Case Report

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Pathology Section

Granular Ameloblastoma of Jaw: A Rare Histopathological Entity

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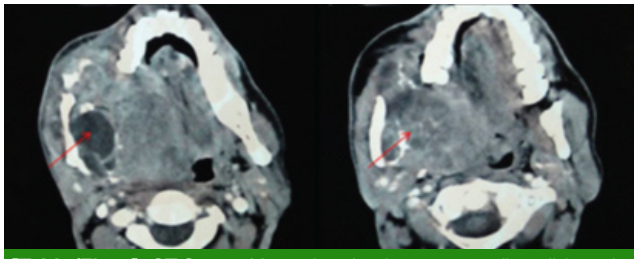
ABSTRACT

Ameloblastoma is a benign odontogenic tumor of epithelial origin. Granular ameloblastoma is a rare subtype of ameloblastoma. In most of the cases, it is found admixed with other patterns of ameloblastoma. Pathogenesis of granular change in tumor cells seems to be age-related; however, ultrastructural and immunohistochemical studies showed that cytoplasmic granularity is caused by lysosomal overload. We report a case of granular ameloblastoma in mandible of a 45-year-old male. The unique microscopic features of granular ameloblastoma help in differential diagnosis from other odontogenic and non odontogenic tumors with granular cell component. Radical excision with adequate margin of uninvolved tissue is important as it has a high recurrence rate.

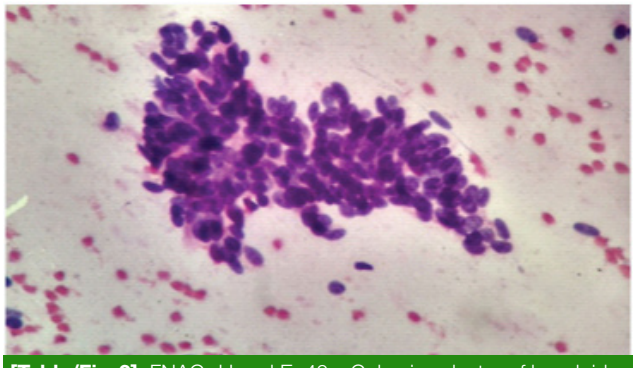
Keywords: Granular cell, Lysosomes, Odontogenic tumor, Recurrence

CASE REPORT

A 45-year-old male presented in ENT Outpatient Department with a swelling on the right cheek for 10 years and pain for 15 days. Swelling was insidious in onset and gradually increased in size leading to facial asymmetry. On extraoral examination, a hard fixed tender swelling measuring 8x6 cm in size was observed. There was a sinus with purulent discharge on overlying skin. Intraorally, swelling was hard and involved alveolar margin of lower jaw, soft palate and posterior pharyngeal wall. There was no palpable regional lymph node. Routine biochemical and hematological investigations were within normal limits. Computed tomography showed a large expansile solid cystic enhancing mass lesion involving right half of the body, ramus and coronoid process of mandible with mild lateral subluxation of temporomandibular joint, mass effect on adjacent tongue and lateral pharyngeal wall with narrowing of pharyngeal lumen. Possibility of giant cell tumor was suggested [Table/Fig-1]. Fine needle aspiration (FNA) of the swelling showed cohesive clusters of basaloid cells with round to oval nuclei and fine granular chromatin. Occasional stromal fragments were also seen. Osteoclastic giant cells were not seen. The possibility of benign odontogenic tumor was suggested [Table/Fig-2]. An incisional biopsy was done. Sample from right gingivobuccal region was taken which on histopathological examination showed islands of tumor cells arranged in plexiform pattern and lined by ameloblastic cells with reverse polarity of nuclei, vacuolated cytoplasm, arranged in palisading pattern. Centre of the islands had



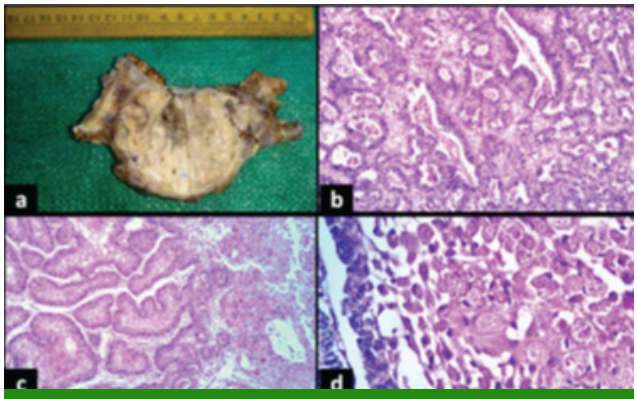
[Table/Fig-1]: CT-Scan of face showing large expansile solid cystic enhancing mass lesion.



[Table/Fig-2]: FNAC- H and E, 40x, Cohesive cluster of basaloid cells.

oedematous spindled stellate reticulum-like cells suggesting ameloblastoma [Table/Fig-3b]. Since, ameloblastoma has a high recurrence rate with enucleation so patient was planned for radical excision. Hemimandibulectomy specimen with a firm greyish white to greyish brown globular mass measuring

8x6 cm in size received. Cut surface showed areas of hemorrhage and necrosis [Table/Fig-3a]. Histopathological examination showed predominant follicular pattern of ameloblastoma with areas of granular cell change [Table/Fig-3c].These granular cells had coarse granular eosinophilic cytoplasm [Table/Fig-3d]. So, a final diagnosis of granular ameloblastoma was given. Post operative period was uneventful and the patient is on regular follow-up for last one year with no recurrence.



