Case Report

Hybrid Ameloblastoma of Anterior Maxilla: A Rare and Puzzling Pathologic entity – Case Report with Systematic Review

Abstract

Hybrid ameloblastoma has a variable clinical, radiological, and histopathological presentation. They contain two or more different histologic types and their biologic comportment is still arguable. We herein present a case of a hybrid variant of desmoplastic ameloblastoma which is the first of its kind to have ever been reported due to its unusual location in the maxillary anterior region, along with systematic review of clinicopathologic features of reported cases immunohistochemical markers may act as an adjunct in the accurate diagnosis of these lesions.

Keywords: *Desmoplastic ameloblastoma, hybrid ameloblastoma, immunohistochemistry, odontogenic tumor, systematic review*

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Introduction

Ameloblastomas are the odontogenic tumors generally present in the jaw bones. They begin as a painless swelling of the jaws and gradually cause facial deformity, mobility, displacement, and root resorption of the involved teeth.[1] Most of the lesions occur in mandible ascending ramus and cause grotesque deformities. Radiologically, it appears as a mixed radiopaque-radiolucent lesion with well- or ill-defined margins having unilocular or multilocular appearance.[2]

The most common types of ameloblastomas are the follicular and plexiform types also called the "classic/conventional types," followed by acanthomatous and granular cell types. In 1987, Waldron and El-Mofty presented a distinctive variant of ameloblastoma, which was called hybrid ameloblastoma displaying capricious combination of the histological features of desmoplastic ameloblastoma along with conventional ameloblastoma.[3] Being a rare entity, only a few cases of hybrid ameloblastomas have been reported globally, accounting for about 1.1%–4.3% of ameloblastomas. The literature also reports clinically and histologically different benign and locally invasive malignant lesions with some similar radiological features, thereby mimicking each other.[4-6] This diagnostic dilemma can be simplified by detailed three-dimensional imaging modalities such as cone-beam computed tomography (CBCT). Our case of hybrid ameloblastoma is by far the first of its kind owing to its inimitable combination of follicular, plexiform, and desmoplastic variants and involvement of anterior maxilla which is a very unusual site for ameloblastoma of any kind. The objective of this paper is to report histologically established hybrid ameloblastoma with areas of misdiagnosed as periapical cyst. It further reviews the clinicoradiological features and immunohistochemical markers of hybrid ameloblastoma and presents a systematic review of clinicopathologic features of hybrid ameloblastoma.

Methodology

The present systematic review was conducted according to the guidelines provided by the PRISMA statement. A bibliographic search was performed in the main databases: PUBMED (www.pubmed.gov); ScIELO (www.scielo.org), Google Scholar (www. scholar.google.com.br), BVS (http://bvsalud.org/) e LILACS (http://lilacs.bvsalud.org), which we collected papers along with cross-references that were published from 1984 to 2018. It included laboratory studies, case reports, and systematic reviews as well as literature

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that were developed in the human species. Articles with cases of peripheral, malignant, metastatic, and recurrent ameloblastoma were excluded from the study. Through the bibliographic research, 85 articles were selected, all of which were extracted from: PUBMED (www.pubmed.gov); ScIELO (www.scielo.org), Google Scholar (www.scholar.google.com.br), BVS (http://bvsalud.org/) e LILACS (http://lilacs.bvsalud.org), previously reported. Keywords included a combination of "hybrid ameloblastoma" and/or "hybrid odontogenic tumours" ([MeSH Terms]).

Results

The paper reviews a total of 49 cases. Clinical, radiological, and histopathological characteristics of each reported case have been identified and analyzed from papers published in the English Medical literature. These clinicoradiological and histopathological features are described in Tables 1 and 2.

