Ameloblastoma with granular cell pattern - A bizarre presentation

Jesmith Elsa Jacob[1*], Asish Rajasekharan[2], Tinky Bose C[3], Ramesh .S[4], Sunu Ramachandran[5], Akhilanand Chaurasia[6]

[1]Senior Resident, [2]Associate Professor and Head, [3]Professor and HOD, [4,5]Assistant Professor, Dept. of Oral Medicine & Radiology, [1,2,4]Government Dental College, Alappuzha, Kerala, [3,5]Government Dental College, Thiruvananthapuram, Kerala, [6]King George Medical University, Lucknow, Uttar Pradesh, India

***Corresponding Author: Jesmith Elsa Jacob**
Email: jesmithjacob7@gmail.com

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. Furthermore, this histologic subtype is considered to be controversial in its potential of recurrence after surgical treatment because cases of recurrence have been described in which the secondary tumor was more aggressive. This article is aimed at portaying a case report of granular cell variant of ameloblastoma affecting a 48-year old male.

Keywords: Ameloblastoma, Granular Cell Odontogenic Tumor, Lysosome like organelles.

Introduction
Ameloblastoma, a benign epithelial odontogenic tumor of the jaws accounts for 1% of all oral tumors and 9–11% of odontogenic tumors with an incidence of 3/10 million. It occurs in three different clinical‑radiographic patterns: conventional intraosseous solid and multicystic (86%), unicystic (13%) and peripheral (1%). The common histological patterns include the follicular (32.5%) and plexiform (28.2%) ones, less common being the acanthomatous (12.1%), granular, desmoplastic (8.6‑13%) and basal (2%) forms.[1]

Despite current nomenclature using the term "granular cell ameloblastoma", this subtype is not classified as such by the latest update of the World Health Organization Classification of Head and Neck Tumours. Granular cell ameloblastoma (GCA), a relatively rare histologic subtype, is characterised by large round/cuboidal eosionophillic cells with granular cytoplasm and, in most instances, it is blended with a follicular subtype. 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. The hallmark of this tumor is its locally aggressive behavior owing to its alarming growth rate which may sometimes reach enormous proportions. Modern day radiographic techniques however overcome this problem and facilitate early diagnosis.[2]

Although the treatment and prognosis are virtually the same (with the possible exception of more aggressive desmoplastic variant), knowledge of various histopathologic subtypes is a prerequisite for accurate diagnosis and management. 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. When this granular cell change is extensive in an ameloblastoma, the designation of granular cell ameloblastoma is appropriate.[3]

The purpose of this article is to present a case of unusual variant of ameloblastoma highlighting its unusual clinical appearance.

Case Description
48 year old male patient, manual labourer by profession residing in vithura presented with a slow growing swelling associated with vague intermittent pain involving left side of the lower jaw for 2 year duration. Associated symptoms like paraesthesia and occasional bleeding were present. Extraorally, facial asymmetry was noted on left side of face. The swelling was seen over the left body of mandible 4x2cm in size extending antero-posteriorly from parasymphysis to angle of mouth and superoinferiorly from ala tragus line to inferior border of mandible on left side (Fig. 1). Tender on palpation and was firm in consistency. On Intraoral examination (Fig. 2) a well-defined localised swelling of size approximately 4 x 6cms was noted on the left edentulous mandibular alveolar ridge extending posteriorly from the 32–35 region with obliteration of buccal and lingual sulcus. Swelling was mildly tender on palpation, variable consistency ranging from firm to soft near 35 region buccally. Marked expansion of the lingual cortex with firm to hard in consistency and egg shell crackling was elicited near 35 on palpation. The swelling was seen displacing the tongue laterally. Linear ulceration of size 2 x 0.5cm with pseudomembranous floor and sloping margins seen on anterior mucosal surface. Dusky red colour seen on mucosa overlying the nodule on anterolateral to the ulcer. The remaining surface appears stretched with dilated and prominent blood vessels. A provisional diagnosis of ameloblastoma was considered. Therefore, in the current case, the differential diagnosis included the main variants of ameloblastoma, such as keratocystic odontogenic tumor, central giant cell lesion, and odontogenic myxoma, based on the location of the tumor.

