

CASE REPORTS

Granular ameloblastoma: report of two cases with atypical cytological aspects

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Abstract

Ameloblastoma is an aggressive odontogenic tumor, which arises from odontogenic epithelium. Ameloblastomas can present in several clinical and histomorphological patterns. The granular cell variant accounts for only 3.5% to 5% of ameloblastomas. We have presented two cases of granular cell ameloblastoma (GCA) occurring in a 44-year-old and 50-year-old man, respectively. Case No. 1 on incisional biopsy was diagnosed as unicystic ameloblastoma (UA), which later after excisional biopsy was finally diagnosed as GCA owing to the features observed in excisional biopsied tissue. Case No. 2 on incisional biopsy showed darker and lighter stained cells arranged in small follicular pattern, and anastomosing cords. Meticulous immunohistochemistry, histochemical examination and careful literature search helped us to diagnose it as GCA. We have made an attempt to elucidate the diagnosis of GCA especially in cases of GCA with unusual granular component.

Keywords: ameloblastoma, granular cell, plexiform.

Introduction

Odontogenic tumors occur exclusively in the jaws that are derived from the epithelial and/or ectomesenchymal component of the tooth or tooth forming structures [1]. *World Health Organization* (WHO) classification of odontogenic tumors divides ameloblastoma into four types: solid/multicystic, extraosseous/peripheral, desmoplastic, and unicystic types [2]. Granular cell ameloblastoma (GCA) is one of the histological variant of solid type of ameloblastoma, which is characterized by presence of granular cells [3]. According to *Armed Forces Institute of Pathology* (AFIP) *Atlas of Tumor Pathology*, GCA consists of granular cells containing eosinophilic cytoplasmic granules, which may be seen in the center or in the peripheral columnar or cuboidal cells of the follicular or plexiform ameloblastic variants [4]. This is the classical presentation of GCA and it was observed in Case No. 1. However, there are few reported cases in the literature wherein the GCA showed presence of granular cells in the absence of classical ameloblastomatous features giving rise to diagnostic dilemmas [5–7]. Our Case No. 2 showed the atypical features of granular cells without the presence of classical ameloblastomatous pattern. Both cases presented here are two ends of the spectrum, showing common (Case No. 1) and uncommon (Case No. 2) features. The primary purpose is to give an overview to the pathologists to arrive at the diagnosis in cases of diagnostic difficulties, particularly for GCA cases.

Case presentations

Case No. 1

A 44-year-old male patient reported to the Outdoor Patient Department of Maulana Azad Institute of Dental

Sciences, New Delhi, India, with a chief complaint of swelling in the right lower back tooth region since 4–5 months. Patient was apparently well 4–5 months back when he first noticed a swelling inside the mouth in the lower right front tooth region. Extra-orally swelling was in the region of right mandibular parasymphseal region. It was soft, fluctuant and non-tender. Intra-orally swelling was involving lower buccal vestibular region with respect to mandibular right lateral incisor to first molar. Teeth were grade I mobile. On palpation buccal and lingual cortical plate expansion was noted (Figure 1a). Orthopantomograph (OPG) showed multilocular radiolucency extending from left lateral mandibular incisor up to distal root of right mandibular first molar (Figure 1b). The patient was diagnosed with ameloblastoma. Incisional biopsy was performed for histopathological examination. Multiple Hematoxylin and Eosin (HE) stained sections showed cystic lining composed of columnar basal cells with hyperchromatic nuclei and reversal of nuclear polarity, and stellate reticulum like superficial cells. At places, odontogenic epithelium was noted in the connective tissue stroma. Background stroma was collagenous and vascular. The lesion was diagnosed as unicystic ameloblastoma (luminal and intraluminal type) (Figure 1c).

Finally, excision of the lesion was done and histopathological examination revealed cystic areas lined by non-keratinized epithelium lined by tall columnar basal cells with stellate superficial cells. Fibrovascular connective tissue showed numerous follicles and interlacing strands of odontogenic epithelium showing tall columnar basal cells with reversal of polarity and stellate central cells. Numerous granular cells were seen in the central and peripheral odontogenic cells. This directed us to the diagnosis of GCA (Figure 1d).

