Case Report

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Granular Cell Ameloblastoma: A Rare Entity

Nilesh D. Pardhe[1*] Vikram Khare[2] Anshuman Jamdade[3] Punit Chitlangia[4] Baljeet S. Hora[5] Vidhi Dhakray Khanna[6]

[1]Professor and Head, Department of Oral & Maxillofacial Pathology, NIMS Dental College & Hospital, Jaipur, Rajasthan, India.
[2]Professor and Head, Department of Oral Medicine & Radiology, Mahatma Gandhi Dental College & Hospital, Jaipur, Rajasthan, India.
[3]Professor, Department of Oral Medicine & Radiology, Mahatma Gandhi Dental College & Hospital, Jaipur, Rajasthan, India.
[4]Assistant Professor, Department of Oral & Maxillofacial Surgery, Mahatma Gandhi Dental College & Hospital, Jaipur, Rajasthan, India.
[5]Professor and Head, Department of Conservative Dentistry & Endodontics, Kalka Dental College, Meerut, Uttar Pradesh, India.
[6]Senior Lecturer, Department of Oral & Maxillofacial Pathology, Maharana Pratap College of Dentistry & Research Centre, Gwalior, India.

ABSTRACT

Background: Ameloblastoma is a benign, slow-growing neoplasm of odontogenic epithelial origin characterized by local invasiveness and high frequency of recurrence, however, with rare metastases. Granular cell amelablastoma is a rare histological sub-type of ameloblastoma characterized by groups of cuboidal, columnar or round granular cells having abundant cytoplasm filled with eosinophillic granules. Ultrastructural and histochemical studies have identified the granules to be lysosomal aggregates. This paper describes the clinical and microscopic features of a huge granular cell amelablastoma occurring in the mandible of a 38 year old female patient, with an emphasis on its distinction from other jaw lesions having granular cell composition.

Keywords: Ameloblastoma, Granular cell ameloblastoma; Lysosomal aggregates; Multilocular.

INTRODUCTION

Ameloblastoma is the most widely recognized odontogenic tumor representing roughly 11% of all odontogenic tumors and 1% of all tumors in the head and neck locale. About 85% of ameloblastoma's occur in the mandible, predominantly in the molar-ramus region presenting radiographically as a unilocular or multilocular radiolucency.[1] The distinct clinico-radiographic types of this tumor include solid/multicystic, unicystic, desmoplastic and peripheral ameloblastomas, and the histologic sub-types are follicular, plexiform, acanthomatous, granular cell and basal cell.[2] The most common variants are follicular and plexiform accounting to 32.5% and 28.2% respectively, followed by the acanthomatous sub-type with 12.1% and the extremely uncommon is desmoplastic variant with incident rates ranging from 4-13%. Less common subtypes are the granular cell and basal cell ameloblastoma.[3]

Granular cell ameloblastoma (GCA) is a relatively rare histologic sub-type, accounting for 3.5% of all ameloblastomas and in most instances is found as an admixture with other histologic patterns, particular the follicular sub-type.[1] The lesional epithelial cells undergo granular transformation and the transformed cells possess coarse, granular and eosinophillic cytoplasm and these granules have been identified as lysosomal aggregates.[4] This granular transformation has been ascribed to a maturing or degenerative change in long standing lesion; however, it may also affect young individuals. The GCA is known to be highly aggressive with a marked tendency for recurrence and it is imperative to differentiate GCA from other ameloblastoma's because of higher incidence of malignancy and metastases. Hence, the tumor was

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***Correspondence Dr. Nilesh Pardhe.**
Department of Oral & Maxillofacial Pathology,
NIMS Dental College & Hospital, Jaipur, Rajasthan, India.
Email: drpardhenilesh@hotmail.com

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recognized deserving of presentation and we present a case of GCA in a 38 year old female patient with purpose of highlighting its unique microscopic features that allow its distinction from other jaw tumors with granular cells.