Routine blood examination were within normal range. Panoramic radiograph (Fig. 3) revealed a solitary, unilateral

lesion with ill-defined corticated multilocular radiolucency of size approximately 7 x 8cm involving the left side of mandible. The lesion extended posteriorly from the symphysis region to the posterior body of mandible. Superior-inferiorly it extended from the alveolar crest to the inferior border causing the inferior border to expand below its level. Multiple areas of increased radiolucency suggestive of cortical perforations were noted within the lesion. Internal structure of the lesion showed a predominantly radiolucent lesion with multiple thin radiopaque lines suggestive of bony septae giving multilocular, soap bubble appearance to the lesion with effacement of left mandibular canal. Relatively increased radioopacity corresponding to soft tissue shadow was seen surrounding the lesion.

CT scan (Fig. 4) exhibited an ill-defined expansile heterogenous soft tissue density lesion involving anterior half of the body of mandible on left side. Antero-inferiorly, it is extending upto symphysis without crossing the midline. The cortex appeared markedly thinned out with multiple areas of cortical perforations. Post contrast: The lesion showed moderate heterogenous enhancement with peripherally enhancing cystic areas in the medial aspect of the lesion. The lesion measured about 3.9 (TR) x 4.6 (AP) x 3.8 cm (CC). Anterolaterally, the lesion was seen compressing the subcutaneous tissue producing a focal buldge in contour with effacement of subcutaneous fat in few areas. No definite skin breach or thickening of skin noted. There was lateral bulging and displacement of left buccinato muscle with the inferior end of left buccinators not separately seen from the lesion, possibly infilterated. Medially, the lesion was having mass effect on tongue, which is displaced mildly laterally. There was poorly distinct fat plane with left mylohyoid muscle and in few areas it was not separately visualised from the lesion possibly, infilterated. Superiorly, the lesion was seen extending into the floor of mouth with well-defined fat plane with the ventral surface of tongue. The margins with anterior belly of digastric was maintained.

Bilateral multiple level IA, IB and II lymph nodes noted, largest measuring 8-9 mm in SAD. Rest of the visualised soft tissue structures of neck, appeared grossly unremarkable.

FNAC from Submental node revealed scattered polymorphous population of lymphoid cells with predominance of mature lymphocytes, few plasma cells, centrocytes, and occasional centroblasts with occasional scattered tangible body macrophages were seen. Features were suggestive of reactive hyperplastic lymph node.

Sections of the formalin-fixed paraffin-embedded tissue, stained with the hematoxylin and eosin (Fig. 5) shows fibrous connective tissue exhibiting numerous odontogenic epithelial islands with peripheral tall columnar cells showing a reversal of polarity. The center of the island showed stellate reticulum like cells. The connective tissue also shows the presence of extensive coarse granular eosinophilic cells distributed throughout the section. Most of the odontogenic islands also reveals such granular cells within them. The central stellate cells may be replaced by large eosinophilic rounded or polyhedral granular cells. The granular cells may take up a complete epithelial island, and then even the basal cells are granular. Histopathological differential diagnosis included granular cell myoblastoma. Marginal bone resection of the lesion was performed through an intraoral approach, followed by peripheral ostectomy of the remaining bone with a drill, apposition, and fixation of a premolded 2.4-mmtitaniumplate.The final diagnosis of Granular Cell Ameloblastoma was rendered.