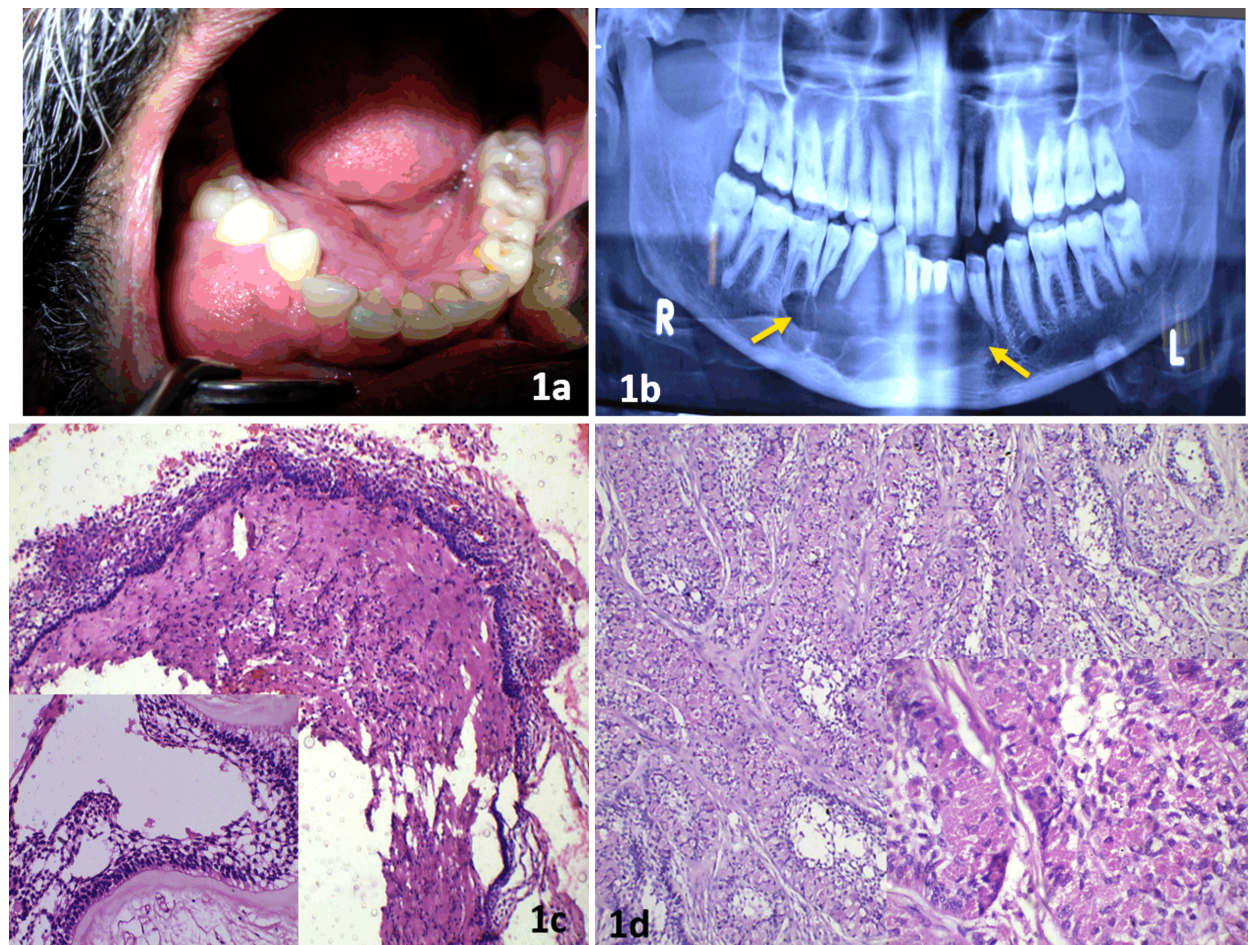


Figure 1 – Case No. 1: (a) Intra-oral swelling in the right mandible extending from right lateral incisor to right mandibular first molar; (b) OPG showing multilocular radiolucency extending from left lateral mandibular incisor up to distal root of right mandibular first molar; (c) Microphotograph showing a cystic lumen lined by ameloblast-like cells with stellate superficial cells (HE staining: $\times 100$; inset, $\times 400$); (d) Microphotograph showing numerous granular cells in the central and peripheral odontogenic follicles (HE staining: $\times 100$; inset, $\times 400$). OPG: Orthopantomograph; R: Right; L: Left.