CASE REPORT

The patient, a 38 year old female, presented with a large, slowly growing swelling of the lower jaw. The swelling was of 5 year duration, painless but causing definite discomfort and facial disfigurement. There was no history of prior facial trauma, draining sinus or pus discharge and no signs of inflammation. Patient was moderately nourished with normal physical status and was of poor socio-economic status. The medical, surgical and family histories were non contributory.

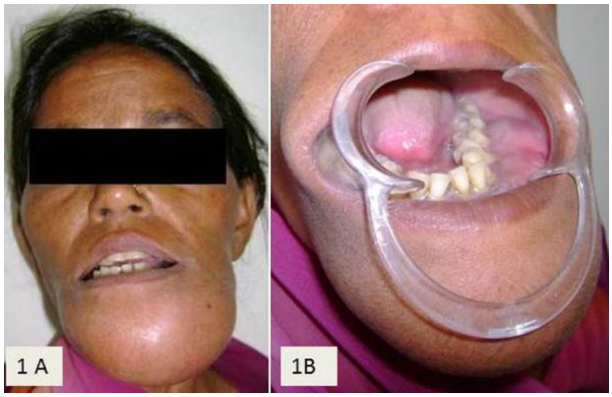

Fig 1: A) Clinical image showing a large extra-oral swelling of the mandible.B) Intraoral swelling causing obliteration of labial and buccal vestibule with lingual displacement of teeth.

On extra-oral examination a large, well defined swelling measuring approximately 12cm × 6cm × 5cm was seen involving the body of the mandible, extending from lower left posterior border of the body of the mandible crossing the midline up to the mid-body region of the right side (Fig.1A). The swelling was firm to hard in consistency with normal overlying stretched skin and no associated lymphadenopathy. Intra- orally there was a large swelling extending from the lower left 2nd molar area up to the midline causing obliteration of the buccal and labial sulcus with displacement of lower teeth (Fig.1B). Computed Tomography showed a large, well-defined, hypodense, multilocular, expansile lytic lesion of the mandible causing bi-cortical expansion and thinning. There was destruction of the buccal cortex

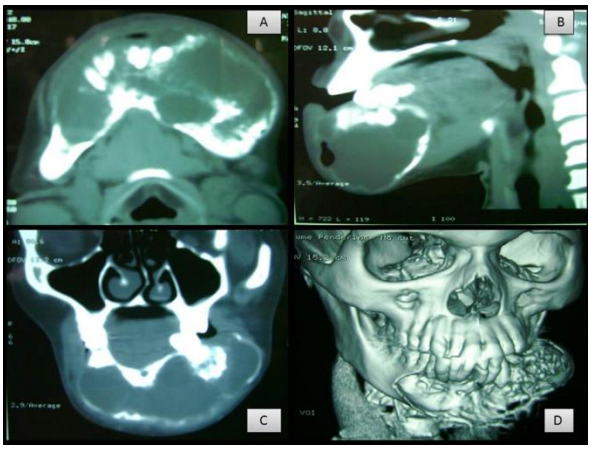

Fig 2: A) Axial CT scan showing a well defined multilocular lesion with bicortical expansion and multiple perforations. B) Sagittal CT section showing a large hypodense lesion with bicortical expansion and perforation with soft tissue invasion. C) Coronal CT showing a large expansile lytic lesion with multilocular soap bubble appearance. D) 3D CT showing a large destructive lesion of mandible extending from right first molar to left third molar region.

