

Case Report

An Unusual Case of Granular Cell Ameloblastoma of the Anterior Mandible

Shilpa C Natesan^{1*}, Justin Mathew^{2**}, Bindhu P Ramakrishnan^{2*}, Priya Thomas^{3*}

¹PG Student, ²Professor, ³Reader,

*Department of Oral Pathology and Microbiology, Annoor Dental College and Hospital,
Puthuppady P O, Perumattom, Muvattupuzha.

**Malabar Dental College and Research Center, Manoor Chekanoor Road, Mudur (PO), Edappal, Kerala.

Corresponding Author: Shilpa C Natesan

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ABSTRACT

World health organization defined ameloblastoma as a benign, locally invasive epithelial odontogenic neoplasm of putative enamel organ origin. Granular cell ameloblastoma is a rare and extremely aggressive histological variant of ameloblastoma. It has been suggested by many authors that granular cell ameloblastoma has a marked proclivity for recurrence and metastasis than any other variants of ameloblastoma. Though posterior mandibular region is the common site of ameloblastoma, only a handful of cases have been reported in anterior region. This paper reports a case of granular cell ameloblastoma occurring in a 37 year old female patient in the mandibular anterior region.

Keywords: Granular cell ameloblastoma, Ameloblastoma, odontogenic tumor.

INTRODUCTION

Odontogenic tumors are unique to the jaws and originate from tissues associated with tooth development. Ameloblastoma is the second most common odontogenic tumor which accounts for approximately 10% of all tumors originating from gnathic bones. ^[1] It is described as a locally aggressive neoplasm of odontogenic epithelium with a wide spectrum of histologic patterns resembling early odontogenesis. ^[2] The name ameloblastoma is derived from the old French word “amel,” which means enamel, and the Greek word “blastos,” meaning germ or bud. Posterior mandibular region is the common site of occurrence of ameloblastoma with males and females having somewhat equal predilection and the peak age of occurrence is the third decade. ^[3]

Ameloblastoma is believed to be having varied origin and majority of the speculators propose that it is derived from the rests of enamel organ, thus recapitulating embryologic ameloblasts and stellate reticulum. Recent concept believes it to occur as a result of alterations or mutations in the genetic material of cells that are embryologically preprogrammed for tooth development. Environmental factors and individual patient variables are also likely to have role in modulating the incidence of the disease. ^[3]

Solid ameloblastoma has various histologic variants out of which granular cell ameloblastoma (GCA) is considered as one of the rare and aggressive variant. It accounts for 1.5-3.5% of the ameloblastomas occurring in the jaws. ^[4] It was first identified by Krompecher in 1918 and the granular cells were called as

pseudoxanthomatous cells. [5] GCA is characterized by the marked transformation of cytoplasm of stellate reticulum like cells into coarse granular eosinophilic appearance. It is said to have a high recurrence rate and metastatic potential. [6]

Only a very few cases of GCA have been reported in the anterior region of mandible. [7] This article reports an unusual case of GCA occurring in the anterior mandibular region of three months duration in a 37 year old female patient.

CASE REPORT

A 37 year old female patient reported with a history of swelling in the lower mandibular anterior region with difficulty in swallowing and speech since three months. The patient noticed the swelling of peanut size two months back and thereafter it has increased rapidly to the present size (4x2cms). No associated pain or discharge was present.

Intraoral examination revealed a diffuse, bony swelling of the mandible, extending from the right second premolar region to the left canine. Both buccal and lingual cortical expansion was noted and the swelling on the lingual side was seen protruding onto the floor of the mouth (Figure 1). On palpation, the lesion was firm and non-tender with no evidence of palpable lymph nodes. Right mandibular premolars associated with the lesion exhibited grade III mobility.

Panoramic view revealed multilocular radiolucency extending from the distal aspect of 45 to mesial aspect of 33. Root resorption in relation to 45 and 44 were also noticed (Figure 2). With clinical and radiographic correlation a provisional diagnosis of ameloblastoma was given.

Excisional biopsy of the area with extraction of all the teeth in the line of the lesion was done. Macroscopically, the soft tissue specimen was firm in consistency with grayish white color (figure 3).



Figure 1: Intraoral photograph showing mandibular swelling with both buccal and lingual cortical expansion



Figure 2: Radiographic picture showing multilocular radiolucency extending from distal aspect of 45 to mesial aspect of 33



Figure 3: Gross specimen including the two soft tissue bits and the extracted teeth (45 to 32)

Histopathology showed solid ameloblastomatous areas composed of odontogenic epithelium arranged in follicles

or islands with peripheral tall columnar cells exhibiting reversal of polarity and subnuclear vacuolization (figure 4). The central cells consist of granular eosinophilic cytoplasm with peripherally arranged vesicular nuclei (Figure 5). Cystic degeneration was noticed in a few islands. Special staining with periodic acid Schiff (PAS) revealed positive cytoplasmic granules within the central cells (figure 6). Based on the histopathological findings, a final diagnosis of granular cell ameloblastoma was given. The patient underwent surgical resection with no signs of recurrence till date (1 year).

