Case Report

Granular cell ameloblastoma: A rare and unique variant

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ABSTRACT

Ameloblastoma is a slow-growing and locally invasive epithelial odontogenic tumor of the jaw that runs a benign course in most cases. Granular cell ameloblastoma is a rare subtype of ameloblastoma, showing the granular transformation of its cytoplasm. It is considered as an aggressive variant of ameloblastoma. Herein, we report the case of a 34-year-old male patient who presented with a swelling in the left cheek for a 1-year duration with a recent rapid increase in size. Examination showed a 4 × 3 cm growth involving the left buccal mucosa and retromolar area. Imaging studies showed expansile lytic lesion mandible. Biopsy revealed neoplasm with odontogenic epithelial islands showing peripheral palisading of tall columnar cells with reversal of polarity and the center of the islands showing stellate reticulum-like cells which were markedly replaced by granular cells. Granular cells can appear in various odontogenic and non-odontogenic tumors. When there is extensive granular cell change in ameloblastoma, it should be differentiated from other oral lesions with granular cells including granular cell odontogenic tumor, granular cell tumor, and congenital epulis.

Key words: Aggressive variant, Granular cell ameloblastoma, Odontogenic tumor

Ameloblastomas are tumors of odontogenic epithelial origin with varied microscopic patterns. The usual clinical presentations are painless slow-growing swelling with an associated facial deformity, malocclusion, and tooth loss. Six histopathologic subtypes of ameloblastoma are recognized: Follicular, acanthomatous, granular cell, basal cell, desmoplastic, and plexiform. Granular cell ameloblastomas are uncommon lesions accounting for about 3–5% of all histologic subtypes of ameloblastoma [1-3]. Granular cell ameloblastoma is diagnosed by the presence of granular cells, which typically occur within the central area of the tumor and progressively replace the stellate reticulum [1]. It appears to be aggressive in nature, with an increased risk for recurrence and metastasis [2,4-6]. The histological differential diagnosis of granular ameloblastoma includes granular cell odontogenic tumor, granular cell tumor, and congenital epulis. Accurate diagnosis of this lesion is important especially in small biopsies for planning further treatment.

CASE REPORT

A 34-year-old male patient presented with swelling of the left cheek of 1-year duration. A sudden increase in the size of the swelling with associated severe pain was noted for the past 2 months.

Extraoral examination showed facial asymmetry with a 4 ×3 cm proliferative growth involving the left buccal mucosa, retromolar trigone, and lower gingivobuccal sulcus.

Computerized tomography scan showed an expansile lytic lesion (4 cm anteroposterior) in the left mandible. Magnetic resonance imaging showed 5 × 4.5 × 4.5 cm mixed solid-cystic lesion retromolar trigone displacing tongue to the right of midline (Fig. 1a and b).

Biopsy showed a neoplasm with odontogenic epithelial cells arranged in islands, cords, and a few follicles surrounded by fibrous connective tissue. Odontogenic epithelial islands showed peripheral palisading of tall columnar cells with reversal of polarity. The center of the island showed stellate reticulum-like cells which were markedly replaced by granular cells. Granular cells exhibited abundant cytoplasm filled with eosinophilic granules. Features were suggestive of granular cell ameloblastoma (Fig. 2a-d).

The left hemimandibulectomy with the left upper alveolectomy was done. Intraoperatively, 6 × 6 cm growth was noted in the lower alveolus extending from the first premolar extending posteriorly reaching up to the anterior tonsillar pillar. Frozen section examination confirmed the diagnosis of granular cell ameloblastoma with adequate margin clearance.

