



CASE REPORT

Granular Cell Ameloblastoma: Report of an Unusual Case and Review of Literature

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ABSTRACT

Ameloblastoma is an epithelial odontogenic tumor of the jaws and exhibits diverse microscopic patterns. Granular cell ameloblastoma is a rare variant of ameloblastoma, making up to 3.5% of all ameloblastomas. The granular change is thought to be a dysfunctional status of neoplastic cells leading to degenerative changes in long standing lesions. The pathogenesis of this tumor seems to be related to lysosome like organelles seen as eosinophilic granules in the cytoplasm. The granular cell ameloblastoma, in most instances is found as an admixture with other histologic patterns, particularly follicular subtype. This report describes an unusual case of granular cell ameloblastoma along with a review of literature.

Keywords: Degenerative changes, Granular cell ameloblastoma, Lysosome like organelles.

How to cite this article: Cherian LM, Sood A, Heera R. Granular Cell Ameloblastoma: Report of an Unusual Case and Review of Literature. *Oral Maxillofac Pathol J* 2014;5(2):517-519.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Ameloblastoma is a true neoplasm of odontogenic epithelial origin which is also the second most common odontogenic neoplasm.^{1,2} Histologically, there are two main patterns, follicular and plexiform, in which various cellular changes such as squamous metaplasia and granular transformation are commonly seen, and when these are extensive, the terms acanthomatous type and granular cell type are applied, respectively.³ World Health Organization (WHO) has categorized ameloblastomas solid/multicystic, extraosseous, desmoplastic and unicystic ameloblastoma.

The granular cell ameloblastoma is a relatively rare histologic subtype, and in most instances, it is found as an admixture with other histologic patterns, particularly the follicular subtype.^{1,2,4} Granular cell change in ameloblastoma was first seen by Krompecher in 1918 and was called

pseudoxanthomatous cells. Granular cells can appear in various odontogenic and nonodontogenic tumors.⁵

The granular cell subtype of ameloblastoma is characterized by the groups of granular cells, which have abundant cytoplasm filled with eosinophilic granules that resemble lysosomes, both ultrastructurally and histochemically.⁶ The acquisition of granular cell phenotype has been attributed to an aging or degenerative change in long-standing lesions; however, it may also affect young patients.⁷

Even though many cases have been reported in literature regarding the recurrence of granular cell ameloblastoma, only one case exists in the literature regarding the recurrent ameloblastoma occurring in a graft.⁸ Also, one case exists of recurrent ameloblastoma as granular cell variety with the initial lesion being of follicular variety.¹⁹ To the best of our knowledge, this is probably the second case of recurrent ameloblastoma in a graft.

CASE REPORT

A 38-year-old woman reported to the department of Oral and Maxillofacial Surgery at Government Dental College, Kottayam with complaint of pain and pus drainage with respect to the angle of the mandible on the right side. Upon further investigation, it was revealed that the patient had a history of similar symptoms, 5 years back with respect to the same site. Five years ago, the patient had undergone resective surgery with placement of rib graft in the area of surgery, respectively. The resected part of the mandible (Fig. 1) was sent for the histopathological diagnosis, which had been given as follicular ameloblastoma. Now, 5 years later, in view of the symptoms presented by the patient, an incisional biopsy was done with respect to same site and was sent to the department of Oral pathology and Microbiology of Government Dental College, Kottayam for histopathological diagnosis. The radiographs revealed complete replacement of the graft by the tumor in the form of radiolucency in the respective area. The microscopic examination revealed numerous follicles lined by tall columnar cells showing reversal of basal polarity, palisaded appearance and subnuclear vacuolization. The central portion of the follicles was occupied by stellate reticulum-like cells (Fig. 2). In majority of the follicles, the stellate reticulum-like cells had been replaced by large polygonal cells displaying eosinophilic granular cytoplasm (Fig. 3). Some of the follicles displayed cystic degeneration along with the granular change in their central portion

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(Fig. 4). The follicles were separated by moderately collagenous connective tissue.

