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Granular Cell Transformation in Plexiform Ameloblastoma: Case Report and Literature Review

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ABSTRACT

Ameloblastoma is the most common odontogenic tumor, primarily occurring in the posterior mandible. It is a slow-growing yet locally invasive epithelial tumor that generally follows a benign course. Granular cell ameloblastoma is a rare variant differentiated by the nests of large eosinophilic granular cells resulting from cytoplasmic transformation. This variant is considered to be more aggressive than any other variant. We report a rare case of plexiform ameloblastoma with granular cell transformation in a 50-year-old male patient presenting as a painless swelling on the right side of the body of the mandible. While granular cell ameloblastoma transformation is well documented in follicular ameloblastoma, its presence in the plexiform variant is extremely rare. This case expands the histologic spectrum of ameloblastoma and underscores the importance of recognizing such variations to avoid diagnostic confusion. Additionally, we re-evaluate the widely held belief regarding its aggressiveness, highlighting emerging evidence that challenges its traditionally aggressive nature. The patient underwent surgical excision in December 2024 and remains under early postoperative follow-up, with long-term monitoring planned to assess recurrence and progression.

1. Introduction

Ameloblastoma is the most common benign odontogenic tumor, originating from remnants of the dental lamina, enamel organ, epithelial lining of odontogenic cysts, or basal cells of the oral mucosa.[1] First described by Broca in 1868,[2] Robinson later defined it as a "unicentric, non-functional, intermittent in growth, anatomically benign and clinically persistent" tumor.[3] Although benign, ameloblastoma exhibits locally aggressive behavior with a high tendency for recurrence if not completely excised. It primarily affects the posterior mandible and is most commonly diagnosed in the third to fifth decades of life, with no significant gender predilection.[4] Clinically, ameloblastomas present as slow-growing, painless swellings, often leading to facial deformity, malocclusion, and mobility of associated teeth. Radiographically, they appear as uni- or multilocular radiolucencies with well-defined or scalloped borders, sometimes associated with impacted teeth. Histologically, ameloblastomas display diverse microscopic patterns, with follicular and plexiform being the most common subtypes. Other less frequent variants include acanthomatous, basal cell, desmoplastic, and granular cell ameloblastomas.[5] Granular cell ameloblastoma is a rare histologic variant characterized by large eosinophilic granular cells within the epithelial islands, attributed to cytoplasmic lysosomal accumulation.[6] While traditionally considered more aggressive, recent studies propose that granular cell transformation may not necessarily indicate increased aggressiveness but could instead represent a matured or degenerative phase of tumor progression.[2] Some cases of hybrid ameloblastoma tumors exhibiting multiple histological patterns within the same lesion have been reported, further complicating the histopathologic classification. Understanding such variations is crucial for accurate diagnosis and prognosis. This article reports a rare plexiform ameloblastoma with granular cell transformation and an unusual histologic presentation. Additionally, we review the literature to re-evaluate the widely held belief regarding the aggressive nature of granular cell transformation.

2. Case presentation

A 50-year-old male patient presented to our institution in 2024 with a chief complaint of a gradually increasing swelling in the left mandibular body region. The swelling had been present there for 4 months and was painless, with no associated numbness, ulceration, or difficulty chewing. The patient had a history of plexiform ameloblastoma diagnosed in 2017, for which he underwent surgical excision followed by reconstruction with a reconstruction plate. There was no prior history of any other systemic illness. Extra oral examination showed diffuse swelling in the left lower jaw with mild facial asymmetry(Fig. 1a). The overlying skin appeared normal, and no cervical

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lymphadenopathy was noted. Intraoral examination revealed a firm, non-tender swelling in the left mandibular body region, with evidence of cortical expansion. The overlying mucosa was intact; there were no signs of ulceration (Fig. 1b).

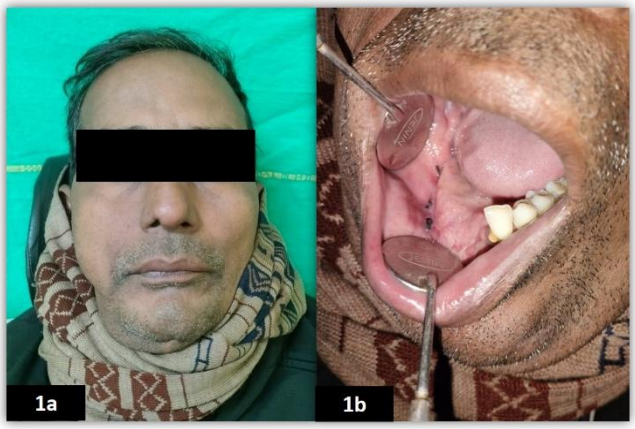


Fig. 1 (a) Extraoral view showing diffuse swelling in the left lower jaw with mild asymmetry, (b) Intraoral view showing a firm, non-tender swelling with cortical expansion.

The 2017 preoperative panoramic radiograph (OPG) showed a well-defined multilocular radiolucent lesion in the left mandibular body, leading to a plexiform ameloblastoma diagnosis (Fig. 2a). Following surgical excision and reconstruction with a reconstruction plate, the 2017 postoperative OPG confirmed the absence of any residual lesion, with the plate intact (Fig. 2b). At the time of the 2024 recurrence, no recent OPG was available; however, clinical findings and histopathology confirmed the presence of a recurrent lesion. OPG was planned but not available for documentation.