Fig. 1: Localized ovoid swelling over left body of mandible

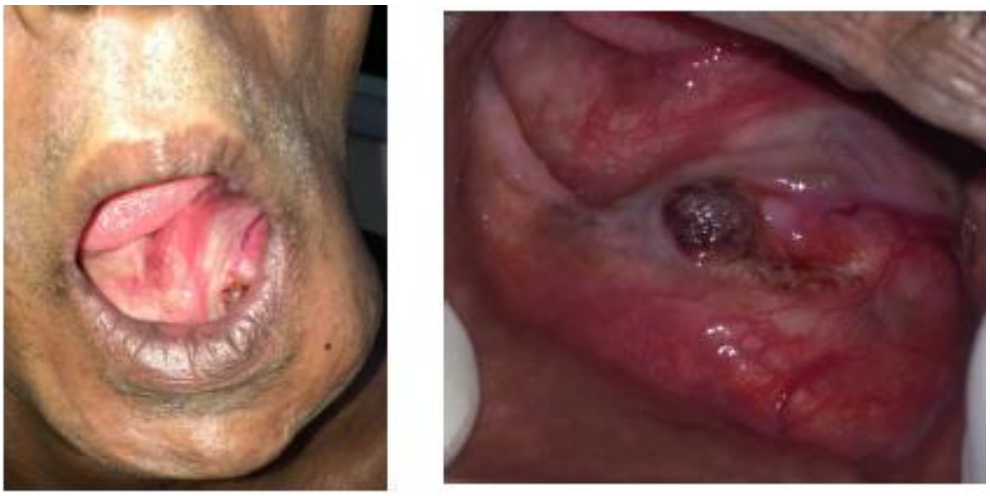

Fig. 2: well-defined localized swelling with linear ulcer and nodule.

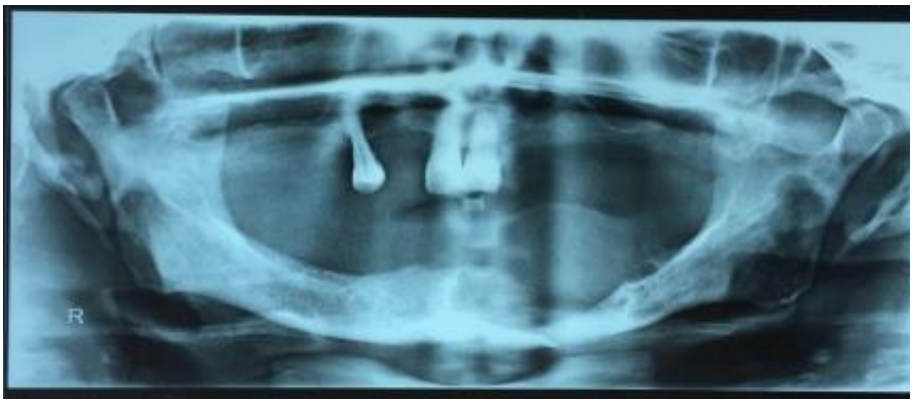

Fig. 3: Multilocular radiolucency with thinned lower border of mandible

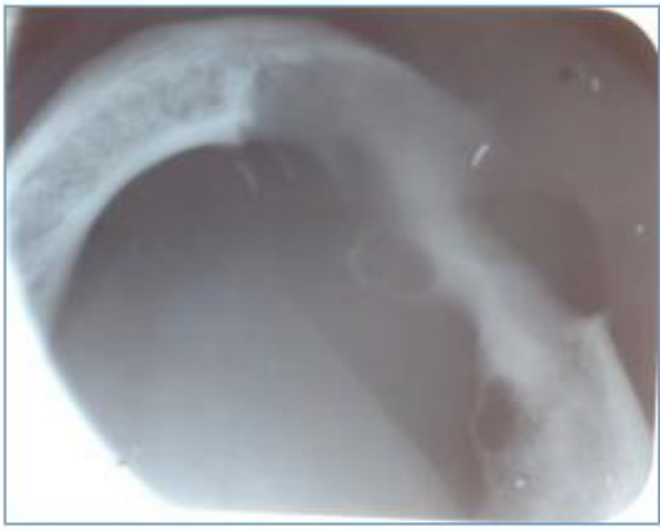

Fig. 4: Buccolingually expansile multilocular radiolucency with cortical perforations