Case Report

A 35-year-old female patient reported to our department of Oral Medicine and Radiology complaining of pain in the upper front tooth region for the past six months. Patient revealed a past history of trauma in the same region 10 years back. Her previous medical and familial history was noncontributory. Extraorally, no swelling, no facial deformity, or expansion of cortical bone was observed. Cervical lymph nodes were not palpable. Intraoral hard tissue examination revealed intact maxillary anterior teeth. Soft-tissue examination revealed vestibular obliteration and tenderness present in relation to left maxillary anterior teeth; however, overlying mucosa was intact with no signs of infection and sinus tract formation [Figure 1]. Based on history and clinical features a provisional diagnosis of radicular cyst was given and the patient was subjected for chairside investigations such as tooth vitality and fine-needle aspiration cytology (FNAC). Pulp vitality tests were performed for 21, 22, and 23 and the teeth did not respond to electric and thermal stimuli and were found to be nonvital. FNAC was nonproductive. Hematological findings were within normal limits.

Patient was advised for panoramic radiograph to visualize the extent of the lesion before surgical management could be planned. The panoramic radiograph revealed well-defined radiolucency extending from mesial to 21 involving 22 up to distal of 23. The border of the radiolucency was not corticated and internal structure revealed unclear radiolucency. There was no resorption of involved teeth with the radiolucency and no involvement of maxillary sinus on the left side [Figure 2]. A nonproductive FNAC, unclear superioinferior margins of the lesion and unclear internal structure of the lesion, raised doubts overdiagnosis of lesion, and patient was subjected for CBCT to uncover these doubts.

CBCT multiplanar and axial sections [Figure 3], with three-dimensional reconstructed image [Figure 4], revealed solitary, oval, ill-defined, unilocular, complete radiolucency, with nonsclerotic border, surrounding the apical aspect of root of 21, 22, 23 causing complete destruction of labial plate at coronal aspect extending toward alveolar crest in 21, 22 region and superiorly leading to destruction of nasal floor, medially up to nasal septum, and distally till the distal aspect of root of 23. The lesion is measuring about 19.8 mm mesiodistally, 13.6 mm superioinferiorly and 15 mm buccolingually. Blunting or root of 21 and 22 was noted. Thinning of mesial aspect of the nasopalatine canal was also noted. The radiographic diagnosis of infected radicular cyst of 21 and 22 was given. Surgical enucleation of the lesion was performed and the surgical specimen was sent to histopathological examination.

Microscopic examination of the hematoxylin and eosin-stained slides reveal mature densely collagenized connective tissue stroma showing odontogenic epithelial cells forming a network of interconnecting strands [Figure 5]. These strands are bounded by a layer of columnar cells resembling ameloblast-like cells in the

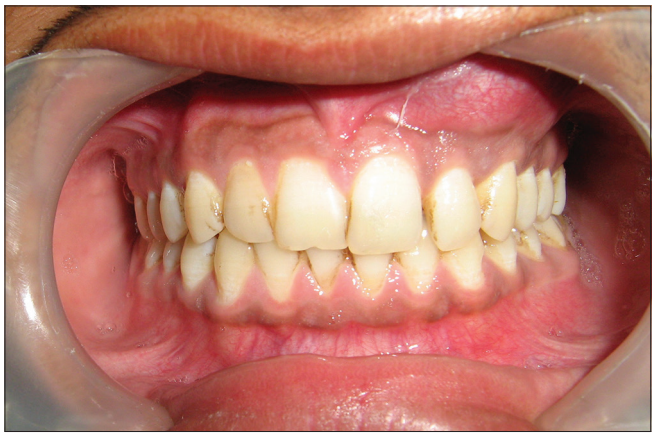

Figure 1: Clinical preoperative picture showing vestibular obliteration in the left maxillary anterior region

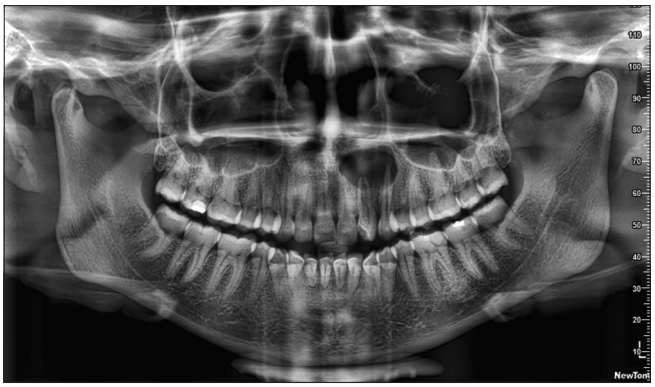

Figure 2: Panoramic radiograph with well-defined radiolucency extending from 21, 22, and 23

