. Photomicrograph displaying follicular ameloblastoma intermingled with focal occurrence of adenomatoid odontogenic tumor-like areas (H&E stained, original magnification: 4x).

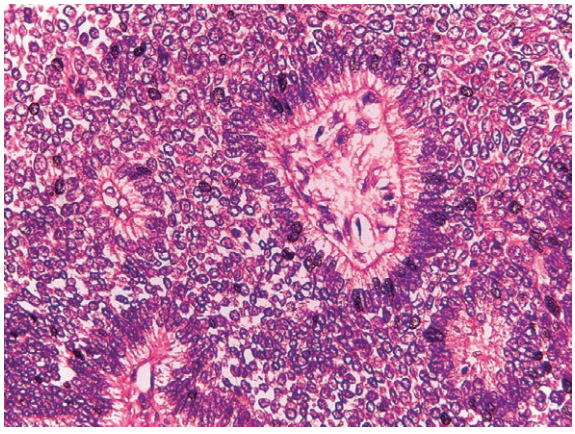

Figure 2. Photomicrograph showing higher magnification of the rosette and duct-like structures along with solid nests of neoplastic cells of hyperchromatic nuclei (H&E stained, original magnification: 40x).

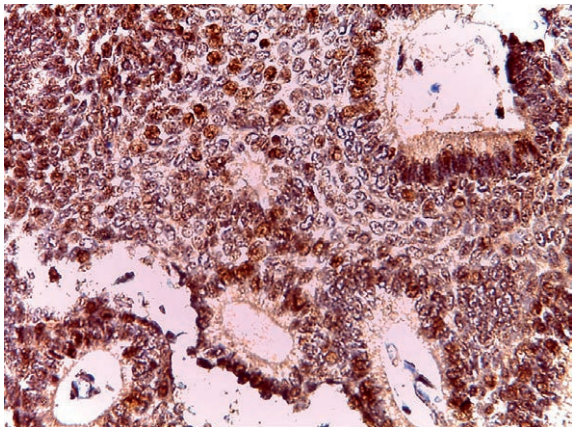

Figure 3. Photomicrograph showing positive expression for calretinin by ameloblastic and by duct-like cells (original magnification: 40x).

noid ameloblastoma (aka adenomatoid ameloblastoma), was specified for such rare phenotype which reveals an impressive occurrence of AOT-like areas.[11]

Adenoid ameloblastoma (AA) demonstrates features of both ameloblastoma and of AOT. Other than ameloblastic elements, AA displays epithelial whorls, evidence of induction in the form of duct-like structures, and sometimes ghost cells. The ameloblastic structures usually dominate the histological fields; yet, AOT-like areas may predominate, overshadowing the ameloblastomatous areas - rendering a confusing composite odontogenic tumor.[4-7]

Paradoxically, the present benign case displayed nuclear vacuolization, cellular atypia, some mitotic figures, and hyperchromatic tumoral cells. Although these findings were not abundant enough for highlighting a malignancy, this picture of AA was rarely reported. Complicating matters, the present case of AA demonstrated some focal aggregations of basaloid and clear cells.

Immunohistochemically, calretinin (calbindin-2), a 29-kDa calcium-binding protein, acts as a mediator of signaling intra-cellular calcium ions which are considered as second messengers intervening in cellular proliferation and differentiation.[12] Calretinin has been considered as a specific immunohistochemical marker for neoplastic ameloblastic epithelium, which is expressed only in ameloblastoma and in keratocystic odontogenic tumor but not in AOT.[13,14] The homogenous immunoreactivity for calretinin in this case confirmed the native ameloblastic nature of the AOT-like areas and established the diagnosis of AA.

By the same token, p53, a tumor suppressor protein, was also detected in ameloblastic lesions and in AOT.[15] In this study, the lesion exhibited a strong positive expression for p53; confirming the risky transforming potential and the relatively high neoplasticity. This should prompt renewed speculations about the higher neoplastic nature of AA and should necessitate a longer interval of follow-up. Given the formidable effort, which has been ushered to attribute a clinical significance of an ameloblastic phenotype over another, the amalgamation of the numerous cytodifferentiated areas in the present case, and in slew of other reported cases in the literature, criticizes the validity of investigating such histological-clinical correlation.

Conclusions

Overall, this introduced lesion, given the clinicopathological and immunohistochemical findings, cast light on a rare variant which adds to the pathogenetic background of the commonest odontogenic tumor: ameloblastoma. This atypical case of adenoid ameloblastoma, given the above-mentioned characteristics, has rendering itself to be suspicious. Accordingly, similar cases should be scrutinized histologically and immunohistochemically. Also, longer follow-up schedule should be considered.

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