ABSTRACT:
Granular cell ameloblastoma is a rare variant, accounting for 1-5% (3.5%) of ameloblastomas. It has clinical behavior similar to other subtypes, and show high tendency to recur on conservative surgical approaches. It can also show metastasis, hence the treatment plan should include regular follow up of the patients, after radical surgery. Here we are presenting a case report of granular cell ameloblastoma occurring in a 45 years old male patient clinically, the lesion was occurring in the left posterior mandible creating soap bubble appearance on radiography. Histopathologically, granular cell changes were prominent. The granular appearance is due to lysosomal aggregation and their presence indicates degenerative change or related to aging phenomenon rather than aggressiveness. The lesion was treated by surgical resection and a period of 3 years follow up showed no recurrence.

Keywords: Granular cell ameloblastoma, Degenerative process, Metastasis, Surgical resection.

INTRODUCTION:
"Ameloblastoma is a true neoplasm of enamel organ type which does not undergo differentiation to the point of enamel formation". It is the second most common odontogenic neoplasm, after odontoma. Although benign and slow growing, its high incidence and locally invasive clinical behavior make it the most significant odontogenic neoplasm. It may arise from rests of dental lamina, developing enamel organ, epithelial lining of odontogenic cysts, or from the basal cells of the oral mucosa. It is currently classified as multicystic (solid) (86%), unicystic (13%) and peripheral (1%) types according to their presentation and occurrence.

Histopathologically, six types are recognized, of which follicular and plexiform patterns are the most common and acanthomatous, granular cell, basal cell and desmoplastic types are less common. The case being presented, granular cell ameloblastoma (GCA) is a rare histological variant of ameloblastoma “with marked transformation of the cytoplasm of stellate reticulum like cells into a coarse, granular eosinophilic appearance”. Granular cell changes are more common in the solid variant but, can also be seen in unicystic or cystic types. All histological types of solid/multicystic ameloblastomas may recur or metastasize with conservative surgical treatment. GCA has a higher chance of recurrence and metastasis to distant sites such as lungs.

CASE REPORT:
A 45 year old male patient presented with a swelling in the left lower side of the face which had been gradually increasing since 1 year. The patient experienced intermittent mild pricking pain since one month, which was aggravated on mastication.

Examination of the lesion:
Extraorally there was a diffuse swelling measuring about 7x5 cm on the left side of the mandible extending antero-posteriorly from symphysis region (Fig 1) to 2 cm in front of the angle of mandible. Supero-inferiorly, the swelling extended from the line joining the corner of mouth to the tragus of the ear extending 2 cm below the angle of mandible. The skin over the swelling showed a scar with an erythematous area in the center. Detailed history and enquiries from the patient could not elicit the cause for the scar. On palpation, the temperature of the skin over the swelling was normal, and the lesion...
was bony hard in consistency, with irregular surface and indistinct borders. Right and left submandibular lymph nodes were enlarged, movable and non-tender, measuring about 0.5x1 cm in dimensions. Intraorally the swelling was obliterating the buccal vestibule (Fig 2, 3) and extended from distal aspect of 31 upto distal aspect of 38. The swelling was non-tender, firm to bony hard in consistency and showed buccal cortical plate expansion with well-defined anterior border. All the teeth on the left side of the mandible were clinically mobile, and the anterior teeth showed gingival recession. Patient chewed betel nut once or twice a day for the past 8-10 years. Staining of teeth, attrition and poor oral hygiene were noted (Fig 2, 3).

Electrical pulp vitality test revealed 33,34,35,36,37 were non-vital. The panoramic radiograph showed a well-defined multilocular radiolucency with soap bubble appearance extending from 31 to angle of mandible with thinning of the cortical plate and root resorption in relation to 33,34,35,36 and 37 (Fig 4). Mandibular occlusal view showed buccal displacement of 35 and buccal cortical plate expansion. CT scan was suggestive of ameloblastoma.

