

Case Report

Granular Cell Ameloblastoma: A Case Report

Sangeeta R. Patankar, Ankit Mehta

Abstract

Granular cell ameloblastoma is a rare condition, accounting for 3.5% of all ameloblastoma cases. The granular cell ameloblastoma, in most instances is found as an admixture with other histologic patterns, particularly the follicular subtype. A 58 year old male patient reported with a swelling in the lower left posterior region of the face since 2 years. Orthopantomograph showed radiolucency extending from lower left central incisor to retromolar area with compartmented appearance. Histopathologically, diagnosis of granular cell ameloblastoma of the excised specimen was made. Follow-up data suggest that the presence of granular cells in an ameloblastoma might be of some prognostic significance in terms of initial treatment performed.

Keywords: Granular Cells;Ameloblastoma;Jaw Neoplasms;Head and Neck Neoplasms; Odontogenic Tumors;Enamel Organ;Recurrence.

Sangeeta R. Patankar, Ankit Mehta. Granular Cell Ameloblastoma: A Case Report. International Journal of Oral & Maxillofacial Pathology; 2011;2(4):63-67. ©International Journal of Oral and Maxillofacial Pathology. Published by Publishing Division, Celesta Software Private Limited. All Rights Reserved.

Received on: 29/06/2011 Accepted on: 23/08/2011

Introduction

Ameloblastoma is a true neoplasm of enamel organ type tissue which does not undergo differentiation to the point of enamel formation. The first neoplasm of this nature reported in the scientific literature is credited to Broca in 1868.¹ Ameloblastoma is the most common odontogenic tumor, accounting for 1% of all tumors in the head and neck region and approximately 11% of all odontogenic tumors.² It is usually a locally aggressive and destructive tumor with a strong tendency for recurrence³ but rarely metastasizes. Though predominantly seen in the middle age group, it is also known to occur in children (8.7% to 15.0%). Approximately 85% of ameloblastoma arise in the mandible, especially in the molar-ramus region, and present radiographically as a multilocular or unilocular radiolucency.⁴

The granular cell ameloblastoma is an unusual variant showing marked transformation in the cytoplasm of tumor cells, which are usually stellate reticulum-like cells. The transformed cells possess very coarse, granular, eosinophilic cytoplasm. Reichart et al. reviewed all available literature on ameloblastoma of the jaws from 1960 to 1993 and reported that out of a total of 1593 cases with available data on histologic subtypes; there were only 56 (3.5%) cases of the granular cell variant.²² The granular cells, which occur singly or in large masses within the central area of the tumor follicles, replace wholly or in part, the stellate reticulum like cells. Several ultra-structural studies and a histochemical examination, described the granules as

lysosomes.⁵ It was speculated that granular-cell ameloblastoma occurs due to the altered function of tumor cells and the age factor is related to the pathogenesis of this tumor.⁵ It has been emphasized that this granular cell variant appears to be an aggressive lesion with a marked proclivity for recurrence. Hence we present a case of granular cell ameloblastoma in a 58 years old male patient.

Case Report

A fifty eight year old male patient reported with a chief complaint of swelling in the lower left jaw region since one year and pain in the same region since one month. The swelling was noticed after extraction of left mandibular second molar and increased gradually till it reached the present size of 4 x 3 cm.

Extraorally the swelling was present at the angle of the mandible extending from the corner of the mouth anteriorly to the ear lobe posteriorly (Fig 1). Intraorally swelling occurred in the region of left mandibular premolars and molars causing buccolingual expansion of the cortical plates obliterating the buccal vestibule. The swelling was bony hard and tender to palpation and did not have well defined borders. The swelling appeared pink in color, oval in shape with smooth surface. The mucosa and the overlying skin were normal in color (Fig 2).