Access this article online	
Received - 28 February 2022 Initial Review - 25 March 2022 Accepted - 03 December 2022	Quick Response code
DOI: 10.32677/ijcr.v8i11.3359	

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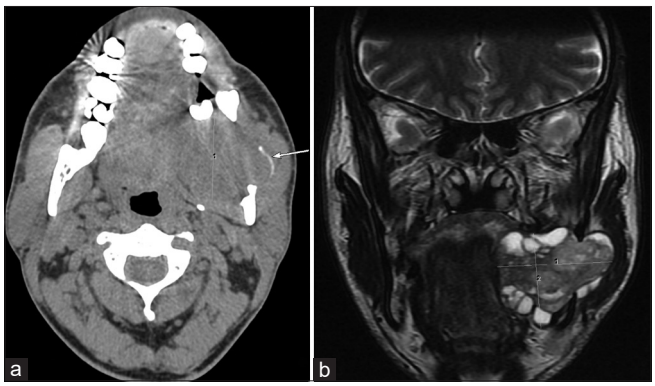

Figure 1: (a) Mixed solid-cystic lesion (5 cm transverse x 4.5 cm superoinferior) with well-defined margins seen in left mandible in coronal T2- weighted MRI image; (b) Lingual (inner) cortex is destroyed & part of buccal (outer) cortex is thinned (arrow) in axial CT image (soft tissue window) of expansile lytic lesion (4 cm anteroposterior) in left mandible.

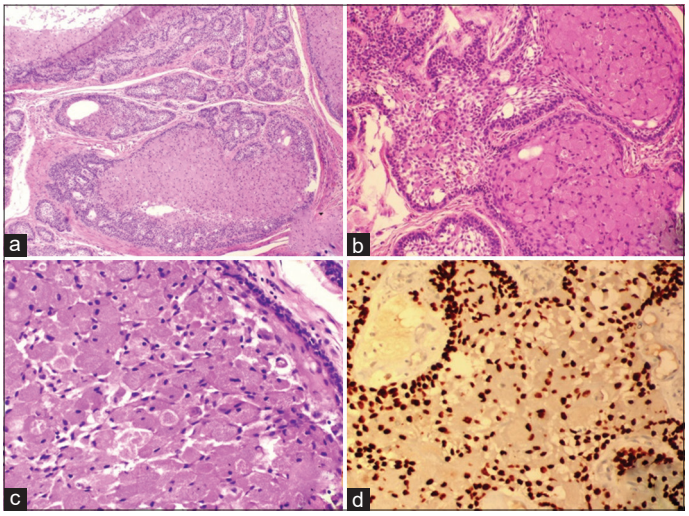

Figure 2: (a) Odontogenic epithelial islands showing peripheral palisading of tall columnar cells with reversal of polarity (H&E, 40X); (b) The center of the islands showing stellate reticulum like cells which were markedly replaced by granular cells. (H&E, 100X); (c) Granular cells with abundant cytoplasm filled with eosinophilic granules (H&E, 200X); (d) Granular cells showing p63 positivity (IHCX200)

DISCUSSION

Ameloblastoma is a benign and locally aggressive tumor of odontogenic epithelium. Around 80% of cases occur in the mandible with 2/3rd of the cases affecting the posterior mandible. It is usually asymptomatic and found incidentally on routine dental examinations. It can present as painless swelling with an expansion of the jaw and associated facial deformities.

Histology is characterized by odontogenic epithelial islands with peripheral palisading of columnar cells showing reverse polarization, central stellate reticulum cells, and no evidence of dentin or enamel formation. Many subtypes have been described. The follicular variant is the most common subtype showing islands of odontogenic epithelium in fibrous connective tissue. Acanthomatous type is characterized by squamous metaplasia and variable keratinization of stellate reticulum-like cells. Cords and sheets of anastomosing odontogenic epithelial cells are the features of the plexiform type. Basaloid type is the least common variant which shows nests or islands of hyperchromatic basal cells without stellate reticulum-like cells [1,2].

Granular cell ameloblastoma is a rare histological subtype of solid/multicystic ameloblastoma. The characteristic feature is odontogenic epithelial islands with peripheral tall columnar cells showing reversal of polarity with the center of the island showing granular cells replacing the stellate reticulum-like cells. The granular cells are cuboidal, columnar, or round and the cytoplasm is filled with acidophilic granules. In granular cell ameloblastoma, the granular cells should be diffusely present and predominate. It should be differentiated from classical ameloblastoma with the focal presence of granular cells only [1].