Table 1: Clinicoradiological and pathological features of hybrid ameloblastoma

Authors	Age (years)	Sex	Location	Locularity	Borders	Radiodensity	Tooth resorption	Tooth displacement	Histopathological features
Waldron *et al*. (1987)	25-82	Female	Max P	NA	NA	NA	NA	NA	Des + Fol
		Female	Mand P	NA	NA	NA	NA	NA	Des + Fol
		Female	Mand P	NA	NA	NA	NA	NA	Des + Fol
		Male	Mand P	NA	NA	NA	NA	NA	Des + Fol
		Male	Mand P	NA	NA	NA	NA	NA	Des + Fol
Higuchi *et al*. (1991)	70	Male	Mand P	Multiloc	Ill	RL	NA	NA	Des + Amel
	58	Male	Mand A + P	Multiloc	Ill	RL	NA	NA	Des + Amel
Hong SP (1991)	NA	NA	NA	Multiloc	Ill	RL	NA	NA	Amel + CCOT
Tajima (1992)	NA	NA	NA	Multiloc	Well	Mixed	NA	NA	Amel + CCOT
Philipsen *et al*. (1992)	55	Male	Mand A + P	Multiloc	NA	Mixed	Yes	NA	Des + Fol + Plex
Ashman *et al*. (1993)	53	Male	Mand A	Multiloc	Well	Mixed	NA	NA	Des + Plex
Raubenheimer (1995)	NA	NA	NA	Uniloc	Ill	Mixed	NA	NA	Amel + CCOT + AOT
Takata *et al*. (1999)	48	Male	Mand A + P	Multiloc	Ill	RL	NA	NA	Des + Fol
Wakoh *et al*. (2002)	35	Female	Mand A + P	Multiloc	Well	Mixed	NA	NA	Des + Fol
Li TJ (2003)	NA	NA	NA	NA	Ill	Mixed	NA	NA	Amel + CCOT
Ide F (2005)	NA	NA	NA	NA	Ill	Mixed	NA	NA	Amel + CCOT
Hirota *et al*. (2005)	17	F	Max A + P	Uniloc	Well	RL	NA	NA	Des + Plex + Acant + Basal cell pattern with desmoplasia
Seim *et al*. (2005)	53	Male	Max P	Uniloc	NA	NA	NA	NA	Foll + Plex + CEOT
dos Santos (2006)	36	Male	Mand A + P	Uniloc	Ill	RL	No	NA	Des + Fol
Desai *et al*. (2006)	32	Male	Mand P	Uniloc	Well	RL	No	NA	Des + Fol
Zhang W *et al*. (2006)	NA	NA	NA	NA	NA	NA	NA	NA	Amel + CCOT + AOT
Jivan V (2007)	NA	NA	NA	NA	NA	NA	NA	NA	Amel + CCOT + AOT
Nosrati K (2009)	NA	NA	NA	NA	NA	NA	NA	NA	Amel + CCOT
Shivapathasundaram (2009)	31	Female	Mand A + P	Uniloc	Well	Mixed	NA	NA	Des + Fol
	40	Male	Max A + P	Uniiloc	Ill	Mixed	NA	NA	Des + Fol
Yazdi *et al*. (2009)	48	Female	Mand A	Multiloc	Ill	Mixed	No	NA	Des + Fol
Etit *et al*. (2010)	62	Female	Max P	NA	NA	NA	NA	NA	Fol + Plex + CEOT
Brooks *et al*. (2010)	66	Female	Mand A	Multiloc	Well	Mixed	NA	NA	Des + Acant
Gade *et al*. (2010)	35	Female	Max A	Uniloc	Well	Mixed	Yes	NA	Des + Fol
Vardhan *et al*. (2011)	29	Female	Mand A + P	NA	Well	RL	NA	NA	Des + Amel
Lawal *et al*. (2011)	50	Female	Mand A	Multiloc	Well	Mixed	NA	Yes	Des + Amel
	29	Male	Mand A	Multiloc	Well	RL	NA	NA	Des + Amel
Acharya *et al*. (2011)	50	Male	Mand	NA	NA	NA	NA	NA	Des + Fol
Angadi *et al*. (2011)	64	Female	Max A + P	NA	Ill	Mixed	No	NA	Des + Fol
Mahadesh *et al*. (2011)	46	Male	Mand P	Multiloc	Well	RO	NA	NA	Fol + Acanth + + Des
Bavle *et al*. (2013)	28	Female	Mand A	NA	Ill	Mixed	NA	NA	Desmoplasia with osteoplasia + Fol + Acanth + Basaloid
Effiom *et al*. (2013)	50	Female	Mand A + P	NA	NA	Mixed	NA	NA	Des + Fol with osteoplasia
Rastogi *et al*. (2013)	34	Female	Mand A	NA	NA	Mixed	NA	NA	Des + Fol