Panoramic view of the patient showed multilocular radiolucency in body of the mandible extending from the lower left central incisor to the retromolar area

reaching up to the inferior border and involving roots of 34, 35, & 36, with resorption of the roots of 36 (Fig 3). Based on clinical and radiological examinations the lesion was provisionally diagnosed as ameloblastoma. The incisional biopsy specimen was sent to the department of oral pathology for histopathological confirmation. Hematoxylin and eosin stained sections showed varied histopathological features in the different sections. One section showed fibrous connective tissue stroma with ameloblastic follicles having peripheral pre-ameloblast like cells and central stellate reticulum like cells (Fig 4). Odontogenic epithelium in the form of anastomosing strands interdigitating with each other giving plexiform pattern was noted in another section. The connective tissue stroma was loose and well vascularized. The third section showed large ameloblastic follicles lined by pre-ameloblast like cells. The center of the follicles exhibited cystic degeneration as well as replacement of stellate reticulum like cells by granular cells (Fig 5 & 6). The granular cells were large with an oval to polyhedral outline. The nucleus was displaced to the periphery of the cells. Prominent coarse granules were seen distending the cytoplasm. The connective tissue was composed of dense bundles of collagen fibers. The final histopathological diagnosis was given as "Granular cell ameloblastoma".

Discussion

The granular cell ameloblastoma is an unusual variant showing marked transformation in the cytoplasm of tumor cells, which are usually stellate reticulum-like cells. The transformed cells possess very coarse, granular, eosinophilic cytoplasm.^{5,7} The granular cell ameloblastoma in most instances, is found as an admixture with other histologic patterns. The defining characteristic of granular cell ameloblastoma is the presence of granular cells in the central portion of the epithelial islands, stands, and cords. The granular cells tend to be large and have an oval to polyhedral outline. The nucleus is displaced to the periphery of the cells. Prominent coarse granules pack and distend the cytoplasm, imparting the distinctive appearance responsible for the name of these cells. The granular cells sometimes show a sharply delineated cell border, but most often the cell membranes are poorly demarcated and the cytoplasm of adjacent cells merges imperceptibly. The cytoplasmic granules

tend to stain weakly eosinophilic, producing a prominent color change compared with the staining of the peripheral columnar cells. This eosinophilic staining is typically less dramatic than that seen in the acanthomatous ameloblastoma. However, a thin rim of stellate reticulum-like cells that separates the granular cells from the peripheral columnar layer may or may not be present. Occasionally, granular cell change also affects the peripheral columnar cells.²⁴ Previous ultrastructural and immunohistochemical studies of cytoplasmic granules of tumor cells have revealed that they are lysosomal aggregates.^{5,8} Lysosomal aggregation within the cytoplasm is caused by dysfunction of either a lysosomal enzyme or lysosome-associated protein involved in enzyme activation, enzyme targeting or lysosomal biogenesis. These defects lead to the accumulation of substrate that would normally be degraded in the endosome-lysosome system.⁹

Kumamoto and Ooya demonstrated that the granularity might be caused by increased apoptotic cell death & associated phagocytosis by neighboring neoplastic cells.⁶ Altini et al reported two cases of what they termed "plexiform granular cell odontogenic tumor".²³ However, the contents of the lysosomal aggregates within the granular cells in ameloblastoma are largely undefined. Many authors have already reported the immunohistochemical findings of granular cell ameloblastoma¹⁰⁻¹² The granular appearance of the tumor cells can be seen in various oral tumors, such as granular cell ameloblastoma, granular cell myoblastoma, congenital epulis and granular cell ameloblastic fibromas. The morphology of all granular cells is similar, but their origins are different. As per histogenesis, granular cell ameloblastoma is epithelial, while the others appear to be of mesenchymal origin.¹³⁻¹⁵ In ameloblastoma, granular-cell change usually occurs in the central portion of tumor follicles, but it can also occur in a plexiform type. The granular appearance was ascribed to the lysosomes on the basis of both histochemical and electron-microscopic findings.