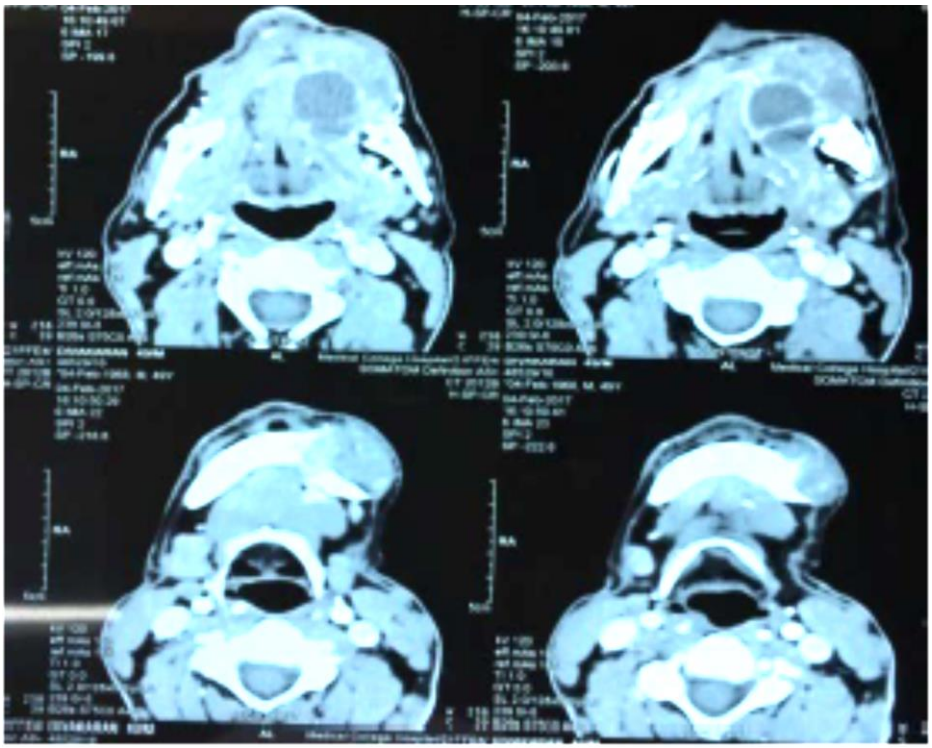

Fig. 5: Ill-defined expansile heterogenous hypodense lesion

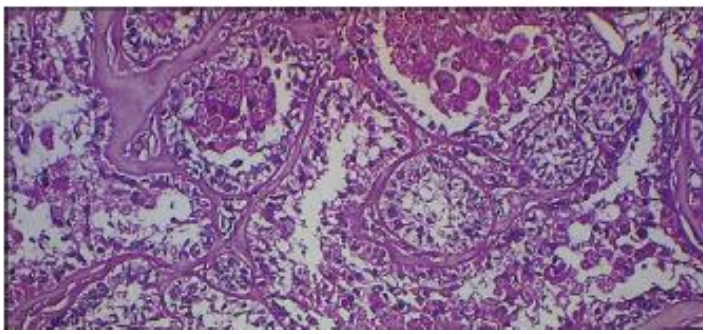

Fig. 6: The microscopic appearance exhibiting fibrous connective tissue with numerous odontogenic epithelial islands with peripheral tall columnar cells showing reversal of polarity. The center of the island shows stellate reticulum like cells which is replaced by granular cells (under x 10 magnification)

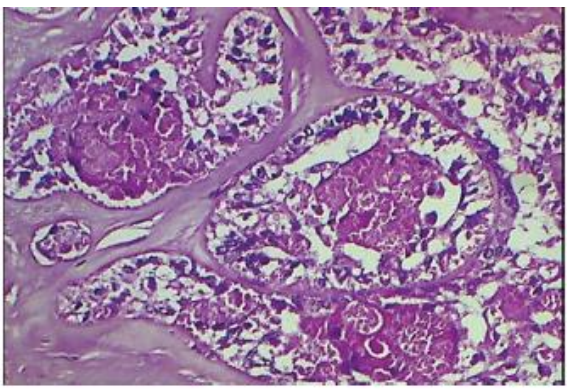

Fig. 7: The microscopic appearance shows central stellate cells replaced by large eosinophilic rounded or polyhedral granular cells (under x10 magnification