Contd...

Table 1: Contd...

Authors	Age (years)	Sex	Location	Locularity	Borders	Radiodensity	Tooth resorption	Tooth displacement	Histopathological features
Yamazaki *et al*. (2013)	31	Female	Mand P	Uniloc		Mixed			Amel + CEOT + AOT
Chaubey SS *et al*. (2014)	17	Male	Mand P	Uniloc	Ill	Mixed	Yes	Yes	CCOT + Plex
Raj rai (2014)	50	Female	Max A + P	Uniloc	NA	Mixed	NA	NA	Des + Plex
Joshi PS *et al*. (2014)	55	Female	Max A	NA	Ill	Mixed	No	Yes	Des + Acant + Osteoplasia
Wadhwan V (2015)	65	Female	Max P	NA	NA	RO	NA	NA	Plex + CEOT
Chaitanya B *et al*. (2016)	50	Female	Mand A + P	Multiloc	Well	Mixed	NA	NA	Des + Foll
Lakshmi *et al*. (2016)	40	Male	Max A + P	Multiloc	Well	RL	No	No	Des + Fol + Acant
Gupta S *et al*. (2016)	38	Male	Mand P	Multiloc	Well	Mixed	NA	NA	Des + Fol
Iwase *et al*. (2017)	40	Male	Mand P	Multiloc	Well	Mixed	Yes	No	Des + Fol
Rai HK *et al*. (2017)	55	Male	Mand P	Uniloc	Well	NA	NA	NA	Adenoid Amel + Dentinoid
Present case	35	Female	Max A	Uniloc	Ill	RL	No	No	Des + Fol + Plex

NA: Not applicable; Max P: Maxilla posterior; M and A: Mandible anterior; M and P: Mandible posterior; Multiloc: Multilocular; Uniloc: Unilocular; RL: Radiolucent; RO: Radiopaque; Ill: Ill defined; Well: Well defined; Des + Fol: Desmoplastic and follicular; Des + Plex: Desmoplastic and plexiform; Fol + Plex + Ade: Follicular; plexiform and adenomatoid odontogenic tumor; Am + CCOT: Ameloblastoma and calcifying cystic odontogenic tumor; Am + AOT: Ameloblastoma and adenomatoid odontogenic tumor; Am + CEOT: Ameloblastoma and calcifying epithelial odontogenic tumor; Am + CCOT + AOT: Ameloblastoma; adenomatoid odontogenic tumor and calcifying cystic odontogenic tumor

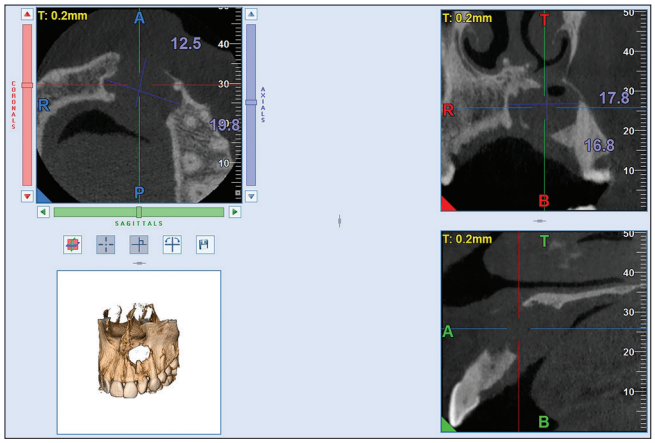

Figure 3: Multiplanar view illustration in sagittal, coronal, and axial sections from cone-beam computed tomography