During normal amelogenesis, an increase in autophagic lysosomes has been also observed in ameloblasts between the secretory and absorptive stages.^{16,17} Recently, an accumulation of granular cells associated with the enamel organ of a developing deciduous incisor was noted

from a stillborn, female infant of 37 weeks gestation.¹⁸ The causative agent of this phenomenon was not discussed, but an accumulation of granular cells is suggestive of a lysosomal insufficiency or of an overproduction of unused materials in the odontogenic epithelium. Thus, the odontogenic epithelium seems to be able to undergo granular change under certain conditions.



Figure 1: The frontal view showing the extra oral extent of the lesion and the resultant disfigurement.



Figure 2: The intraoral photograph showing buccal expansion of the mandible.

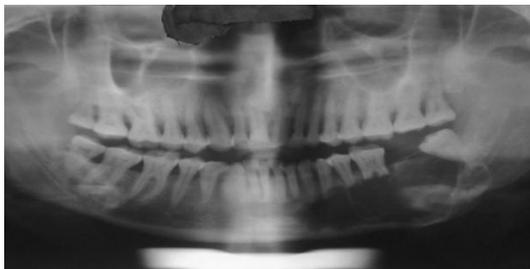


Figure 3: Orthopantomogram showing multilocular radiolucency in the body of mandible reaching up to the inferior border and involving roots of 34, 35 and resorption of 36.

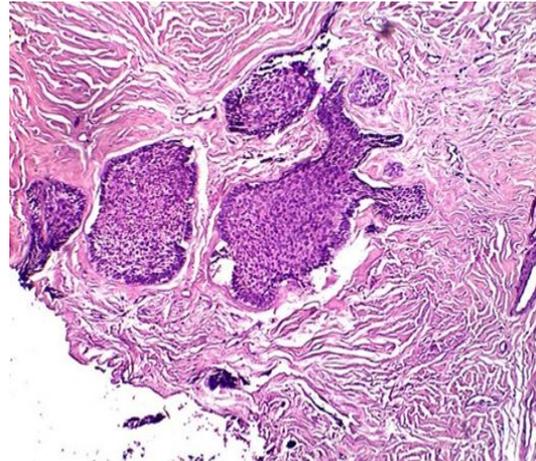


Figure 4: The hematoxylin & eosin stained photomicrograph shows fibrous connective tissue stroma with ameloblastic follicles having peripheral pre-ameloblast like and central stellate reticulum like cells. (10 X)

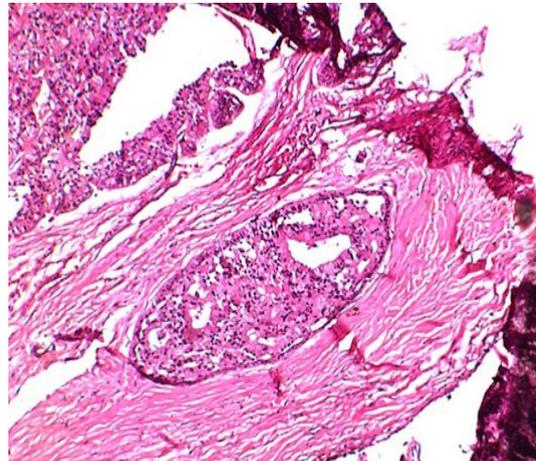


Figure 5: The hematoxylin & eosin stained photomicrograph shows a large ameloblastic follicle with granular cell change at the center. (10 X)

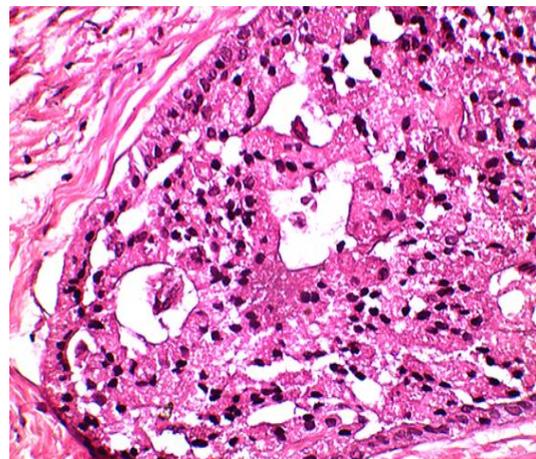


Figure 6: The hematoxylin & eosin stained photomicrograph shows granular cells in the center of the follicle. (40 X)

