INTRODUCTION
Odontogenic tumors comprise complex group of lesions of diverse histopathological types and clinical behavior.[1] Ameloblastoma, a true neoplasm of enamel organ type tissue, is a slow growing but locally invasive benign epithelial tumor of jaws accounting for about 11% of odontogenic tumors. Ameloblastoma occurs over a broad age range with average age range being fourth decade of life. It shows a definite predilection for the mandibular posterior region. Radiographically, often presents as expansile lesion with a multilocular appearance and with thinning of the cortical plate. According to the 2005 histological classification of tumors of the World Health Organization, ameloblastoma are classified into – solid/multicystic, extraosseous/peripheral, desmoplastic and unicystic. Histopathological variants include follicular, plexiform, granular, basal cell, acanthomatous and desmoplastic ameloblastoma. Granular cell ameloblastoma (GCA) is a less common lesion accounting for 3–5% of all histologic subtypes of ameloblastoma.[2] This article attempts at highlighting this relatively less common tumor - GCA involving the lower jaw.

CASE REPORT
A 55-year-old male patient reported with a painless swelling on right side of the lower jaw. Patient gave a history of swelling in mandibular right molar region 12 years back for which he got his molar extracted. He developed a swelling in the same region a year later and was treated for the local infection with incision and drainage. The swelling persisted for 6 years swelling and then gradually increased to the present size. Extraorally, the swelling was ovoid in shape, firm in consistency and extended from right mandibular molar region to anterior region of the mandible. Intraorally, the swelling extended from mandibular right third molar region to lower left first premolar area with obliteration of buccal and lingual vestibule [Figure 1]. Overlying mucosa was intact. Regional lymph nodes were palpable. The medical history of the patient was not contributory. Past medical history was not relevant. Panoramic view revealed a large multilocular radiolucency extending from lower right third molar region to lower left first premolar region [Figure 2]. An incisional biopsy was carried out which histopathologically revealed tumor cells arranged in form of follicles within a fibrous connective tissue stroma [Figure 3]. The follicles were lined by tall columnar ameloblasts like cells organized in palisaded pattern and with stellate reticulum like cells in the center. Most of the follicles showed the presence of large granular cells forming the central mass of the
A diagnosis of GCA was made. The lesion was surgically excised, and the gross specimen was sent for histopathological examination. Gross specimen revealed section of the mandible extending from lower right third molar region to lower left second premolar with buccal and lingual cortical plate expansion [Figure 5]. On further histopathological examination, similar presentation was observed, and a diagnosis of GCA was confirmed.

**DISCUSSION**

Ameloblastoma are tumors of odontogenic epithelial in origin.[1] Though benign, they are locally aggressive in nature with a propensity for recurrence. Ameloblastoma accounts for 1% of all oral tumors and 11% of all odontogenic tumors.[2] Central lesions develop more frequently in molar ramus region in mandible, in molar region in maxilla followed by maxillary sinus and floor of the nose. GCA is a relatively rare lesion and in most instances, it is found as an admixture with other histologic patterns, particularly follicular subtype.[4] It accounts for 3–5% of all histological subtype. Granular cell change in ameloblastoma is a rare histological entity. It was first seen by Krompecher in

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**Figure 1:** Clinical image shows intraoral swelling

**Figure 2:** Orthopantomogram showing multilocular swelling

**Figure 3:** Histopathological image shows follicles with central granular cells (H and E, x10)

**Figure 4:** Histopathological image shows eosinophilic granular cells in the center of follicle and peripheral ameloblast like cells (H and E)

**Figure 5:** Gross specimen
GCA exhibit large eosinophilic granular cells forming the central mass of tumor islands. There is a marked transformation of cytoplasm of stellate reticulum like cells so that they appear coarse granular and eosinophilic. Granular cells may be cuboidal or rounded. At times, a layer of stellate reticulum may be seen at the periphery separating the granular cells from tall columnar cells. Occasionally granular change may also affect peripheral columnar cells. Different views have been put forth to describe the nature of these granules. It has been suggested that these granules are lysosomal aggregates. Ultrastructural studies also suggest that these are lysosomal aggregates and are responsible for granularity of cells.

