Original article

# GRANULAR CELL AMELOBLASTOMA: A clinicopathologic multi-center study of 46 cases

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## ABSTRACT

OBJECTIVE: The aim of this study was to examine the clinico-pathologic aspects of granular cell ameloblastoma seen in five tertiary health facilities in Nigeria.
METHODS: All cases of ameloblastoma, diagnosed from five University Teaching Hospitals over a 21-year period were retrieved from the histopathology archives from the various centres. The Haematoxylin and Eosin (H&E) slides were reviewed and granular cell ameloblastoma diagnosed amongst these cases were put together. Clinical parameters such as age, gender, size and duration of affectation were retrieved from case files of patients. The data was entered into and analyzed with the SPSS software version 20. Simple descriptive analyses were done, with the level of statistical significance set at $p \leq 0.05$.
RESULTS**:** Forty-six cases of GCA representing 3.4% of total number of ameloblastoma were reported. There were 24 males and 22 females giving a 1.1:1 male: female ratio. The mandible was the commonest site of occurrence with 38 (82.2%) cases, while only 4 (8.7%) cases occurred in the maxilla. Multilocular radiolucency was the most common radiographic pattern with 17 (37.8%) cases, while the unilocular and mixed radiolucencies presented with 4 (8.9%) and 1 (2.2%) cases respectively.
CONCLUSION: This study reported one of the largest series of GCA and showed that GCA was indeed a rare variant of ameloblastoma, and many of the clinical findings were similar to those of the solid/multicystic variant of ameloblastoma.

**Keywords:** Ameloblastoma; Granular cell ameloblastoma; Mandible; Maxilla

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## INTRODUCTION

Ameloblastoma is a common benign odontogenic tumour, known as a locally invasive tumour of the jaws that usually runs a benign course.[1] The mandible is affected more often than the maxilla with posterior mandible being the preferable part of the mandible affected. [2, 3]Ameloblastoma is most commonly reported in middle aged adults and most authors have reported no particular gender predilection. [4,5]

Three main clinical types of ameloblastoma have been identified; the conventional

ameloblastoma, which is usually radiographically multilocular; the unicystic ameloblastoma, which is radiographically unilocular and commonly related to impacted teeth, and the peripheral ameloblastoma which is basically a soft tissue tumour presents on the gingiva.[6] Several microscopic subtypes of the ameloblastoma, especially of its solid/multicystic variant, are recognized, although these microscopic patterns are generally believed to have little bearing on the behaviour of tumour.[6] The follicular and plexiform patterns are the most frequent. Less common histopathologic subtypes include the acanthomathous, granular cell, desmoplastic, and basal cell.[7]

Granular cell ameloblastoma (GCA) is a rare variant of ameloblastoma. They represent 3-5% of all histologic subtypes of ameloblastomas.[8] GCA is a variant of ameloblastoma in which nests of large, eosinophilic granular cells are found replacing the central stellate reticulum-like cells. [9] The granules in GCA have been subject of controversies. While some authors believe that they represent a degenerative aging process, a more recent study has suggested that they may be associated with increased apoptotic cell death of the lesional cells and the phagocytosis by neighbouring neoplastic cells.[9]

Possibly because of the rarity of GCA, most previous studies on GCA have been limited to case reports.[7,15] Therefore, the aim of this study was to examine the clinico-pathologic aspects of GCA seen in five Tertiary Health facilities in Nigeria, and contribute to the global data on GCA.

## MATERIALS AND METHODS

All cases of ameloblastoma diagnosed from University Teaching Hospitals of Lagos, Ile-Ife, Ibadan, Port Harcourt, and Benin over the last 21 years (1999-2019) were retrieved from the histopathology archives from the various centres. The Haematoxylin and Eosin (H&E) slides were reviewed and GCA was diagnosed amongst them. Ameloblastomas in which eosinophilic granular cells replaced the central stellate reticulum-like cells were diagnosed as GCA. GCA with granular cell differentiation limited to one or two epithelial islands were termed focal GCA, while ameloblastoma with more global (3 or more islands) granular cell differentiation were termed diffuse GCA.

Collaborators from each centre retrieved clinical parameters such as age, gender, size and duration of affectation from case files of patients. The data was entered into and analyzed with the SPSS software version 20. Simple descriptive analysis was done.

## RESULTS

A total of 1,345 case of ameloblastoma were reported from the five collaborating centres during the study period. Out of these, 46 cases of GCA were seen, representing 3.4% of the total number of ameloblastoma. There were 24 males and 22 females giving a 1.1:1 male: female ratio. The mandible was the commonest site of occurrence with 38 (82.2%) cases while only 4 (8.7%) cases occurred in the maxilla (Table 1). A case was reported in the soft tissue (cheek).

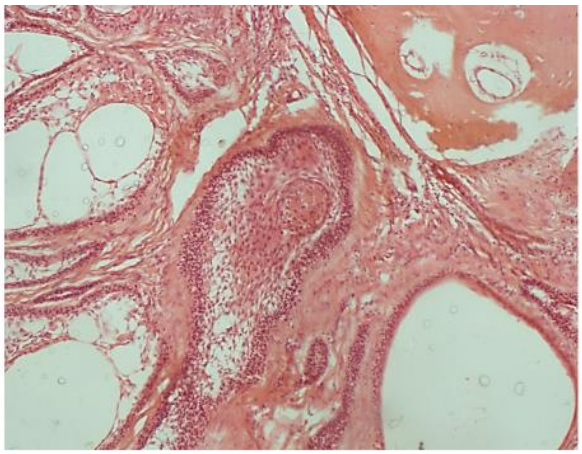

**Fig 1: Focal granular cell ameloblastoma in a follicular pattern (H&Ex40)**

Concerning the histologic variants, the focal variant (Fig 1) was the most common, representing 55.6% of case, while the 31.1% of cases were diffuse. Multilocular radiolucency was the most common radiographic pattern, with 17 (37.8%) cases, while the unilocular and mixed (radiolucency and opacity) presented with 4 (8.9%) and 1 (2.2%) cases respectively. Majority (75.6%) of the cases presented within a duration of 10 months and a median duration of presentation of 3 months. On the other hand, the

mean widest diameter of lesion at presentation was 13.3±8.0 cm with lesions presenting with widest diameter range of 2cm to 30cm.