Histopathological examination of the incisional biopsy revealed dense connective tissue stroma with areas of odontogenic epithelial islands in follicular pattern (Fig 5). Most of the islands had peripheral lining of ameloblast like cells (all columnar cells with reversal of polarity, hyperchromatic nuclei and subnuclear vacuolization (Fig 7) and the center of the islands showed large round to oval cells with eosinophilic granular cytoplasm and prominent, eccentric nuclei (Fig 6,7). Other islands showed stellate reticulum like cells at the center with cystic degeneration in focal areas. Hyalinization was noticed around few of the odontogenic islands (Fig 5). The surrounding stroma was highly collagenous in nature, with fibroblasts, blood vessels and mixed inflammatory infiltrate. Based on the above features, the lesion was diagnosed as a granular cell ameloblastoma.

Patient was treated by partial mandibulectomy under general anesthesia. Risdon’s extraoral approach was used, to raise the cervical skin flap and expose the tumor. The dissection was done...
starting from 42 region extending posteriorly to the mid ramus region of the left mandible by employing “inverted L” osteotomy. The continuity was bridged using stainless steel reconstruction plate. On microscopy, the excised specimen confirmed the diagnosis of granular cell ameloblastoma and a period of 3 years follow up showed no recurrence.

**DISCUSSION:**

Granular cell changes in ameloblastoma are rare seen in 1-5% of ameloblastomas (Reichart et al - 3.5%). These changes were first identified and described by Krompecher in 1918, who called these cells as pseudoxanthomatous cells.

Such granular cell changes are seen in a number of pathological entities like granular cell odontogenic fibroma, granular cell epulis and granular cell tumor. Among these lesions, granular cell changes in ameloblastoma are more common. Most authors currently agree that these cell changes do not change the prognosis of GCA from conventional ameloblastomas.

Conventional solid or multicystic ameloblastomas occur in a wide age group (10-90 years), with the average age of diagnosis being 33-39 years that shows no gender or race predilection, but some studies indicate a greater frequency in blacks.

**Fig 5:** Granular cells replacing the stellate reticulum cells in the ameloblastic follicles (H&E, 20x)

**Fig 7:** Cellular details of ameloblast like cells and granular cells (H&E, 40x)

Granular cell ameloblastoma is a histopathological diagnosis characterized by the occurrence of granular cells within the central area of ameloblastic tumour follicles (sometimes granular change can be seen in plexiform type also) and progressively replaces the stellate reticulum. This may also extend to include the peripheral columnar or cuboidal cells as well. The granular cells may be cuboidal, columnar, or round, their cytoplasm is filled with acidophilic granules, identified ultrastructurally as lysosomal aggregates. The nuclei of these granular cells are pyknotic and hyperchromatic. The term granular cell ameloblastoma is used when there is predominantly granular cell change.

Earlier, granular cell ameloblastoma was believed to be a more aggressive variant, but currently granular cell changes are believed to indicate degenerative changes or related to aging phenomenon.

Histopathologically, granular cell lesions like granular cell odontogenic fibroma, granular cell tumor (GCT) and congenital granular cell epulis need to be differentiated from GCA. In granular cell odontogenic fibroma, the granular cells occur in the tumor stroma whereas, in GCA, it is within the odontogenic islands. GCT is a soft tissue lesion, and congenital epulis occurs in newborn.
Immunohistochemical differentiation can also help as granular cell ameloblastoma is of epithelial origin and other lesions in the differential diagnosis are mesenchymal in origin. Special stains like Periodic Acid-Schiff (PAS), Phosphotungstic Acid–Hematoxylin (PTAH) help in differentiating GCA cells from granular cells of mitochondrial origin like oncocytes.

Irrespective of the histological subtypes, for large ameloblastomas without cortical perforation, Sammartino et al have recommended conservative treatment like curettage as the mode of treatment with regular follow up to avoid cosmetic problems. Therefore, radical surgical methods are recommended. As GCA may metastasize and as the recurrences have occurred even after 8 years of initial treatment, the patients should be kept under periodic observation. Thus, the recognition of this histological variant plays a key role in treatment plan and also “follow up data suggest that the presence of granular cells in an ameloblastoma might be of some prognostic significance in terms of initial treatment performed”.

REFERENCES: