

# Nature of granular cells in granular cell ameloblastoma



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## IMMUNOHISTOCHEMICAL STUDY

Objective: To evaluate the nature of granular cells in granular cell ameloblastoma

Study Design: Tissue specimens of five patients with granular cell ameloblastoma were fixed in buffered formalin and later embedded in paraffin wax. Blocks were sliced into 3micron thick sections for immunohistochemicalanalysis using a panel of markers CD68, Bcl2, S100, P53, Cytokeratin(AE1/AE3), vimentin and desmin

Results: All five cases were strongly positive for cytokeratin and CD68. S100 was negative in three cases and showed mild positivity in two cases . Bcl2, P53, Vimentin and Desminwere negative in all the five cases.

Conclusions: This study presents a heterogenous nature of the granular cells, however further validation is required with a larger sample size.

### INTRODUCTION:

Ameloblastoma is a benign odontogenic tumour usually located in the jaw bone [1]. It is considered to be the most common odontogenic tumor. It is a tumor of the enamel organ without formation of enamel. Robinson has defined it as: Unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent. The importance of this tumor lies in its common occurrence, locally invasive behavior which causes marked deformity and serious debilitation. They also demonstrate increased recurrence rate after surgery. [2]It has a distinctive microscopic appearance characterized by the presence of peripheral columnar cells with

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hyperchromatic, reversely polarized nuclei, arranged in a palisaded pattern. [3]

Conventional solid or multicysticameloblastoma exhibits six microscopic subtypes namely follicular, plexiform, acanthomatous, granular cell, desmoplastic and basal cell ameloblastoma. [4]. The follicular and plexiform patterns are the most frequent. Less common histopathologic subtypes include the acanthomathous, granular cell, desmoplastic, and basal cell [1, 5] Granular cell ameloblastoma (GCA) is one of the rare histological variants of ameloblastomaaccounting for only 3. 5% of ameloblastomas. [5]

Granular cell ameloblastoma is characterized by nests of large, eosinophilic granular cells. [6] Aggressive behaviour has been ruled out by many studies and suggest that granular cells are just a transitional or matured phase in the life cycle of ameloblastomas, starting with normal stellate reticulum-like cells, leading to a production of granules and finally leading to degeneration and formation of cystic areas. [7] Whether granular cell change in ameloblastoma is a degenerative process or a harbinger of a more aggressive course is a matter of debate. [8] [Figure 1& 2]

Previous studies have carried out ultrastructural, histochemical and immunohistochemical methods to characterize the nature of the granular cells , though the mechanism involved is poorly understood.

The present study attempts to do an immunohistochemical analysis with a panel of markers to study the nature of granular cells in granular cell ameloblastoma. Due to its rarity accounting to 3. 5%, literature search revealed that majority of them were single case studies . This study is the <https://assignbuster.com/nature-of-granular-cells-in-granular-cell-ameloblastoma/>

first of its kind to report antigenic characterization in five such cases with a wide range of markers.

## **MATERIALS AND METHODS:**

### **Case Selection:**

Formalin-fixed paraffin-embedded tissue blocks of granular cell ameloblastoma were retrieved from the archives of Department of Oral and Maxillofacial Pathology, SRM Dental College, Chennai. The clinical data of the patients are listed in table 1.

### **Immunohistochemical Analysis:**

Immunohistochemical analysis was performed on 3 $\mu$  tissue sections on poly-L-Lysine coated slides (Biogenix Life Sciences Limited, CA, US). Pre-diluted ready to use primary monoclonal mouse anti - CD-68, anti - Bcl2, anti-S 100, anti-P53, anti-cytokeratin antibody (AE1/AE3), anti-Vimentin and anti-Desmin(Biogenix Life Sciences Limited, CA, US)were used followed by thesuper sensitive polymer HRP detection system(Biogenix Life Sciences Limited, CA, US). Colored reactions were developed by incubating with 3'3'-diaminobenzidine and subsequently counterstained with Harris hematoxylin. Positive and negative controls were included in all reactions. Presence of brown coloured end product at the site of target antigen was indicative of positive immunoreactivity. Evaluation of theimmunoreactivity was based on staining intensity and wereclassified asweak, moderate, and strong. Localization of positively stained cells in peripheral ameloblast-like cells, central stellate reticulum like cells, and granular cells were also evaluated.