Discussion

Granular cell ameloblastoma is diagnosed by the presence of granular cells, which typically occur within the central area of tumour and progressively replace the stellate reticulum. Originally they were considered to represent an aging or degenerative process, but recent immunohistochemical studies suggest that this phenomenon is related with increased apoptotic cell death of the lesional cells and the phagocytosis by neighbouring neoplastic cells.[4] Granular cells are just 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 and formation of cystic areas. It was speculated that, with age, the unnecessary aged components progressively increase in the cytoplasm of some of the tumor cells, while the ability of lysosomes to eliminate these materials decreases; hence, their cytoplasm becomes packed with lysosomal granules. The first studies considered

granular cells to be phagocytic with the accumulation of a peculiar metabolite that was subsequently identified as the presence of numerous cytoplasmic lysosomes. Immunohistochemical investigation proved that the granular cells are positive 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.[5]

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.[6] All tumors occurred in the mandible, majority affecting the posterior regions. Compared to the other ameloblastoma subtypes, no distinguishing radiographic findings have been reported. The granular cell ameloblastoma thought to behave more aggressively, with a greater tendency to metastasize.[6]

The differential diagnosis of granular cell ameloblastomas includes other oral lesions with a similar morphology of granular cell accumulation, including granular cell odontogenic tumour, granular cell tumour and congenital epulis. These lesions have different biologic behavior and should be discriminated from granular cell ameloblastomas.[7]

The granular cell odontogenic tumour is a type of odontogenic tumour featuring a proliferation of large cells with eosinophilic granular cytoplasm, which appear similar to the cells of granular cell ameloblastoma. They are very rare lesions which have been reported in patients of a wide age range with a female predilection. Radiographically, they appear as multilocular or unilocular radiolucent lesions with occasional radiopacities. In contrast to granular cell ameloblastoma, the granular cells of granular cell odontogenic tumour are not located within epithelial islands but constitute part of the tumour stroma. 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.[8] The tumour is usually treated with enucleation and vigorous curettage, rarely recurs and its prognosis is very good.[9]

The granular cell tumour is an uncommon benign soft tissue neoplasm that shows predilection for the oral cavity. The most common site is the tongue, followed by the buccal mucosa. Differential diagnosis from a granular cell ameloblastoma is necessary when there is peripheral localization or cortical perforation and soft tissue extension of the ameloblastoma. Granular cell tumour usually occurs in the fourth to sixth decades of life and shows a female predilection. Clinically, it appears as an asymptomatic sessile nodule of small size. Microscopic examination reveals large polygonal cells with abundant, pale, eosinophilic granular cytoplasm, with a small vesicular nucleus, arranged into sheets or nests.

The granular cell tumour is treated with conservative local excision and recurrence is uncommon.

Congenital epulis is an uncommon soft tissue tumour 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 occurrence of the latter in patients of older age. The lesion is treated with conservative excision and there have been no reports of the recurrence. Additionally, it appears to stop growing after birth and may even diminish in size. In recent years, research efforts have attempted to elucidate the molecular factors that govern the pathogenesis and progression of ameloblastoma and its subtypes by regulating critical cell processes, such as cell proliferation, apoptosis and differentiation. Interestingly, the granular cells in granular cell ameloblastomas showed immunoreactivity for these BH3-only proteins, while other subtypes like acanthomatous ameloblastomas showed no reactivity, suggesting a possible additional role of these proteins in tumour cell differentiation. The prognosis of AGC is considered favorable when treated early; however, a recurrence rate of over 30% has been reported, implying a potentially unknown, aggressive behavior on the part of the AGC.[10]

Conclusion

Granular cell ameloblastoma is a unique lesion which shows a high rate of recurrence and an aggressive nature. The granular cell ameloblastoma is a rare condition 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, early diagnosis and prompt surgical treatment in granular cell ameloblastoma is of prime importance owing to is high recurrence rate. 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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None.

Disclosure Statements

The authors report no conflicts of interest related to this study.

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