Case No. 2

A 50-year-old male patient reported to the Outdoor Patient Department of Maulana Azad Institute of Dental Sciences, New Delhi, India, with a chief complaint of pain in the left lower back tooth region since one year. Patient experienced pain, 8–9 months back, which was insidious in onset and dull aching in character. Past dental history revealed extraction of left mandibular first molar was done 3–4 years back. Extra-orally, mild swelling was present on the left angle of the mandible, which was non-tender on palpation. Intra-orally, there was mild obliteration of the buccal vestibule (Figure 2a). OPG revealed large multilocular radiolucency seen in the left angle of the mandible extending into the ramus. The case was provisionally diagnosed as ameloblastoma (Figure 2b). Based on these findings, incisional biopsy was planned and histopathological examination was done. Multiple HE-stained sections at low magnification ($50\times$) showed encapsulated growth with abundant darkly staining cells and very little stroma (Figure 2c). At $\times 100$ magnification, the darkly stained cells appeared to be arranged in small follicular pattern and anastomosing cords. These follicles and anastomosing cords were interspersed by intervening

septa (Figure 2d). At $\times 400$ magnification, along with hyperchromatic cells, some light stained cells composed with intracellular eosinophilic granules were also noticed (Figure 2d). No mitotic activity was observed in the given sections. Background stroma was vascular and collagenous. Based on HE histopathological features, the differential diagnosis of odontogenic tumor and salivary gland tumor were considered. Since there was presence of granular cells, a special Periodic Acid–Schiff (PAS) with diastase staining and PAS with Alcian blue were also done.

Immunohistochemical staining was planned with panel of markers – cytokeratin (CK) AE1/AE3, S-100, MIB-1, epithelial membrane antigen (EMA) to elucidate the origin of tumor cells. Cytokeratin staining was found to be strongly positive (Figure 3a). EMA, S-100, MIB-1 were negative. PAS with diastase showed dark pink color staining of the cells and PAS with Alcian blue was negative (Figure 3b).

We established a pathological diagnosis of GCA based on the above-mentioned examination.

Finally, segmental resection of the left mandible was planned and histopathological examination report was consistent with the incisional biopsy report.

