GRANULAR CELL AMELOBLASTOMA- A RARE ENTITY

Dr Jatin Gupta
MDS- Oral Medicine and Radiology
Alwar, Rajasthan, India- 301001
Email-id – drjatin18@gmail.com

Abstract
Ameloblastoma is a neoplasm of odontogenic epithelium, especially of enamel organ-type tissue that has not undergone differentiation to the point of hard tissue formation. It accounts for approximately 10% of all tumors originating from gnathic bones. It exhibits diverse microscopic patterns which occurs either singly or in combination with other patterns. Granular cell ameloblastoma is an uncommon variant of ameloblastoma, which is clinically aggressive and histopathologically has numerous large eosinophilic granular cells. These cells usually form the central mass of the epithelial tumor islands and cords. The clinical, radiographical and histopathological features of this tumor with its biological behavior are discussed.

KEYWORDS: ***Granular cell ameloblastoma (GCA); tumor islands; body of mandible; ameloblastoma variant.***

INTRODUCTION

Odontogenic tumors (OT) are a group of heterogenous lesions derived from epithelial and/or mesenchymal elements that are part of the tooth-forming apparatus. Ameloblastoma is well recognized as a locally invasive benign neoplasm thought to arise from the cellular components of the enamel organ. It is an epithelial odontogenic tumor of jaw and exhibits diverse microscopic patterns which occurs either singly or in combination with other patterns. It has been postulated that the epithelium of origin is derived from one of the following sources:

1- Cell rests of enamel organ.
2- Epithelium of odontogenic cysts.
3- Disturbances of developing organ.
4- Basal cells of surface epithelium.
5- Heterotrophic epithelium in other parts of body[8].

They are unique to the jaws and if left untreated, often lead to extensive tissue destruction and deformity. They comprise a complex group of lesions that exhibit diverse histological patterns and various clinical behaviors. These developmental associated tumors are generally benign, although several reveal a neoplastic nature and show locally invasive behavior with a high risk of recurrence. Due to their histological similarities to the developing tooth tissues in normal odontogenesis, the correlation among them is the basis for their classification[1].

The granular cell ameloblastoma is an uncommon variant of ameloblastoma which has been reported to be clinically aggressive[2]. Usually it resembles follicular type but epithelium in the centers of the tumor islands, forms sheets of large eosinophilic granular cells resembling those of granular cell tumors. This change may be so extensive that peripheral columnar cells are replaced and the tumor is difficult to recognize from a small biopsy specimen.

DISCUSSION

Ameloblastomas sometimes exhibit granular transformation of cytoplasm, usually occurring in central stellate reticulum-like cells, and this change often extends to peripheral columnar or cuboidal cells. Numerous theories have been proposed on the origin and nature of these granular cells in ameloblastomas. These granular cells are epithelial in origin and several ultrastructural and histochemical studies have described them as lysosomes. 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[8].

Granular cells are just a transitional or matured phase in the lifecycle of ameloblastomas, starting with normal stellate reticulum like cells leading to production of granules and finally leading to degeneration and formation of cystic areas[8]. It is well known that ameloblastoma is locally invasive and has marked tendency to local recurrence[4]. GCA represents a rare variant of ameloblastoma. Moreover, cases of classical ameloblastoma with only focal presence of granular cells have to be differentiated from the pure variant of GCA, in which the neoplastic granular cells are diffusely present and predominate[5].

Concerning histogenesis, the granular cells of ameloblastomas are of epithelial nature, and arise from ameloblasts. Conversely, the granular cells found in other lesions of the oral cavity are of mesenchymal derivation[5]. During normal amelogenesis, ameloblasts show an increase in autophagic lysosomes between the secretary and absorptive stages and from reduced ameloblasts to squamous epithelium. Thus, the odontogenic epithelium seems to undergo granular changes under certain conditions. The high activity of acid phosphatase could confirm that the cytoplasmic granularity is due to high lysosome content, as shown in the histochemical studies[5].

It is currently thought that the granular change probably occurs as a consequence of an altered function of tumor cells, a hypothesis supported further by the finding that this tumor is age-related. In some cases granular cells show intracytoplasmic crystalloids, which probably constitute variant types of lysosomes, possible due to cellular degeneration[5].

Hartman has reported a series of 20 cases of GCA and emphasized that this granular cell type appears to be an aggressive lesion with marked proclivity for recurrences unless appropriate surgical measures are instituted at the first operation[6].

Granular cell ameloblastoma is diagnosed by the presence of granular cells, which typically occur within the central area of tumour and progressively replace the stellate reticulum. Originally they were considered to represent an aging or degenerative process[9,10], but recent immunohistochemical studies suggest that this phenomenon is related with increased apoptotic cell death of the lesional cells and the phagocytosis by neighbouring neoplastic cells[11]. Immunohistochemical investigation proved that the granular cells are positive for cytokeratin, CD68, lysozyme and alpha-1-antichymotrypsin, but negative for vimentin, desmin, S-100 protein, neuron-specific enolase and CD15, indicating epithelial origin and lysosomal aggregation[11].

Dina et al.[12] also showed that the granular cells exhibited membranous positivity for cytokeratin and cytoplasmic positivity for CD68. The differential diagnosis of granular cell ameloblastomas includes other oral lesions with a similar morphology of granular cell accumulation, including granular cell odontogenic tumour, granular cell tumour and congenital epulis. These lesions have different biologic behaviour and should be discriminated from granular cell ameloblastomas[13].

The granular cell tumour is an uncommon benign soft tissue neoplasm that shows predilection for the oral cavity. The most common site is the tongue, followed by the buccal

mucosa[14]. Differential diagnosis from a granular cell ameloblastoma is necessary when there is peripheral localization or cortical perforation and soft tissue extension of the ameloblastoma. Granular cell tumour usually occurs in the fourth to sixth decades of life and shows a female predilection. Clinically, it appears as an asymptomatic sessile nodule of small size[14]. Microscopic examination reveals large polygonal cells with abundant, pale, eosinophilic granular cytoplasm, with a small vesicular nucleus, arranged into sheets or nests[14,15].

Congenital epulis is an uncommon soft tissue tumour which occurs almost exclusively on the alveolar ridges of newborns or rarely on the tongue. Although this lesion is also composed of granular cells, the necessity of distinction from a granular cell ameloblastoma appears unlikely, considering occurrence of the latter in patients of older age. Interestingly, immunohistochemical investigation is negative for S-100 protein. The lesion is treated with conservative excision and there have been no reports of the recurrence. Additionally, it appears to stop growing after birth and may even diminish in size[14].

The prognosis of granular cell ameloblastoma is similar to that of the classical ameloblastomas. Few cases have been described with an aggressive biological behaviour, with high recurrence rate.

As previously mentioned this is the of the case of recurrence which is showing metastasis to the submandibular lymph nodes and only few cases are reported in literature with metastasis to cervical lymph nodes and metastasis to lungs[4], so to conclude thorough examination of whole body is necessary in GCA cases.

CONCLUSION

GCA is a rare condition with unique histopathologic and immunohistochemical findings. GCA should be differentiated from the other variants of ameloblastoma and also from other granular cell lesions because of its high recurrence rate. Patients should be kept under periodic observation because of reports of recurrences even up to 8years after initial treatment.[8]

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