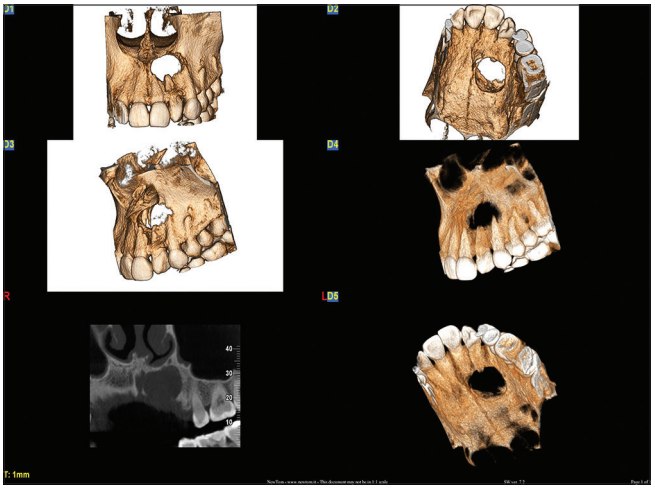

Figure 4: Three dimensional illustration of pathology present from different views in different aspects

periphery with nuclei arranged away from the basal region of the cell showing reverse nuclear polarity. Between these layers, stellate reticulum-like cells are present. Fibrous stoma along with blood vessels is enclosed between the network of odontogenic cells and appears to be compressing or squeezing the odontogenic cell network [Figures 6 and 7]. In another section, small-to-medium-sized discrete compressed follicles of tumor cells with few areas of cystic degeneration can also be seen. The compressed follicles are surrounded by hyalinized stroma in various areas [Figures 8 and 9]. Myxomatous degeneration is also appreciable in certain areas. These findings were consistent with desmoplastic-plexiform-follicular (hybrid) ameloblastoma.

Discussion

Clinical and histopathological features of hybrid ameloblastoma

According to Waldron and El-Mofty, hybrid ameloblastoma is a rare variant of ameloblastoma which shows a unique combination of the histological features of desmoplastic ameloblastoma along with conventional ameloblastoma.[7]

As per the reported cases, the mandible is the most common site for involvement of hybrid ameloblastomas as compared to the maxilla.[8-10] Moreover, if the tumor occurs in the maxilla, then the posterior region is the most affected.[11,12]

Table 2: Summary of data on 36 compiled cases of hybrid ameloblastoma

	Percentage
Patient age: Mean age (years)	36.6
Site	
Maxillary anterior	4.0
Maxillary posterior	10.2
Mandible anterior	14.2
Mandible posterior	24.4
Mandible anterior and posterior	20.4
Maxillary anterior and posterior	10.2
Gender	
Male	38.7
Female	44.8
Radiographic features	
Periphery and shape	
Multilocular	34.6
Unilocular	22.4
Ill defined	30.6
Well defined	24.4
Effect on surround	
Root resorption	8.16
Structure - tooth displacement	8.16
Internal structure	
Radiolucent	20.4
Radiopaque	4.0
Mixed	46.9
Histopathologic features	
Desmoplastic and follicular	40.8
Desmoplasia and ameloblastoma	10.2
Ameloblastoma and calcifying cystic odontogenic tumor	10.2
Desmoplastic, follicular, and plexiform	4.08
Desmoplastic and plexiform	4.08
Ameloblastoma, adenomatoid odontogenic tumor, and calcifying cystic odontogenic tumor	8.16
Desmoplastic, plexiform, acanthomatous, basal cell pattern with desmoplasia	2.04
Follicular, plexiform, and calcifying epithelial odontogenic roconvulsive therapy tumor	4.08
Desmoplastic and acanthomatous	2.04
Desmoplastic, follicular, and acanthomatous	4.08
Plexiform and calcifying cystic odontogenic tumor	2.04
Plexiform and calcifying epithelial odontogenic tumor	2.04
Desmoplastic, acanthomatous, and osteoplasia	2.04
Desmoplastic and follicular with osteoplasia	2.04
Follicular, acanthomatous, desmoplasia with osteoplasia, and basaloid	2.04

Whereas in the present case, the maxillary anterior region was found to be involved making it a highly unique entity.