[Table/Fig-3a]: Gross- Globular tumor mass with areas of haemorrhage and necrosis. **[Table/Fig-3b]:** Incisional biopsy- H and E, 40x, Tumor cells arranged in plexiform pattern. **[Table/Fig-3c]:** Hemimandibulectomy specimen - H and E,10x, Tumor cells in follicular pattern lined by ameloblastic cells and central stellate reticulum like cells with areas of granular cell change. **[Table/Fig-3d]:** H and E,40x, Granular cells with coarse granular eosinophilic cytoplasm.

DISCUSSION

Odontogenic tumors are derived from epithelial, ectomesenchymal and/or mesenchymal element that are still, or have been part of tooth forming apparatus [1]. Ameloblastoma is a locally aggressive benign odontogenic tumor accounting for 1% of all tumors and cyst of the jaw [2]. It involves odontogenic epithelium with mature fibrous stroma without odontogenic ectomesenchyme [1]. It has a broad age of presentation but usually occurs in third to fifth decade of life and shows predilection for posterior region of mandible [3]. Patient usually presents with slow growing painless mass and seek medical attention only when the swelling reaches considerable size leading to facial deformity. Development of giant sized mass indicates persistent growth of tumor [4].

According to the World Health Organization histological classification of tumors, ameloblastomas is classified into –solid/multicystic, unicystic, desmoplastic and extraosseous/peripheral ameloblastoma. Histopathological patterns include follicular (32.5%), plexiform (28.2%), acanthomatous (12.1%), desmoplastic (8.6-13%), granular (3-5%) and basal (2%) [1,5]. These diverse microscopic patterns may occur singly or in various combinations. Granular ameloblastoma, a rare histopathological entity, is usually admixed with follicular pattern. Granular cell transformation mostly takes place in the cytoplasm of stellate reticulum cells but at times may affect peripheral columnar cells [2].

Numerous theories have been put forth to describe the nature of the granules in granular cells. Some attribute granularity to aging or degenerative changes in tumor cells as usually long standing cases of ameloblastoma exhibit granular cell change. Increased expression of fibronectin, biomarkers for replicative senescence, in granular cells support the theory of degenerative process [6]. Ultrastructural studies suggest that granularity of cells is due to lysosomal overload. There is intracytoplasmic lysosomal aggregation due to dysfunction of enzyme or associated protein. Dysfunction of these proteins affect enzyme activation and biogenesis of lysosomes. On immunohistochemical study, granular ameloblastoma is positive for CD 68, lysozyme and α-1anti-chymotrypsin supporting lysosomal nature of granules [2]. Balaji et al., attributed granularity in granular cell to increased apoptosis of tumor cells and phagocytosis by neighboring tumor cells. This theory is supported by increased expression of Annexin V (apoptotic marker) and decreased expression of Bcl-2 and p53 (antiapoptotic marker) in tumor cells [7].

Cytological reports of ameloblastoma are relatively rare in literature. These lesions are rarely aspirated due to lack of clear criteria for cytological diagnosis. FNA has an advantage over biopsy that sampling from multiple sites and deeper part of tumor can be done. Sometimes, due to the cystic nature of the tumor, adequate sampling from representative area can be missed on biopsy [8].

Histopathological differentials of granular ameloblastoma include granular cell odontogenic tumour, granular cell tumour and congenital epulis. These lesions should be discriminated as they have different biological behavior, treatment and prognosis [2]. Granular cell odontogenic tumour show granular cells arranged in lobules lying in stroma along with islands of odontogenic epithelium, cementum like deposits and dystrophic calcifications. Granular cell tumor can occur at any age with peak incidence in fourth to sixth decade of life. Patient usually presents with sessile mucosal nodule on tongue and microscopically, it shows sheets and nests of large polygonal cells with central vesicular nucleus and abundant granular eosinophilic cytoplasm. Odontogenic epithelium is not seen. The overlying epithelium usually shows pseudoepitheliomatous hyperplasia. Congenital epulis is an uncommon benign tumour which occurs almost exclusively on the alveolar ridges of newborn. It is composed of nests of cells with granular cytoplasm set in a prominent vasculature. Odontogenic epithelium can be seen but pseudoepitheliomatous hyperplasia of overlying epithelium is not seen. On

immunohistochemical study, granular ameloblastoma show membranous positivity for cytokeratin (indicating epithelial origin) and cytoplasmic expression of CD 68 (lysosomal marker).Granular cell odontogenic tumor is positive for vimentin, Bcl-2, CD 68 but cytokeratin and S-100 are negative. Granular cell tumor is strongly and uniformly positive for S-100 (indicating neural origin) and show fine granular cytoplasmic positivity for CD 68. It is cytokeratin negative. Congenital epulis is positive for vimentin but S-100 and cyto keratin are negative [1,3].

Prognosis of granular ameloblastoma depends on the type of treatment. Patients managed by enucleation and curettage often show recurrence as microscopic tumor cells lie beyond the macroscopic and radiological boundary. So, radical excision is the treatment of choice [3]. Reichart et al., reported a higher (33.3%) recurrence rate of granular ameloblastoma compared to the more common follicular, plexiform and acanthomatous subtypes [9].

CONCLUSION

Granular cell ameloblastoma is a rare histopathological variant. It is important to identify and differentiate it from other odontogenic and non odontogenic tumors with granular cell change as it has a higher recurrence rate. Early diagnosis and prompt radical excision reduces recurrence rate.

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