



## CASE REPORT

# Granular Cell Ameloblastoma: An Unusual Variant

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## ABSTRACT

Ameloblastoma is a neoplasm of odontogenic epithelium, especially of enamel organ-type tissue that has not undergone differentiation to the point of hard tissue formation. Granular cell ameloblastoma is a rare condition, accounting for 3.5% of all ameloblastoma cases that shows marked transformation in the cytoplasm of tumor cells, which are usually stellate reticulum like cells. It is also considered an aggressive variant of the ameloblastoma with potential recurrence and malignant transformation. The transformed cells possess very coarse, granular, eosinophilic cytoplasm. The 'granular change' is thought to be due to a dysfunctional status of neoplastic cells, and the pathogenesis of this tumor seems to be age-related. This article describes a case of granular cell variant of ameloblastoma affecting a 64-year-old male.

**Keywords:** Granular cell ameloblastoma, Odontogenic tumor, Lysosomal granules.

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## INTRODUCTION

Ameloblastoma (AB) is a benign, locally aggressive odontogenic tumor arising from odontogenic epithelium with mature fibrous stroma without odontogenic ectomesenchyme.<sup>1</sup> It has been described very aptly by Robinson as being a tumor that is 'usually unicentric, non functional, intermittent in growth, anatomically benign and clinically persistent.'<sup>2</sup> It was first described by Broca in 1868 and constitutes 1 to 2% of all cysts and tumors of the jaw.<sup>3</sup> The common tissue of origin postulated for this tumor are cell rests of enamel organ, epithelium of odontogenic cysts, disturbances of developing organ, basal cells of surface epithelium, heterotrophic epithelium in other parts of body, etc.<sup>4</sup> The microscopic appearance of the tumor is distinct with the presence of peripheral columnar cells containing hyperchromatic, reversely polarized nuclei, arranged in a palisaded pattern.<sup>5</sup> The tumor

usually behaves as an aggressive and destructive one with a strong tendency for recurrence but rarely metastasizes.<sup>6</sup>

Most often these tumors occur between the third to fifth decades of life, without any gender or racial predilection.<sup>5</sup> Approximately, 85% of ameloblastoma arise in the mandible, especially in the molar-ramus region and present radiographically as a multilocular or unilocular radiolucency.<sup>7</sup> The tumor often manifests itself as a hard tissue swelling that may assume very large dimensions if left untreated. Pain and paresthesia are unusual clinical features.<sup>5</sup> Ameloblastomas are divided into three fairly distinct types based on its clinicopathologic criteria which include the solid or multicystic (majority of cases), unicystic and peripheral.<sup>5</sup> In solid or multicystic ameloblastomas, the usual radiographic appearance is a multilocular radiolucency with well defined borders. A unilocular presentation is always associated with unicystic ameloblastomas but also possible for conventional tumors.<sup>8</sup>

Histopathologic variants of ameloblastoma include follicular, plexiform, acanthomatous, granular cell, desmoplastic and basal cell patterns.<sup>9</sup> The granular cell ameloblastoma (GCA) is one of the rarest entities and accounts for only 5% of all ameloblastomas.<sup>3</sup> Approximately, 30 studies on this rare subtype of ameloblastoma has been revealed in the english literature.<sup>9</sup> It is known to be locally aggressive among all the ameloblastomas and there is higher incidence of malignant transformation and metastases.<sup>10</sup> So, it is important to separate GCA from other ameloblastomas.

The granular cell subtype of ameloblastoma is characterized by marked transformation of cytoplasm, usually of stellate reticulum-like cells, which are filled with eosinophilic granules that resemble lysosomes, both ultrastructurally and histochemically.<sup>5</sup> This granular change is attributed to a dysfunctional status of the neoplastic cells and to an aging or degenerative change in long standing lesions; however, it may also affect young patients.<sup>5</sup>

The purpose of this article is to present a case of an unusual histologic variant of ameloblastoma and highlight its unique microscopic features that allow its distinction from other jaw tumors with a granular cell consistency.