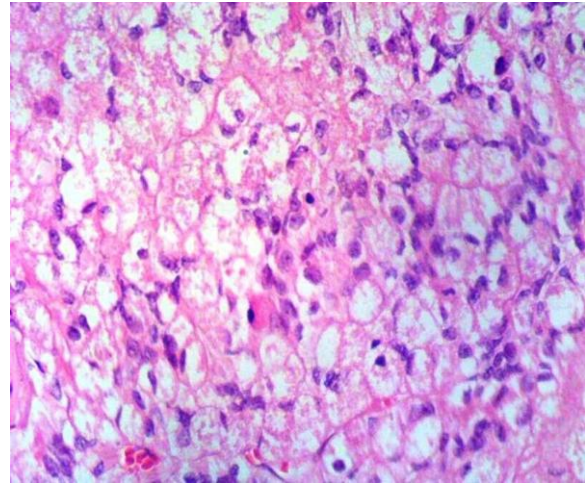


Figure 6: Microscopic picture showing high power view of central cells with coarse eosinophilic granules (40 x magnifications)

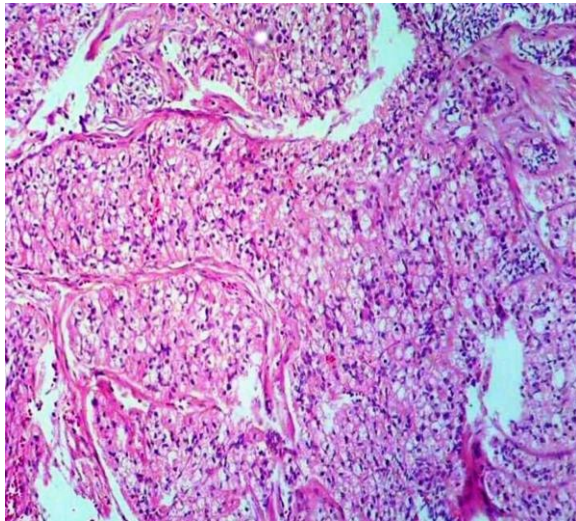


Figure 4: Microscopic picture showing ameloblastomatous islands separated by thin fibrous connective tissue septae (4 x magnifications)

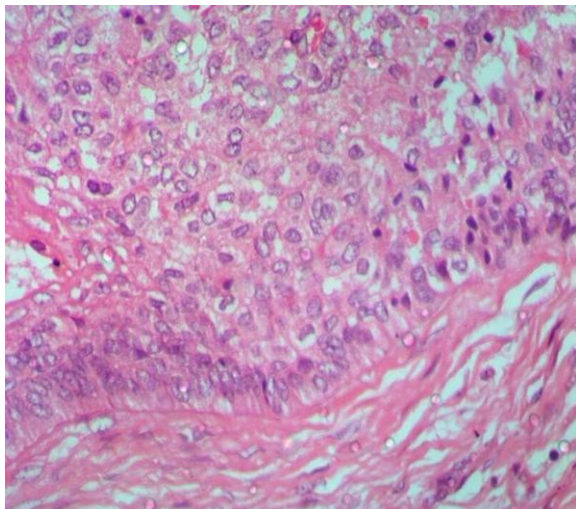


Figure 5: Microscopic picture showing tall columnar ameloblast like cells with central cells showing granular changes (10 x magnifications)

DISCUSSION

Ameloblastomas are divided into four clinicopathological subtypes by Riechart et al as conventional solid/multicystic ameloblastoma (SMA), Unicystic ameloblastoma, Peripheral ameloblastoma and Desmoplastic ameloblastoma including so-called hybrid lesions. [4] Solid or conventional ameloblastoma is the most common type with six reported histopathologic variants; follicular, plexiform, acanthomatous, basal cell, granular cell and desmoplastic.