Lysosomal aggregation within the cytoplasm may be due to dysfunction of either lysosomal enzyme or lysosome – associated protein involved in enzyme activation, enzyme targeting or lysosomal biogenesis. Leading to accumulation of substrate that would normally be degraded in endosome – lysosome system. It was also considered that lysosomes might have resulted from some genetic alterations of granular cells.

Some attribute granularity to aging or degenerative process. It has been suggested that numerous lysosomes accumulate as a result of decrease in the ability of lysosomes to dispose the unwanted components that accumulates in the cell with age. Fibronectin is one of the biomarkers for replicative senescence. An increase in fibronectin expression has been observed in granular cells indicating granular cells changes could be associated with an age-related transformation.

Authors suggest that the granularity in GCA might be caused by increased apoptosis and associated phagocytosis by neighboring neoplastic cells. Balaji et al. have reported occurrence of numerous apoptotic cell fragments with condensed nuclei in granular cell clusters using Annexin V, a marker to detect early apoptosis. They also noted that most of these fragments were phagocytosed by adjacent neoplastic cells. Studies suggest a decreased expression of several apoptosis-related factors such as Bcl-2 family proteins and p53 protein in ameloblastoma.

Immunohistochemical studies have revealed that these granular cells and tall columnar cell lining the follicle are cytokeratin positive indicating epithelial in origin. It has been suggested immunohistochemically granular cells are positive for CD68, lysozyme and α1 antichymotrypsin but negative for vimentin, desmin, S-100 neuron-specific enolase (NSE) and CD15 indicating cytoplasmic lysosomal aggregates are not of mesenchymal myogenic or neurogenic origin. Some studies have suggested the expression of laminin-5 in granular cells and a weak expression in peripheral cells. This might indicate the role of laminin-5 in transformation of granular cells.

The 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. Granular cell odontogenic tumor is a rare odontogenic neoplasm with a tendency to occur in the mandibular posterior region and is composed of granular cells and nests or islands of the odontogenic epithelium. The granular cells are positive for vimentin, CD68, lysozyme, muscle-specific actin, smooth muscle actin, calponin, neuron specific enolase, CD138, and Bcl-2. Granular cell tumor is relatively rare benign neoplasm that occurs in any part of the body including orofacial region. Immunohistochemical studies of granular cell tumors suggest a neural or neuroectodermal origin of the granular cells. Cells exhibit positive staining for S-100, NSE, vimentin, glycoprotein, neurofilament. Histologically congenital epulis does show the presence of large cells with eosinophilic granular cytoplasm within fibrous connective tissue stroma, which stain positively for phosphotyrosine and are S-100 negative. However, these lesions are seen to occur on gum pads of infants. Oncocytomas though rare in the jaws, possibility of occurrence cannot be ruled out. In such rare cases, differential diagnosis is made with immunohistochemistry staining as oncocyes stain positive for mitochondrial antigens.

Treatment of GCA is similar to other subtypes of the solid/multicystic ameloblastoma. Previous studies suggest GCA to be most aggressive lesion, whereas some studies suggest that the granular cell are just a transitional phase in life cycle of ameloblastoma, starting with normal stellate reticulum like cells, leading to production of granules and finally leading to degeneration and formation of cystic areas. The prognosis of GCA is favorable if treatment is initiated in time. However, Reichart et al. have reported a 33.3% recurrence rate for GCA. A regular follow-up is important because of reports of recurrences even up to 8 years after initial treatment.

**CONCLUSION**

Granular cell ameloblastoma is a relatively rare lesion. Nature of granules in GCA has been a matter of discussion. Understanding the nature of granular cells...
not only in GCA but also in similar lesions will aid in differentiating as well as understanding the clinical behavior of the lesion.

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