## CASE REPORT

A 64-year-old male presented with a chief complaint of a painless swelling in the lower left back tooth region since 6 months. The patient had undergone surgery for the same

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1 year back from another hospital but the histopathology report was missing and the lesion recurred. There was no contributory past medical history.

Extraorally the swelling was present on the left body of mandible extending from the corner of the mouth anteriorly to the first molar region posteriorly (Fig. 1). Intraorally swelling extended from distal aspect of left mandibular lateral incisor to mesial aspect of left mandibular first molar causing buccolingual expansion of the cortical plates (Fig. 2). The swelling was bony hard and tender to palpation and did not have well defined borders. The mucosa and the overlying skin were normal in color.

Panoramic view of the patient's mouth showed unilocular radiolucency in the body of the mandible extending from the distal aspect of left lateral incisor toward the mesial aspect of left mandibular first molar with ill-defined border (Fig. 3). Inferiorly, the radiolucency was seen 2 mm above the inferior border of mandible. Root resorption of involved teeth could not be appreciated. Based on clinical and radiological examinations the lesion was provisionally diagnosed as ameloblastoma.

Incisional biopsy was taken and hematoxylin and eosin stained section showed a moderately collagenous connective tissue stroma containing numerous follicles toward one end. The follicles were lined peripherally by columnar cells and the central core contained stellate reticulum like cells. The peripheral columnar cells and most of the central stellate reticulum like cells contained granular eosinophilic cytoplasm (Figs 4 and 5). The stroma contained scanty inflammatory cell infiltrate and few vascular channels. Immunohistochemical investigation proved that the granular cells are positive for CD68 (Fig. 6). The final histopathological diagnosis was given as 'granular cell ameloblastoma'. The patient is kept under regular check-up.

## DISCUSSION

GCA is one of the rarest entities of all reported ameloblastomas.<sup>1</sup> Numerous theories have been proposed on the origin and nature of these granular cells in ameloblastomas. These granular cells are considered to be epithelial in origin. Several ultrastructural and histochemical studies have been done on the nature of these granules which describes them as lysosomes.<sup>3</sup> This lysosomal aggregation within the cytoplasm may be due to dysfunction of a lysosomal enzyme. It can also be due to malfunction of a lysosome-associated protein involved in enzyme activation, enzyme targeting or lysosomal biogenesis.<sup>14</sup>

Granular cells can be considered as a transitional or matured phase in the lifecycle of ameloblastomas, starting with normal stellate reticulum like cells leading to production of granules and finally leading to degeneration.<sup>3</sup> More

recent observation is that the accumulation of lysosomal granules represent a degenerative process. This view is supported by the increased expression of death signaling molecules by the granules.<sup>15</sup> According to Ara et al, the synthesis of signaling molecules, such as  $\beta$ -catenin and



Fig. 1: Extraoral view of the patient shows a diffuse swelling in the left mandibular region