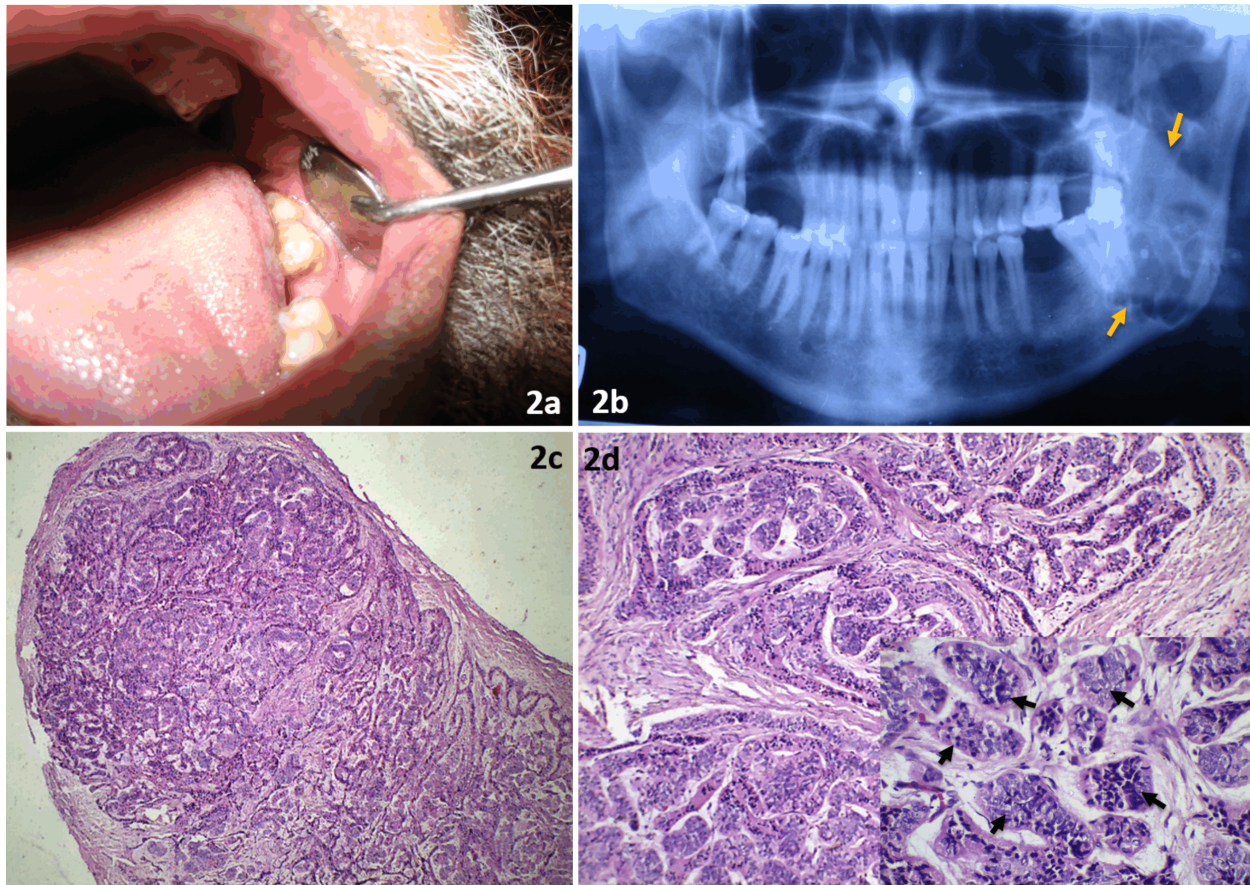


Figure 2 – Case No. 2: (a) Intra-oral mild obliteration of the right posterior buccal vestibule; (b) OPG showing multilocular radiolucency in the left angle of the mandible extending into the ramus; (c) Microphotograph showing encapsulated growth with abundant dark staining cells and little stroma (HE staining, $\times 40$); (d) Microphotograph showing arrangement of tumor cells in small follicles and anastomosing cords – inset showing microphotograph exhibiting lighter staining cells with intracellular eosinophilic deposits as shown by black arrows (HE staining: $\times 100$; inset, $\times 400$). OPG: Orthopantomograph.

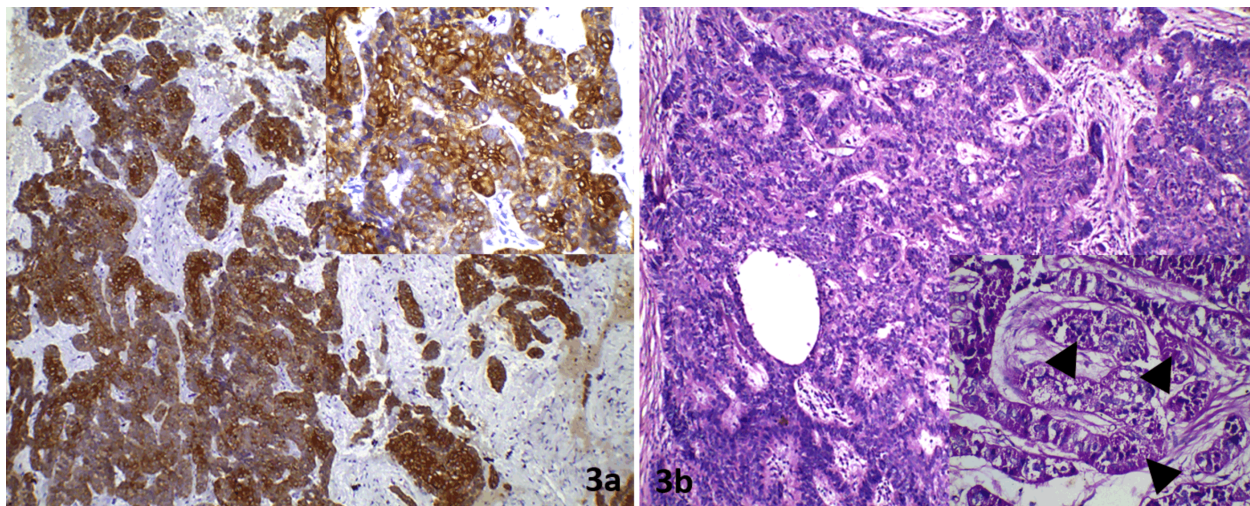


Figure 3 – Case No. 2: (a) Microphotograph showing strong CK AE1/AE3 immunoexpression ($\times 100$; inset, $\times 400$); (b) Microphotograph showing PAS positivity – inset showing granular aspect of the cytoplasm of tumor cells as shown by black arrows (PAS with diastase staining: $\times 100$; inset, $\times 400$). CK: Cytokeratin; PAS: Periodic Acid–Schiff.