Philipsen *et al.* proposed that the hybrid variant was a transitional form of the desmoplastic type, comprising the microscopic features of both desmoplastic and classic follicular or plexiform variants which is in accordance to the histological features present in this case.

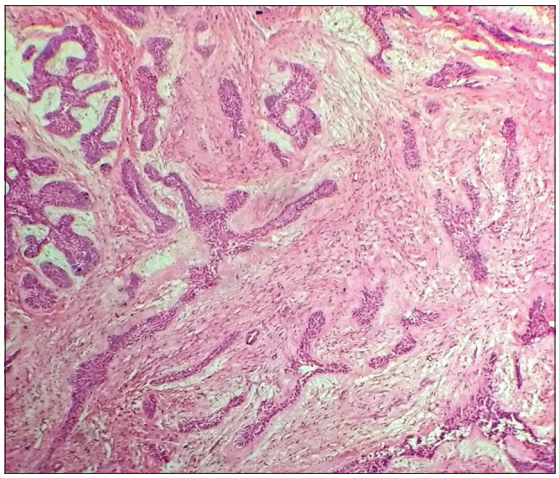

Figure 5: Interlacing strands of odontogenic epithelium in the connective tissue stroma showing plexiform pattern (H and E, ×4)

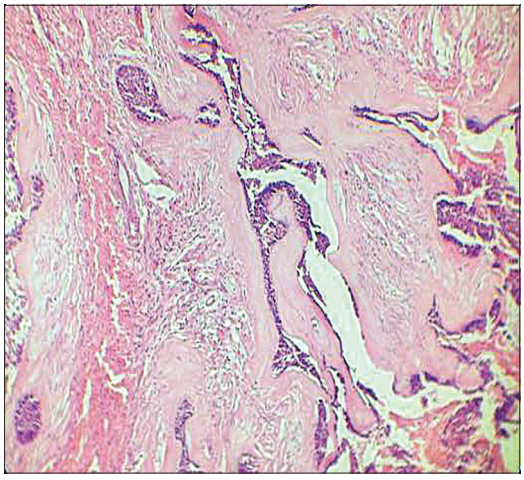

Figure 6: Connective tissue stroma undergoing desmoplastic changes (H and E, ×10)

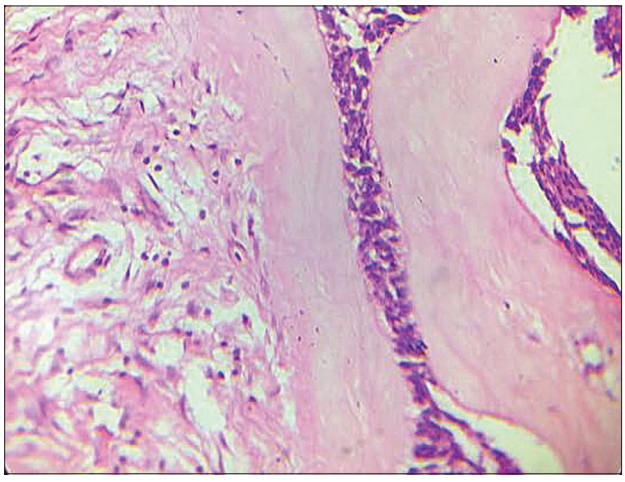

Figure 7: Desmoplastic changes at higher magnification (H and E, ×40)

Radiographically, it mimics fibro-osseous diseases and odontogenic cysts and tumors with mixed