**Table 1: Age, Sex and Site distribution of Granular cell Ameloblastoma**

| | Frequency | Percentage (%) |
|---|---|---|
| **AGE** | | |
| **Age group (years)** | | |
| 0-10 | 2 | 4.3 |
| 11-20 | 6 | 13.1 |
| 21-30 | 12 | 26.1 |
| 31-40 | 5 | 10.9. |
| 41-50 | 7 | 15.2 |
| 51-60 | 5 | 10.9 |
| >60 | 6 | 13.1 |
| Missing | 3 | 6.5 |
| **Total** | **46** | **100.0** |
| Mean | 36.6±17.4 | |
| Minimum | 7 | |
| Maximum | 67 | |
| **GENDER** | | |
| Male | 24 | 52.2 |
| Female | 22 | 47.8 |
| **SITE** | | |
| Cheek | 1 | 2.2 |
| Mandible | 38 | 82.6 |
| Maxilla | 4 | 8.7 |
| Missing | 3 | 6.5 |
| **Total** | **46** | **100.0** |

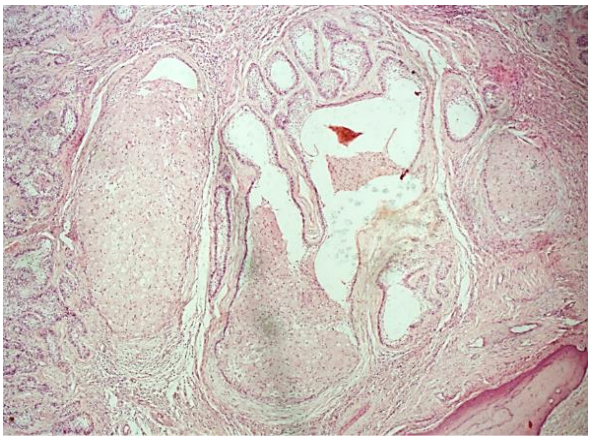

**Fig 2: A diffuse variant of granular cell ameloblastoma with multiple foci of granular differentiation (H&E x40)**

## DISCUSSION

GCA is a rare variant of ameloblastoma characterized by replacement of the stellate reticulum-like cells with cells with eosinophilic granular cytoplasm. The fact that only 46 cases of GCA, representing 3.4% of ameloblastomas were seen in archives of 5 major tertiary health centers in Nigeria, over a twenty-one-year period, seems to confirm the rarity of this variant of ameloblastoma. Previous study reported that GCA represented 3-5% of ameloblastomas.[8]

Kameyama et al.[10] had reported only one case of GCA out of 77 cases of ameloblastomas, representing 1.2% of their reported cases of ameloblastomas. While Reichart et al.[11] reported that only 56 cases of GCA were seen in a 33-year review of histologic types of ameloblastomas representing 1.5% of ameloblastomas seen.

The mean age of occurrence for GCA in this study was 36.6 years. This was slightly less than the mean age of 40.7 years reported by Hartman in a cohort of 20 cases from Armed Forces Institute of Pathology[12]. However, Reichart et al. [11] opined that the mean age of GCA was similar to those of other types of ameloblastoma which they reported as a median of 35 years in that particular study. Some previous studies have reported the mean age of solid ameloblastoma to be similar to the mean age of 36.6 years obtained for GCA in this study [5,13,14]. More detailed comparison of age of occurrence of GCA is not feasible as most previous studies were case reports.

GCA was predominantly in the mandible in this study, with 82.2% of cases occurring in the mandible. Previous studies including most case reports have reported the mandible as the overwhelming preferred site of occurrence for GCA.[7,8,15] Hartman previously reported that all 20 cases of GCA occurred in the mandible.[12] The reason for the obvious mandibular predilection of GCA is not immediately obvious, however, it should be noted that almost all clinical and histological variants of ameloblastoma have an obvious mandibular predilection. Also, findings of more multilocular radiolucency (77.2%) and no obvious gender predilection are in keeping with previous reports on the solid/multicystic ameloblastoma.[4,5]

Two main interpretations have been suggested for the occurrence of granular cell differentiation

in ameloblastomas. First, some believe this to be a metabolic process as supported by ultra-structural studies that showed that the granular cells are made up of lysosomes.[15] Second and most recent interpretation is that this represents a degenerative process and this has been supported by studies that show increased expression of death signalling molecules.[16] A study by Ara et.al. [17], showed that the synthesis of signalling molecules, such as β-catenin and Wnt-5a is up regulated in the granular cells of GCA, but their transportation or secretion is impaired, thereby resulting in their accumulation within granular cells, as auto-phagosomes.

In conclusion, this study reported one of largest series of GCA and showed that GCA was indeed a rare variant of ameloblastoma. Many of the clinical findings were similar to those of the solid/ multicystic variant of ameloblastoma. The study was constrained by the limited available case series studies on GCA for proper comparison, as most previous studies were case reports. Similar multicentre studies from other parts of the world are encouraged. Also, the analysis of the composition and significance of the granular cells in GCA will be interesting to interrogate.

**Conflict of interest:** None declared

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