Several theories have been suggested to explain the granular change in the cytoplasm of neoplastic cells. Many authors proposed that this change is related either to the aging or to the degenerating process.¹⁹ In the case reported by Tsukada et al., granular change appeared 28 years after the onset of the tumor. In another case, granular change was recognized in the ameloblastoma 22 years after the first resection.²⁰

The mean age of 20 patients with granular cell ameloblastoma was 40.7 years at the time of discovery, this is 8 years more than then mean age of the conventional ameloblastoma. It is speculated that the unnecessary or aged components in the cytoplasm of the tumor cells become increasingly more numerous with advancing age; however, the ability of lysosomes to digest or dispose of these materials decreases with age and as a result cytoplasm of the tumor cells becomes packed with lysosomal granules.

Hartman has reported a series of 20 cases of granular cell ameloblastoma and emphasized that this granular cell type appears to be an aggressive lesion with a marked proclivity for recurrence unless appropriate surgical measures are instituted at the first operation. In addition, several cases of this type have been reported as metastasizing. However, all other clinical features of the lesion appear similar to other forms of ameloblastoma.²¹ Thus, recognizing this variant of ameloblastoma definitely has an important role in the treatment plan.

Author Affiliations

1. Dr. Sangeeta R. Patankar, Professor, HOD & PG Guide, 2. Dr. Ankit Mehta, PG student, Department of Oral and Maxillofacial Pathology, Y.M.T Dental College and Hospital, Kharghar, Navi Mumbai, India.

Acknowledgements

We would like to thank all the staff members and students of Oral Pathology Department for their support.

References

1. Shafer, Hine, Levy. Shafer's textbook of Oral pathology. 5th ed. R Rajendran, B Sivapathasundharam. Editors. New Delhi: Elsevier; 2006. 381 p.
2. Odontogenic tumors. In: Regezi JA, Sciubba J (eds). Oral Pathology: Clinical Pathological Correlations. 2nd ed. Philadelphia: Saunders Elsevier, 1993. 363–71 p.
3. Philipsen HP, Reichart PA. Unicystic ameloblastoma: A review of 193 cases from the literature. *Oral Oncol* 1998;34:317–25.
4. Waldron C. Odontogenic cysts and tumors. In: Neville B, Damm D, Allen C, Bouquot J (eds). *Oral and Maxillofacial Pathology*. Philadelphia: Saunders; 2002. 589–642 p.
5. Nasu M, Takagi M, Yamamoto H. Ultrastructural and histochemical studies of granular cell ameloblastoma. *J Oral Pathol* 1984;13:448–56.
6. Kumamoto H, Ooya K. Immunohistochemical and ultrastructural investigation of apoptotic cell death in granular cell ameloblastoma. *J Oral Pathol Med* 2001;30:245–50.
7. Shafer WG, Hine MK, Levy BM. A textbook of oral pathology. 3rd Ed. Philadelphia: W.B. Saunders Co; 1983. 276–86 p.
8. Dina R, Marchetti C, Vallania G, Corinaldesi G, Eusebi V. Granular cell ameloblastoma: an immunocytochemical study. *Pathol Res Pract* 1996;192:541–6.
9. Parkinson-Lawrence E, Fuller M, Hopwood JJ, Meikle PJ, Brooks DA. Immunohistochemistry of lysosomal storage disorders. *Clin Chem* 2006;52:1660–8.
10. Regezi JA, Zarbo RJ, Courtney RM, Crissman JD. Immunoreactivity of granular cell lesions of skin, mucosa, and jaw. *Cancer* 1989;64:1455–60.
11. Mirchandani R, Sciubba JJ, Mir R. Granular cell lesions of the jaws and oral cavity: a clinicopathologic, immunohistochemical, and ultrastructural study. *J Oral Maxillofac Surg* 1989;47:1248–55.
12. Fukumashi K, Enokiya Y, Inoue T. Cytokeratin expression of constituting cells in ameloblastoma. *Bull Tokyo Dent Coll* 2002;43:13–21.
13. Stefansson K, Wollmann R, Jeikovic M. S-100 protein in soft-tissue tumor derived from Schwann cells and melanocytes. *Am J Pathol* 1983;106:261–8.
14. Lack EE, Grawford BE, Worsham CF, Vawter GF, Callihan MD. Gingival granular-cell tumor of the newborn (congenital "epulis"). *Am J Surg Pathol* 1981;5:37–46.
15. White DK, Chen SY, Hartman KS, Coldnel S, Miller AS. Central granular cell tumor of the jaw (the so-called granular-cell ameloblastic fibroma). *Oral Surg* 1978;45:396–406.