Discussion

Prevalence of GCA is considered as 3.5–5% of all ameloblastomas [3, 6, 8]. Hartman [8] studied a series of 20 cases of GCA and reported the average age of patient around 40.7 years, with no significant gender

predilection, and was found predominantly at the posterior region of the mandible [3]. These findings were consistent with our cases except both cases were in males.

Mostly, the diagnosis is usually straightforward for GCA, wherein granular cytoplasmic change is present either centrally or peripherally in the odontogenic

epithelium (follicular or plexiform). On the other hand, when a granular cell pattern was observed in the absence of other typical ameloblastomatous characteristics, it may cause diagnostic dilemmas as in our second case. The same was opined by Argyris *et al.* [7].

Pertaining to our first patient, the diagnosis was crystal clear. At the time of incisional biopsy, we observed cystic lining composed of non-keratinized epithelium lined by tall columnar basal cells with hyperchromatic nuclei and reversal of nuclear polarity and stellate reticulum-like superficial cells both luminal and intraluminal (Figure 1c). So, the case was diagnosed as unicystic ameloblastoma (UA) based on these features. However, later during excisional biopsy, numerous granular cells were seen in the centre and periphery of odontogenic follicles and interlacing strands of odontogenic epithelium and we finally diagnosed the case as GCA (Figure 1d). This may point towards the importance of representative site for the biopsy. The purpose to present this case was so that reader can differentiate between common and uncommon granular cell component in GCA.

Motahhary *et al.* reported granular cell type of a UA in a 57-year-old Indian female patient [9]. They observed the sheets of granular cells confined to cystic lining and opined that granular pattern of lining cells could be related to a degenerative process occurring in a solid tumor that may be leading to the cyst formation [9].

Our second patients' case was diagnostically challenged to us due to the presence of atypical granular cell component. A thorough English language literature search revealed 14 cases have been reported discussing about the atypical granular cell component in absence of ameloblastic features since 1988 to till date (Table 1).

Table 1 – Reported cases of GCA with unusual granular cell component

No.	Year	Reference	No. of reported cases
1.	1986	Altini <i>et al.</i> [10]	3
2.	1989	Yamamoto <i>et al.</i> [11]	1
3.	1991	Siar <i>et al.</i> [12]	2
4.	1993	Siar & Ng [13]	2
5.	1995	Raubenheimer <i>et al.</i> [14]	3
6.	2012	Oza & Agarwal [5]	1
7.	2015	Matsushita <i>et al.</i> [6]	1
8.	2015	Argyris <i>et al.</i> [7]	1
9.	2017	Our report	1

GCA: Granular cell ameloblastoma.

Atypical GCAs have been referred as “plexiform granular cell odontogenic tumor” by Altini *et al.* [10] and “anastomosing GCA” by Matsushita *et al.* [6]. Characteristic histopathological features include anastomosing cords and strands of two-cell layer thick with granular eosinophilic cytoplasm. The same was observed in our second case (Figure 2, c and d).

Published scientific literature suggests that GCA are immune reactive for cytokeratins and non-reactive for S-100 [5–7, 9]. However, few authors have reported about S-100 positivity in their cases [13, 15]. Similarly, our second case expressed strong positivity for CK AE1/AE3 in the peripheral cells and central cells (Figure 3a). Therefore, the tumor was suspected for epithelial in origin.

However, it is easy to differentiate between intra-osseous ameloblastoma and salivary gland tumor based on the location but salivary gland tumors may occur centrally. Case No. 2 had histomorphological features similar to oncocytoma (Figure 2, c and d) but oncocytomas mostly occur peripherally and our case was located centrally in the mandible (Figure 2b). However, there are published cases of GCA showing resemblance to oncocytoma [5–7].

Cytoplasmic granules in GCA are positive for PAS with diastase and exhibits dark pink color. It has been suggested that positive histochemical expression support a lysosomal origin for the GCA granules [8, 9]. The same histochemical expression was observed in our Case No. 2 (Figure 3b). This arouses the suspicious for intraosseous mucoepidermoid carcinoma and acinic cell carcinoma. Following this PAS with Alcian blue was done which was found to be negative and that favored the diagnosis of GCA.

Conclusions

We presented two cases of GCA, one with usual granular cell component and other with unusual granular cell component. We emphasize to include GCA as differential diagnosis in cases of intraosseous tumors showing presence of granular cells without classical ameloblastic features.

Conflict of interests

The authors declare that they have no conflict of interests.

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