DISCUSSION

Granular cell ameloblastoma is a rare variant of ameloblastoma, accounting for only 3.5% of ameloblastoma cases.¹ Hartman reviewed 20 cases of the granular cell ameloblastoma from the files of Armed Forces Institute of Pathology and reported an average age of 40.7 years of occurrence with no distinct gender predilection.⁴ All tumors occurred in the mandible, majority affecting the posterior regions. Compared to the other ameloblastoma subtypes, no distinguishing radiographic findings have been reported.⁹

The granular cell ameloblastomas thought to behave more aggressively, with a greater tendency to metastasize.⁴ Cases with metastasizing granular cell ameloblastoma to lymph nodes, lungs and cervical vertebrae have been reported.^{5,11,12} However, this has been disputed by some authors, because no correlation has been found between

histologic type and clinical behavior.¹⁰ Consensus is that histologic variant should not modify treatment.⁸

Granular cell ameloblastoma is characterized by the presence of granular cells, which typically occur within the central area of tumor and progressively replace the stellate reticulum. The granular cells tend to be large and have an oval to polyhedral outline. The nucleus is displaced to the periphery of the cells. Prominent coarse granules pack and distend the cytoplasm, imparting the distinctive appearance responsible for the name of these cells.² The cytoplasmic granules have been electron microscopically identified as lysozymes.¹⁵

Granular cell changes have been thought to represent aging or degenerative change.⁷ Some authors have suggested that lysosomes might play a role of autophagy and of remodeling the cytoplasm.¹⁵ Recent immunohistochemical studies suggest that this phenomenon is related with increased apoptotic cell death of the lesional cells and the phagocytosis by neighboring neoplastic cells.¹³ Immunohistochemical investigation proved that the granular cells are positive

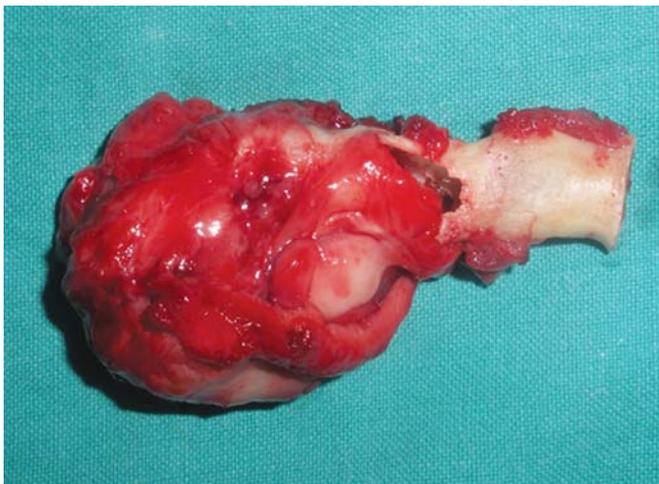


Fig. 1: Biopsy specimen

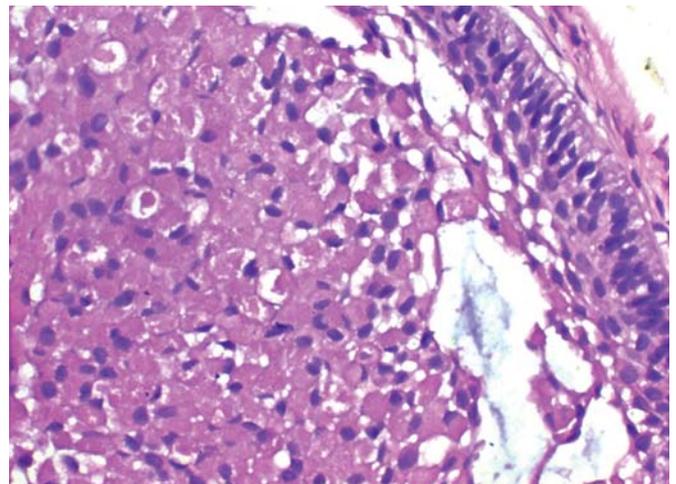


Fig. 3: Ameloblastic follicle, where the stellate reticulum-like cells replaced by large polygonal cells displaying eosinophilic granular cytoplasm