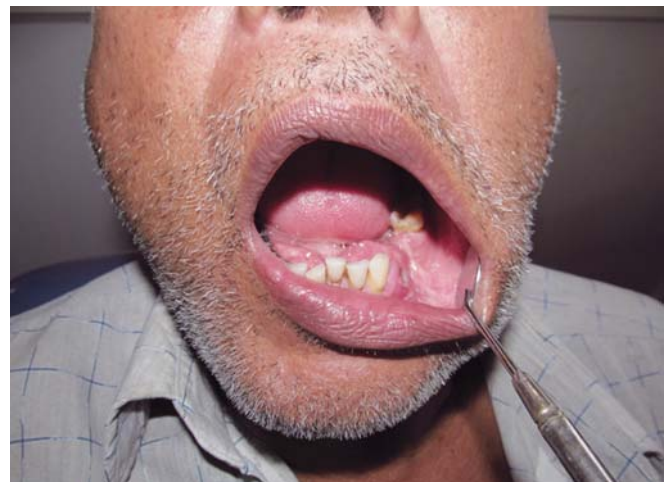


Fig. 2: Intraoral view showing the extension of the swelling

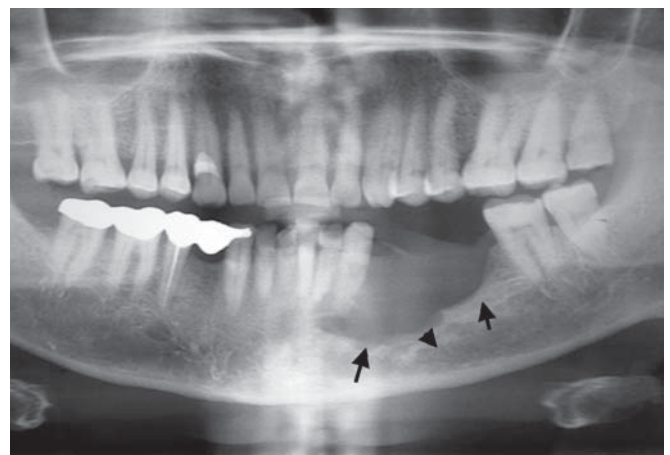
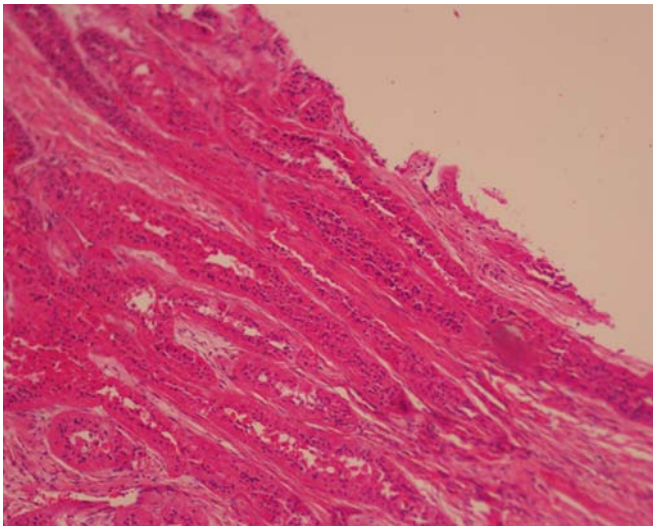
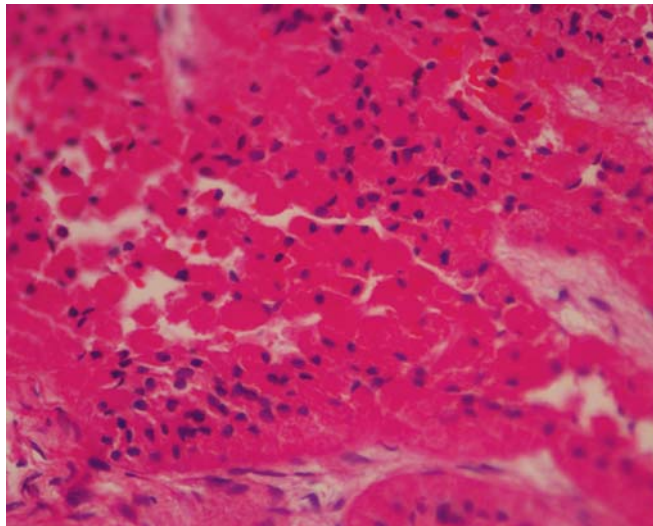


Fig. 3: A panoramic radiograph displays a well-defined unilocular radiolucency with scalloped border extending from the left mandibular lateral incisor to the left mandibular first molar