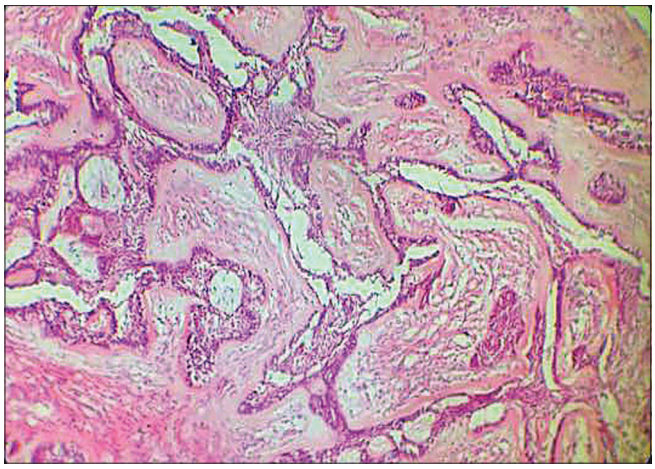

Figure 8: Desmoplastic stroma compressing the epithelial islands (H and E, ×10)

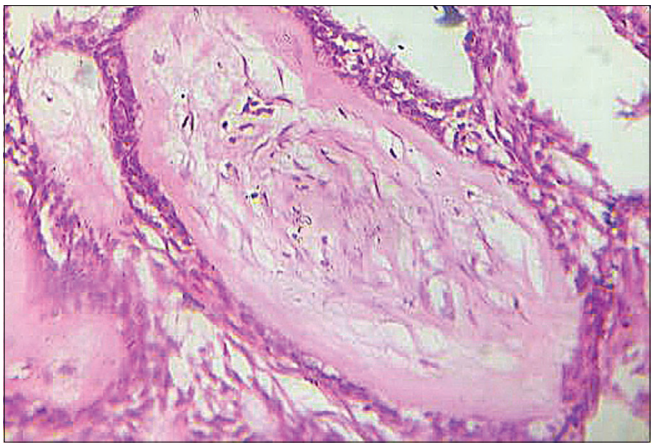

Figure 9: Epithelial island showing desmoplasia (H and E, ×10)

radiolucent-radiopaque internal structure such as ossifying fibromas, fibrous dysplasia, osteoblastomas, osteosarcomas, calcifying epithelial odontogenic tumors, and calcifying odontogenic cysts.[8-10]

The hybrid variant appears such as mixed radiolucent and radiopaque lesions with irregular borders similar to common radiological pattern observed in the desmoplastic variant or fibro-osseous lesions or malignant tumors owing to high infiltrative nature.[11,12] While few cases of hybrid ameloblastomas exhibit a multilocular radiolucent pattern, which is similar to that of conventional ameloblastomas, as was seen in our patient.

The incidence of desmoplastic variant ranges from 4% to 13% making it an extremely rare entity.[13,14] The intriguing relationship of the desmoplastic variant with the conventional variants is the center of interest of many researchers worldwide. The simultaneous occurrence of desmoplastic variant with an additional variant in the hybrid lesion is enigmatic.[15,16] It is still unclear whether the already existing desmoplastic variant transforms into the conventional variant or vice versa. Few researchers even consider it to be a collision tumor.[17,18]

However, the histopathological features shown in our case are in agreement with Waldron and El-Mofty's diagnostic criteria because it showed the synchronized occurrence of desmoplastic variant along with other variants such as follicular and plexiform.[19,20]

Immunohistochemistry of hybrid ameloblastoma

As a result of tumoral modulation in hybrid lesions immunohistochemically, expressions of extracellular matrix proteins, tenascin, fibronectin, and type I collagen, in a hybrid ameloblastoma lesion, have been reported.[21]

Treatment

With limited understanding of its behavior and prognosis, the proper treatment strategies for hybrid ameloblastoma are not entirely defined so far. Based on the present knowledge, the WHO recommends to apply the same treatment modality as for solid ameloblastoma which includes complete resection as enucleation or curettage might result in its recurrence, however, small lesions can easily be enucleated in toto.[22-24]

Conclusion

Hybrid ameloblastoma has a variable clinical, radiological, and histopathological presentation. The biologic comportment of the lesion is still arguable. Immunohistochemical markers may act as an adjunct in the accurate diagnosis of this lesion. Thus, many more clinical, radiological, and histopathological data are required to clearly demonstrate this pathologic entity.

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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Nil.

Conflicts of interest

There are no conflicts of interest.

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