## **RESULTS:**

Immunoreactivity of the markers used in the study are listed in table 2. CD-68 expressed strong positivity in all the five cases. Positivity was observed only in the granular cells. Cytokeratin (AE1/AE3) expressed strong positivity in all the five cases by staining peripheral cells, stellate reticulum like cells and granular cells. Bcl2, P53, Vimentin and Desmin exhibited negative staining in all the five cases.

#### DISCUSSION:

Granular cell ameloblastoma accounts to 3.5% of all ameloblastomas [11]. The lesion presents with marked transformation of the cytoplasm of the stellate reticulum like cells, so that the cells take on a very coarse, granular, eosinophilic appearance. [5] GCA is known to be aggressive histologic variant among all the ameloblastoma. Granular cells have been described in other odontogenic tumor, the granular cell ameloblastic fibroma and oral lesions, such as congenital epulis and granular cell tumor [12]

The nature of various oral granular cell lesions is unclear, and many theories have been proposed for the origin of granules, the principal ones are odontogenic, fibroblastic, histiocytic, myoblastic, and neurogenic. [13] Granular cells are also seen associated with the enamel organ of developing tooth. [14]

The granular appearance has been ascribed to numerous lysosomes based on histochemical and electron microscopic findings. Ultrastructurally, the osmiophilic internal structure of the lysosomes varies considerably. [15]

Many of these granules approach 1µm in size; giant granules of 30µm in diameter are rarely seen. They present with features of finger-print-  
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like membranous structures, myelin figures, small particles, granules, vesicles, lattice structures, and crystalloids. This diversity may represent different materials and stages of digestion of the lysosomal contents. The myelin figures suggest the presence of phospholipid in the granules.

Therefore, it has been concluded by many authors that numerous lysosomes represent increased cellular actions of the tumour ameloblasts to digest unwanted components [14, 16].

Considerable interest about the nature of granular cells in ameloblastoma ever since it was recognized has happened because of its reported aggressive behaviour however recent literature reports speculate that the granular cell transformation in granular cell ameloblastoma may be associated with the aging phenomenon. [17, 18, 19]

The present study was carried out in five cases of granular cell ameloblastoma to ascertain the nature of the granules using a panel of markers CD68, Bcl2, S100, P53, Cytokeratin (AE1/AE3), vimentin and desmin. Strong positivity for cytokeratin and CD68 was noted in all the cases. S100 was negative in three cases and mildly positive in two cases. P53, Bcl 2, Vimentin and desmin were negative in all the five cases. [Table 2]

The nature of granules in granular cell ameloblastoma in the previous studies have reported epithelial origin due to consistent positivity with cytokeratin and negativity with other mesenchymal markers. [Figure 3] Presence of strong positivity with CD68 in granular cells indicates the presence of lysosomal aggregates. [Figure 4]

Negative expression of antiapoptotic factors such as Bcl-2 and p53 proteins in granular cells indicate that there is increased apoptosis in the granular cells. This finding was similar to the report by Kumomoto et al who reported apoptosis in the granular cells [20]. Contradictory to previous reports is the presence of mild positivity with S100 unlike other previously published reports. S100 is normally present in cells derived from the neural crest (Schwann cells, and melanocytes), chondrocytes, adipocytes, myoepithelial cells, macrophages, Langerhans cells, dendritic cells, and keratinocytes. Mild positivity of S100 could be suggestive of transdifferentiation of the cells. Such heterogeneous presentation of granular ameloblastomas evokes more interest to further ratify its true nature.

#### CONCLUSION:

The current immunohistochemical panel could be evolved further for a better understanding of the nature of the granular cells in ameloblastomas. Further studies with more number of cases could help reason out the antigenic heterogeneity of granular cell ameloblastoma.