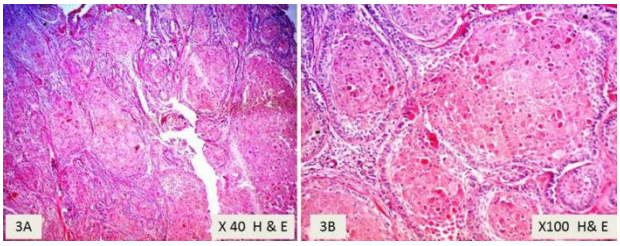

Fig 3: A) Histopathological image showing numerous ameloblastic follicles filled with granular cells in a fibrous connective tissue stroma (x40 H&E stain). B) Photomicrograph showing follicles packed with granular cells and a peripheral layer of palisading columnar cells. A thin rim of stellate reticulum like cells is seen separating the peripheral layer from the central granular cells(x100 H&E stain).

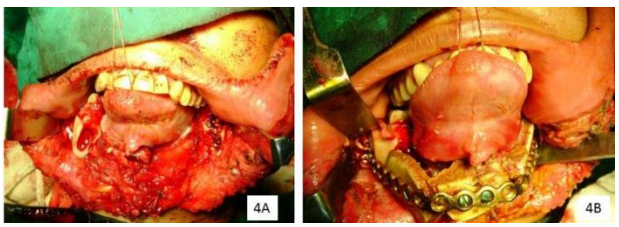

Fig 4: Intra operative photograph.

and lower border of the mandible with few perforations of the lingual cortex (Fig.2A, B & C). 3D image revealed a destructive lesion extending from the lower left 3rd molar area to the lower right 1st

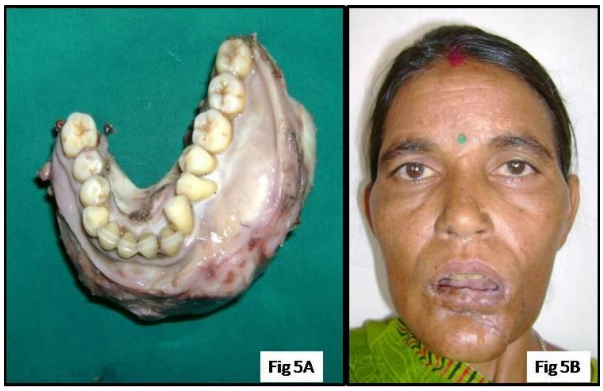

Fig 5: A) Resected mandibular specimen. B) Post-operative photograph of the patient.

molar region with expansion (evident on the left side of the mandible) and perforations of the buccal cortex showing multiple septae and areas of discontinuity of the lower border of the mandible (Fig.2D). A full body examination including chest radiograph and abdominal ultrasonography was done to rule out any metastatic lesion. Complete blood and urine analysis were done, the results of which were all within normal limits.

An incisional biopsy of the lesion was performed under local anesthesia. The H & E stained histopathological sections revealed an encapsulated tumor of odontogenic origin, composed of numerous follicles of variable sizes supported by a fibrous connective tissue stroma. The follicles showed a peripheral layer of palisading columnar cells with hyperchromatic nuclei and reverse polarity. The central areas of almost all the follicles showed the presence of granular cells. These granular cells were oval to polyhedral in shape with coarsely granular eosinophilic cytoplasm and small pyknotic nuclei pushed towards the periphery of the cells (Fig.3A). Some tumor islands showed a thin rim of stellate reticulum like cells separating the central granular cells from the peripheral cells, while in some follicles the granular cell transformation was so extensive that they involved almost the entire follicle (Fig.3B). Based on the histopathological features a diagnosis of "Granular Cell Ameloblastoma" was made.

After explaining the diagnosis to the patient a written informed consent was obtained and the patient was admitted for surgery. Using the lip-splitting incision, mandibulectomy was performed wherein the body of the mandible was resected sparing the angles and ascending ramus of both sides (Fig 4A). Reconstruction was done using iliac crest bone graft and reconstruction plates (Fig 4B).The resected specimen (Fig 5A) was sent for histopathological examination, the findings of which were consistent with that of incisional biopsy. The recovery was uneventful (Fig 5B) and there was no clinical or radiographic evidence of recurrence or any metastases for a follow-up period of two years.