16. Reith EJ. The stages of amelogenesis as observed in molar teeth and young rats. *Ultrastruct Res* 1970;30:111-51.
17. Schroeder HE, Listgarten MA. Monographs in developmental Biology; Fine structure of the developing epithelial attachment of human teeth. 2nd ed. S. Karger AG; Basel: 1977. 23-36 p.
18. Sunderland EP, Sunderland R, Smith CJ. Granular cells associated with the enamel organ of a developing tooth. *J Oral Pathol* 1983;12:1-6.
19. Tsukada Y, De La Pava S, Pieklen JW. Granular-cell ameloblastoma with metastasis to the lung: Report of a case and review of the literature. *Cancer* 1965;18:916-25.
20. Narvarrette AR, Smith M. Ultrastructure of granular-cell ameloblastoma. *Cancer* 1971;27:948-55.
21. Hartman KS. Granular cell ameloblastoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1974;38(2):241-53.
22. Reichart PA, Philipsen HP, Sonner S. Ameloblastoma: biological profile of 3677 cases. *Eur J Cancer B Oral Oncol* 1995;31:86-99.
23. Altini M, Hille JJ, Buchner A. Plexiform granular cell odontogenic tumor. *Oral Surg Oral Med Oral Pathol* 1986;61:163-7.
24. Kessler HP. Intraosseous ameloblastoma. *Oral Maxillofacial Surg Clin N Am* 2004;16:309–22.

Corresponding Author

Dr Ankit Mehta,
Post Graduate Student,
Department of Oral and Maxillofacial
Pathology,
Y.M.T Dental College and Hospital,
Kharghar, Navi Mumbai, India.
Ph: 09819863418
Email: drankymehta@gmail.com

Source of Support: Nil, Conflict of Interest: None Declared.

Important Information

All research work that involves the study of human subjects should state at the appropriate section, that the research was approved by the institutional review board or ethics committee in accordance with national and international guidelines and regulations, e.g., The Declaration of Helsinki.

Acknowledgment

Acknowledge persons who have made substantive contributions to the study. Specify the institution or department where the study was conducted.

Source of support

Specify grant or other financial support, citing the name of the supporting organization and grant number.

Conflict of Interest Statement

Conflict of interest exists when an author (or the author's institution), reviewer, or editor has financial or personal relationships that inappropriately influence (bias) his or her actions (such relationships are also known as dual commitments, competing interests, or competing loyalties).

When there is some relationship between the authors and some public or private entity that could give rise to some conflict of interest, this possibility should be made known on the title page of the manuscript and in the covering letter of submission.

In case there is no conflict of interest, the author should state so (for example: "I declare that I do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted").

Copyright Statement

The whole of the literary matter is the copyright of the Editorial Board. The Journal (IJOMP), however, grants to all users a free, irrevocable, worldwide, perpetual right of access to and a license to copy, use, distribute, perform and display the work (either in pre-print or post-print format) publicly and to make and distribute derivative works in any digital medium for any reasonable non-commercial purpose, subject to proper attribution of authorship and ownership of the rights. The journal also grants the right to make small numbers of printed copies for their personal non-commercial use.