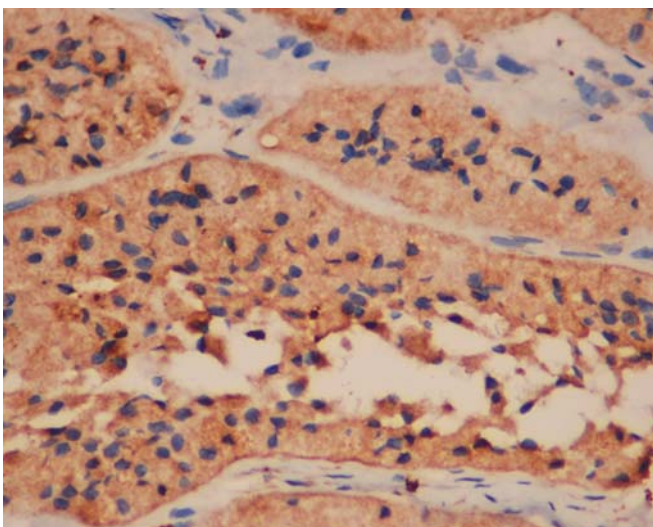




**Fig. 4:** Biopsy specimen reveals ameloblastomatous islands containing central large round cells with eosinophilic granules in the cytoplasm (hematoxylin and eosin stain,  $\times 10$  view)



**Fig. 5:** Large round cells with eosinophilic granules in the cytoplasm (hematoxylin and eosin stain,  $\times 40$  view)



**Fig. 6:** CD 68 showed a strong staining intensity in granular cells

Wnt-5a is upregulated in the granular cells of GCA, but their transportation or secretion is impaired, resulting in their accumulation within granular cells, as autophagosomes.<sup>14</sup> The true nature of these granules still remains a mystery.

A literature review on the ameloblastomas of jaws, from 1960 to 1993, reported that, out of a total of 1593 cases with available data on histologic subtypes, there were only 56 (3.5%) cases of the granular cell variant.<sup>11</sup> An age interval of 21-65 (average age 40.7 years) was reported when 20 cases of GCA was reviewed from the files of Armed Forces Institute of Pathology. All tumors occurred in the mandible, the vast majority of them (19 out of 20) affecting the posterior regions.<sup>12</sup> In our case too, the patient was in the fifth decade, and the posterior mandible was involved.

Usually in GCA, the stellate reticulum-like cells undergoes the greatest changes with very coarse, granular, eosinophilic cytoplasm.<sup>11</sup> This change often extends to peripheral columnar or cuboidal cells. In our case, the peripheral columnar cells were mostly affected along with few stellate reticulum-like cells. The cell membranes of granular cells were poorly demarcated and the cytoplasm of adjacent cells merges imperceptibly but sometimes showed a sharply delineated cell border.

Immunohistochemically, granular cells were positive for CD68, lysozyme and cytokeratins but negative for vimentin, desmin, S-100, neuron specific enolase and CD15, indicating cytoplasmic lysosomal aggregates are of epithelial origin and not of mesenchymal, myogenic or neurogenic origin.<sup>13</sup> In our case also the granular cells were positive for CD68.

Complete surgical excision is the treatment of choice. Ameloblastoma is a tumor that frequently recurs after treatment. The rate of recurrence ranges from 4.5% for *en bloc* resection to 54.1% for conservative therapy. Among all the variants of ameloblastomas, the granular cell type is the most aggressive one. Compared to the more common follicular, plexiform, and acanthomatous subtypes, a 33.3% recurrence rate for GCA is reported, which is quite high.<sup>11</sup> In another study, 11 of 15 patients (73%) developed recurrent lesions.<sup>12</sup>

Differential diagnosis of GCA includes other oral lesions with a similar morphology of granular cell accumulation including granular cell odontogenic tumor, granular cell tumor and congenital epulis. In contrast to granular cell ameloblastoma, the granular cells of granular cell odontogenic tumor are not located within epithelial islands but constitute part of the tumor stroma.<sup>14</sup> Small islands or cords of the odontogenic epithelium may be seen interspersed among the granular cells, while small cementum-like deposits and dystrophic calcifications are often found within the lesion.<sup>15</sup>

Granular cell tumor appears as an asymptomatic sessile nodule of small size. Immunohistochemical investigation is

positive for S-100 protein, which could indicate neural origin whereas in granular cell ameloblastoma, S-100 is negative as it is of epithelial origin.<sup>5</sup>