DISCUSSION

Granular cell ameloblastoma is an uncommon variant of ameloblastoma. Only 1 out of 77 ameloblastoma cases was classified as GCA in the clinico-pathologic study of Kameyama et.al.[5]Reichart et. al.[3]reviewed all available literature on ameloblastoma of the jaws from 1960 to 1993 and 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. Hartman[6]reviewed 20 cases of GCA from the files of Armed Forces Institute of Pathology and reported an average age of 40.7 years (age range: 21 -65 years) with no notable gender preference. The dominant parts of the scores were accounted for in mandible with inclination towards the posterior part of the mandible. Jaw swelling and pain were the most regular introducing indications. Compared to other ameloblastoma sub-types no distinguishing radiographic discoveries for GCA have been reported. Our case indicated comparative clinico-radiographic parameters.

The defining feature for GCA is the presence of granular cells, which typically occur in the central part of the epithelial islands, strands and cords and progressively replace the stellate reticulum. The granular cells have an oval to polyhedral shape and tend to be large. The follicles may have a thin rim of stellate reticulum like cells that separates the granular cells from the peripheral columnar layer and the nucleus is displaced to the periphery of the cells. Conspicuous coarse granules pack and distend the cytoplasm and have a tendency to stain eosinophillic, granting a notable manifestation. Occasionally, granular cell change may affect the peripheral columnar cells.[1] Initially the granular cells were acknowledged to represent a maturing or degenerative process, however later

immuno-histochemical studies proved that this change is due to increased apoptotic cell death of the lesional cells and the phagocytosis by neighboring neoplastic cells.[7]On Immunohistochemical investigation it is seen that the granular cells demonstrate positivity for cytokeratin, lysozyme, CD68 and alpha-1-antichymotrypsin, however are negative for vimentin, desmin, S-100 protein, neuron-particular enolase and CD15, showing epithelial origin and lysosomal aggregation.[8]

Granular cell change in ameloblastoma was first reported by Krompecher[9]in 1918 and was called pseudoxanthomatous cells. The differential diagnosis of GCA incorporates other oral lesions such as granular cell tumor, granular cell odontogenic tumor and congenital epulis.[7] The granular cells in all these lesions have a similar morphology but different histogenesis (GCA is epithelial in origin, while the others have mesenchymal origin)and biologically they behave in a different manner.

Granular cell tumor usually occurs in the fourth to sixth decades of life and shows a female inclination. Clinically, it shows up as a small, asymptomatic sessile nodule commonly involving the tongue and buccal mucosa. Histopathological examination shows sheets or nests of large polygonal cells with plentiful, pale, eosinophilic granular cytoplasm and a small vesicular nucleus. Immunohistochemistry reveals positivity for S-100 protein, which demonstrates neural origin.[4, 7]

In complexity to GCA, the granular cells in granular cell odontogenic tumor are not spotted inside epithelial islands yet constitute part of the tumor stroma. Interspersed among the granular cells are seen small islands or cords of the odontogenic epithelium. Small foci of cementum-like material and dystrophic calcifications are frequently discovered in the lesion.[7, 10]

Congenital epulis is an unprecedented soft tissue tumor which occurs almost exclusively on the alveolar ridge of newborn and infrequently on the tongue. Despite the fact that this lesion is also made up of granular cells, the need of distinction from a GCA shows up implausible, acknowledging the occurrence of GCA in older age. Interestingly, immunohistochemical examination is negative for S-100 protein. Also, it appears to stop growing after birth and may even diminish in size.[4, 7]

CONCLUSION

- Granular cell ameloblastoma is a rare condition with unique histopathological and immunohistochemical findings.
- It is an aggressive lesion with a marked tendency for recurrence and many cases have been reported as metastasizing.
- Recognizing this variant of ameloblastoma and differentiating it from other granular lesions is thus needed and definitely has an important role in treatment planning and long term follow-up.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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