Granular cell change in ameloblastoma is a rare histopathological entity. Compared to the other ameloblastoma subtypes, no distinguishing clinical or radiographic findings have been reported. [5] The age of occurrence is similar to any other conventional ameloblastoma with reported cases ranging from 4 to 92 years. GCA occurs predominantly at the posterior regions of the mandible with no gender predilection and the most frequent presenting symptoms are jaw swelling and pain. The desmoplastic variant is the one which often occur in the anterior or premolar regions of the mandible or maxilla. [8] Only a very few cases of GCA have been reported in the anterior region of mandible. [7]

The usual histological picture of GCA includes follicular or plexiform pattern with peripheral tall columnar cells

and central large cells exhibiting granular cytoplasm. Sometimes the granularity may extend to include the peripheral ameloblast like cells. The central granular cells are usually large (1-30µm), cuboidal, columnar, or round in shape, with the cytoplasm being filled with acidophilic granules. [3] The nuclei of these granular cells are usually described as pyknotic and hyperchromatic. [9] Along with granular cell changes, some follicles also exhibit normal stellate reticulum like cells, cystic degeneration and

squamous metaplasia. GCA shows a striking resemblance to other granular cell lesions like granular cell odontogenic tumor, granular cell myoblastoma and congenital epulis. Histogenetically, the GCA's are of epithelial nature, and arise from ameloblasts. Conversely, the granular cells found in granular cell ameloblastic fibroma, granular cell myoblastoma, and congenital epulis are of mesenchymal derivation. The differentiating features of these lesions with GCA are listed in table 1.

Table 1: Histopathologic differential diagnosis of GCA

| Lesion | Differentiating feature |
|---------------------------------|---|
| Granular cell ameloblastoma | Ameloblastomatous follicles with peripheral tall columnar cells (resembling ameloblast cells) and central granular cells. IHC - positive for CD68 |
| Granular cell odontogenic tumor | Unlike GCA, granular cells are located within the connective tissue stroma rather than the epithelial islands. IHC - positive for vimentin, Bcl2 and negative for cytokeratin, S-100 |
| Granular cell tumor | Granular cells arranged into sheets, cords or nests with indistinct cell borders exhibiting a syncytial appearance IHC - positive for vimentin and S-100 |
| Congenital epulis | Easy to distinguish as it occurs in newborn whereas GCA occurs in adults IHC - negative for S-100 |

Ultrastructurally, it has been revealed that it is the lysosomal overload in the cells of GCA that imparts the characteristic granularity. The reason for granularity has been enumerated by several authors as a degenerative change, metabolic change due to aging phenomena or an increased apoptotic cell death of neoplastic cells and subsequent phagocytosis by neighbouring cells. [5] Though aging is one of the proposed theories, a few cases reported in young patients leave us to further debate. At the molecular level, lysosomal aggregation within the cytoplasm is explained by dysfunction of either a lysosomal enzyme or a lysosome-associated protein, which is related to enzyme activation, enzyme targeting, or lysosomal biogenesis. [10] Granular cells are positive for CD68, lysozyme, α 1antichymotrypsin and apoptotic markers. [11] With the exception of granular cells; the expressions of basement membrane proteins in granular cell ameloblastoma were similar to those in follicular ameloblastomas. [12]

GCA is known for its locally aggressive behavior and high recurrence rate. One of the finest researches on

ameloblastoma occurring in the jaws was conducted by Reichart et al. He reported that out of 1593 cases with accessible information on histologic sub-types of ameloblastoma, there were just 56 (3.5%) cases of the GCA with 33.3% recurrence rate compared to other variants. [6] However a literature search from Pubmed and Google scholar with the keyword 'granular cell ameloblastoma' over the past 10 years detailed more than 30 cases of GCA with only 2 cases of metastasis and none being recurrent. [13,14] In light of this finding we suggest that the recurrent behavior and prognosis of GCA is similar to other histologic subtypes of ameloblastoma and is more dependent on the method of surgical treatment. Recurrence rates are dictated by the adequacy of the surgical margins and extension of ameloblastoma into vital structures, especially maxillary ameloblastomas. [8] As proposed by Gandhi et al, GCA treated by enucleation or curettage exhibit a high recurrence rate due to the fact that the border of the tumour within cancellous bone lies beyond the apparent macroscopic surface and the radiographic boundaries of the lesion.

Therefore radical surgical methods are recommended for any variant of ameloblastoma. [15]

If untreated, ameloblastoma can acquire a larger size and cause potentially life threatening complications. For conventional ameloblastoma, location and extent of local growth of the tumor are the key points to consider while planning treatment. The standard treatment of any variant of ameloblastoma is surgical resection. According to many authors, other than unicystic variant, simple enucleation has no role in the management of ameloblastoma. Also radiotherapy and chemotherapy has been used in a few cases, the efficacy of the same has to be assessed on a large scale clinical trial. A more light into the molecular pathogenesis of ameloblastoma can lead to a better adjuvant chemotherapeutic treatment regimen. [7]

SUMMARY

We report a case of granular cell ameloblastoma occurring in the anterior mandible region. The patient has been under regular follow-up for the last 1 year with no signs of recurrence. Ameloblastomas are slow growing aggressive tumour which can cause extensive bone erosion and destruction with a poorly understood potential for rare metastasis. Therefore early diagnosis and timely surgical treatment is of prime importance in GCA like any other variant of ameloblastoma.

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