The literature search show studies suggesting aggressive clinical behavior of this subtype. Hartman studied 20 cases of granular cell ameloblastoma and emphasized that the granular cell type demonstrates a marked propensity to recur following conservative therapy [6]. Reichart *et al*. in their study found that the recurrence rate is 33.3% which is greater than other common types of ameloblastomas [7].

The nature of granular cells in ameloblastoma has been explained by various theories [8-10]. Granular cells of granular cell ameloblastoma are clearly of epithelial origin and show consistent cytokeratin positivity. Identification of apoptotic markers and death signaling pathways in these granular cells supports the theory of degenerative mechanism as the cause of granular appearance [11]. Electron microscopy studies showed regular nuclei of granular cells and the cytoplasmic granules were identified as lysosomes [1]. The presence of numerous lysosomes indicates active function rather than an aging phenomenon or degenerative changes.

On immunohistochemical investigations, the granular cells showed positivity for cytokeratin, lysozyme, and alpha-1-antichymotrypsin. The cells were negative for vimentin, desmin, S-100 protein, neuron-specific enolase, and CD15. This indicates the epithelial origin and lysosomal aggregation [3,11].

The differential diagnosis of granular cell ameloblastoma includes oral lesions with granular cell accumulation, including granular cell odontogenic tumor, granular cell tumor, and congenital epulis. Biologic behavior, treatment, and prognosis of these lesions are different. This makes discrimination important [2,3].

Granular cell odontogenic tumor is a rare odontogenic neoplasm of the jaw. It is also described as granular cell ameloblastic fibroma and granular cell odontogenic fibroma. It has a striking tendency to occur in the posterior mandible in middle-aged women. Radiographic features include a well-defined radiolucency or mixed radiolucent-radiopaque lesion. Histopathologic examination shows sheets and lobules of large eosinophilic granular cells. The tumor is positive for vimentin, Bcl-2, and CD 68. Negative staining for cytokeratin and S-100 will help to differentiate from other tumors with granular cytoplasm. Granular cell odontogenic tumor is completely benign and responds well to curettage [12]. The granular cell tumor is a benign lesion that occurs at various sites of the body with a

preponderance to the oral cavity. The typical presentation is a sessile mucosal nodule on the tongue. The histopathological examination will show sheets and nests of large polygonal cells with a central vesicular nucleus and abundant granular eosinophilic cytoplasm. Overlying squamous epithelium may show pseudoepitheliomatous hyperplasia. Granular cell tumors will show diffuse and strong positivity for S-100 and fine granular cytoplasmic positivity for CD 68. Cytokeratin is negative in granular cell tumors [1]. Congenital epulis is an uncommon benign tumor that occurs almost exclusively on the alveolar ridges of the newborn. Odontogenic epithelium can be seen but pseudoepitheliomatous hyperplasia of overlying epithelium is not seen. Congenital epulis is positive for vimentin. S-100 and cytokeratin stains are negative [1].

The characteristic ameloblastomatous epithelium in granular cell ameloblastoma helps in ruling out other granular cell lesions. In granular cell ameloblastoma, the granular cells are large oval to polyhedral cells with small nuclei and bulky cytoplasm with coarse eosinophilic granules. The morphology of granular cells is similar in different granular cell-rich lesions of the oral cavity, but their origins are different. As per histogenesis, granular cell ameloblastoma is epithelial, while others appear to be of mesenchymal origin.

CONCLUSION

Granular cell ameloblastoma is a rare histological subtype of ameloblastoma. Odontogenic epithelial islands with peripheral tall columnar cells and the center showing granular cells are the characteristic histological feature. Granular cell odontogenic tumor, granular cell tumor, and congenital epulis are the main differential diagnosis of this entity.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Sukumaran R, Somanathan T, Sen A. Granular cell ameloblastoma: A rare and unique variant. Indian J Case Reports. 2022;8(11):360-362.