Congenital epulis is an uncommon soft tissue tumor which occurs almost exclusively on the alveolar ridges of newborns or rarely on the tongue. Although this lesion is also composed of granular cells, the necessity of distinction from a granular cell ameloblastoma appears unlikely, considering the occurrence of the latter in patients of older age.<sup>5</sup>

## CONCLUSION

The granular cell ameloblastoma is a rare presentation with unique histopathologic and immunohistochemical findings; its treatment and prognosis do not significantly differ from those of the other subtypes of the solid/multicystic ameloblastoma. However, GCA should be differentiated from the other variants of ameloblastoma and also from other granular cell lesions because of its high recurrence rate. Patients should be kept under periodic observation because of reports of recurrences even up to 8 years after initial treatment.

## REFERENCES

1. Dhanuthai K, Chantarangsu S, Rojanawatsirivej S, Phattararatip E, Darling M, Jackson-Boeters L, Said-Al-Naief N, Shin HI, An CH, Hong NT, et al. Ameloblastoma: a multicentric study. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;113(6):782-788.
2. Shafer, Hine, Levy. Cysts and tumours of odontogenic origin. In: Rajendran R, Sivapathasundharam B, editors. *Shafer's Textbook of Oral Pathology*. 7th ed. Mosby: Saunders; 2012. p. 276-283.
3. Gupta S, Grewal H, Saha K. Granular cell ameloblastoma showing desmoplasia. *Ann Saudi Med* 2012;32(5):537-540.
4. Adebisi KE, Ugboko VI, Omoniyi-Esan GO, Ndukwe KC, Oginni FO. Clinicopathological analysis of histological variants of ameloblastoma in a suburban Nigerian population. *Head Face Med* 2006;2:42.
5. Philipsen HP, Reichart PA. Unicystic ameloblastoma: a review of 193 cases from the literature. *Oral Oncol* 1998;34(5):317-325.
6. Waldron C. Odontogenic cysts and tumors. In: Neville B, Damm D, Allen C, Bouquot J, editors. *Oral Maxillofac Pathol*. Philadelphia: Saunders 2002. p. 589-642.
7. Regezi JA, Sciubba JJ, Jordan RCK. In: *Oral pathology: Clinical pathologic correlations*. 4th ed. St Louis, Missouri: WB Saunders 2003. p. 267-274.
8. Laphanasupkul P, Poomsawat S, Chindasombatjaroen J. Investigation of basement membrane proteins in a case of granular cell ameloblastoma. *Int J Oral Sci* 2012;4(1):45-49.
9. Deshpande A, Umap P, Munshi M. Granular cell ameloblastoma of the jaw: a report of two cases with fine needle aspiration cytology. *Acta Cytol* 2000;44(1):81-85.
10. Reichart PA, Philipsen HP, Sonner S. Ameloblastoma: biological profile of 3677 Cases. *Eur J Cancer B Oral Oncol* 1995;31B(2):86-99.
11. Hartman KS. Granular-cell ameloblastoma. *Oral Surg Oral Med Oral Pathol* 1974;38(2):241-253.
12. Nasu M, Takagi M, Yamamoto H. Ultrastructural and histochemical studies of granular cell ameloblastoma. *J Oral Pathol* 1984;13(4):448-456.
13. Sathi GS, Han PP, Tamamura R, Nagatsuka H, Hu H, Katase N, Nagai N. Immunolocalization of cell signaling molecules in the granular cell ameloblastoma. *J Oral Pathol Med* 2007;36(10):609-614.
14. Maria A, Sharma Y. Granular cell-Peripheral ameloblastoma: a rare variant. *J Maxillofac Oral Surg* 2009;8(3):294-297.
15. Meer S, Altini M, Coleman H, Daya N. Central granular cell odontogenic tumor: immunohistochemistry and ultrastructure. *Am J Otolaryngol* 2004;25(1):73-78.