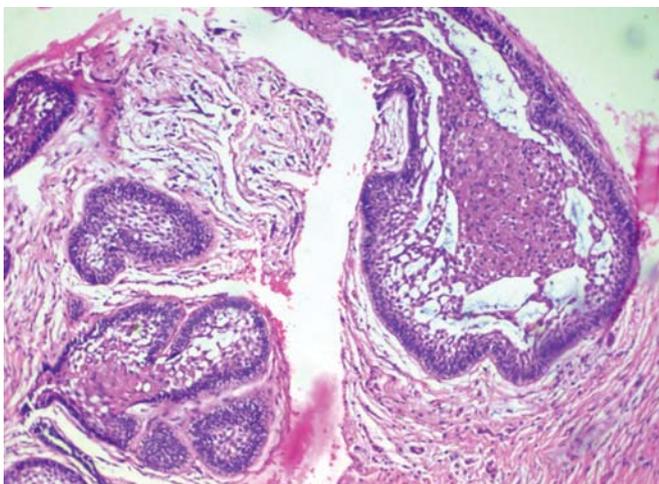


Fig. 2: Odontogenic follicles with central stellate reticulum-like cells

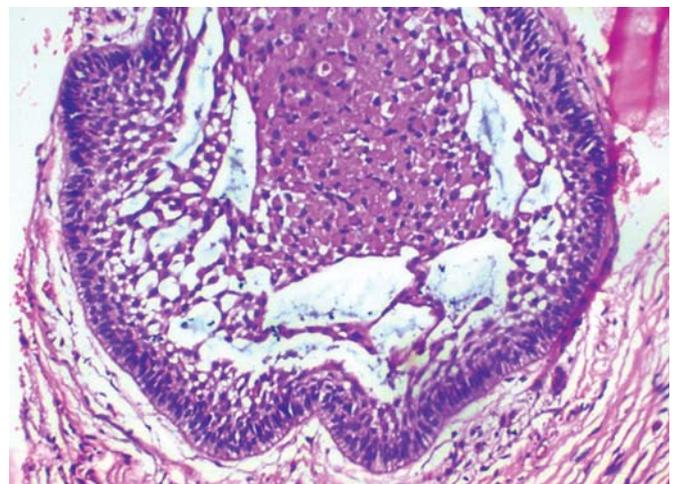


Fig. 4: Ameloblastic follicle with cystic degeneration and granular cells

for cytokeratin, CD68, lysozyme and alpha-1-antichymotrypsin, but negative for vimentin, desmin, S-100 protein, neuron-specific enolase and CD15, indicating epithelial origin and lysosomal aggregation.¹⁴ Granular cells also show strong positivity to laminins 1 and 5 and fibronectin.¹⁶

An investigation of the role of the mitochondria—mediated apoptosis signaling pathway showed decrease or loss of immunoreactivity for the apoptotic protease-activating factor-1, caspase-9 and apoptosis—inducing factor in the granular cells of granular cell ameloblastomas.¹⁷ Kumamoto et al¹⁸ demonstrated that the granular cells in granular cell ameloblastomas showed immunoreactivity for (BH3-only proteins) Bid, Bim, Bad, Noxa and Puma while other subtypes like acanthomatous ameloblastomas showed no reactivity, suggesting a possible additional role of these proteins in tumor cell differentiation.

CONCLUSION

Granular cell ameloblastoma is a unique lesion which shows a high rate of recurrence and an aggressive nature. The future molecular studies might be able to put a better perspective with regard to its pathogenesis. However, keeping in mind the case above, all the ameloblastoma cases should be kept on long-term follow-up.

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