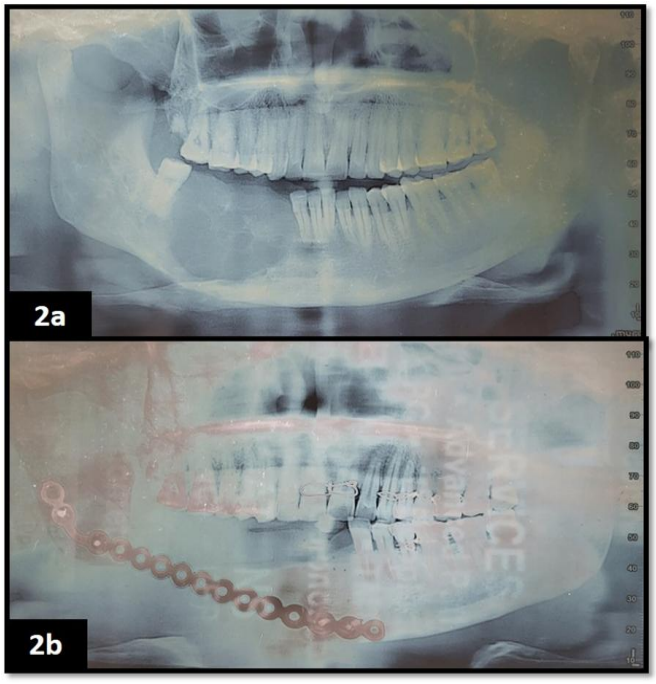
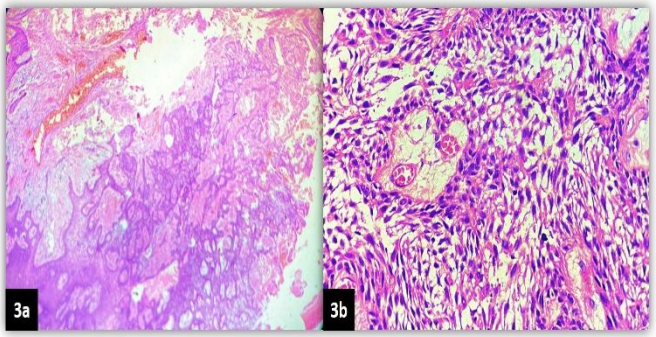
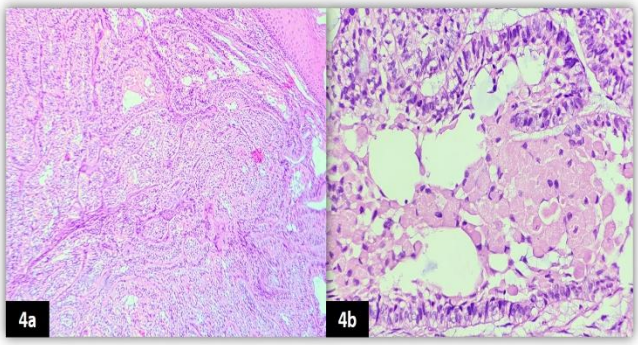


Fig. 2 (a) Preoperative 2017 OPG showing a multilocular radiolucent lesion in the left mandible. (b) Postoperative 2017 OPG confirming lesion excision and intact reconstruction plate.

H & E stained sections from the excised lesion showed features of plexiform ameloblastoma with interconnecting epithelial strands lined by palisading columnar ameloblast-like cells surrounding a central area resembling stellate reticulum. However, in contrast to the previous histology (Figs. 3a and 3b), focal areas demonstrated large eosinophilic granular cells with coarse cytoplasmic granules, indicative of granular cell transformation (Figs. 4a and 4b). Based on the clinical, radiographic, and histopathological correlation, a diagnosis of recurrent plexiform ameloblastoma with granular cell transformation was made. The patient underwent surgical excision, and postoperative recovery was uneventful. He has been advised to have regular follow-ups to monitor for further recurrence.



Figs. 3(a) and (b). Histopathological images of the original plexiform ameloblastoma from 2017 showing interconnecting epithelial strands lined by palisading columnar ameloblast-like cells surrounding a central stellate reticulum-like area (H&E stain, magnification 10X and 40X).



Figs. 4(a) and (b). Histopathological images of the recurrent lesion in 2024 showing areas of granular cell transformation, characterized by large eosinophilic granular cells with coarse cytoplasmic granules, indicative of secondary changes in plexiform ameloblastoma (H&E stain, magnification 10X & 40X).

3. Discussion

Ameloblastoma, the most common odontogenic neoplasm excluding odontoma (which is classified as a hamartoma), is a benign but locally infiltrative tumor composed of ameloblast-like cells and stellate reticulum (WHO 5th edition).[6] This tumor frequently arises between the third and fifth decades of life, with no significant gender or racial predilection. Clinically, ameloblastomas are often asymptomatic and may be discovered incidentally on routine dental radiographs. However, in advanced cases, patients may present with painless jaw swelling, cortical expansion, facial asymmetry,

tooth displacement, or root resorption.[1] Among its various histopathological forms, the solid/multicystic variant exhibits greater local aggressiveness and a higher recurrence rate following local excision than unicystic ameloblastoma, emphasizing the need for comprehensive surgical management and long-term follow-up.[7] Histologically, ameloblastomas exhibit a diverse range of microscopic patterns, with follicular and plexiform subtypes being the most common, followed by acanthomatous, granular cell, basal cell, and desmoplastic variants. Granular cell ameloblastoma (GCA) was first identified by Krompecher in 1918 and has historically been considered an aggressive variant due to its distinct histological features.[8, 9] The presence of large eosinophilic granular cells within ameloblastic islands led to speculation regarding its higher recurrence rate and invasive potential. Most documented cases of granular cell ameloblastoma have been associated with the follicular pattern, with only a few cases reported in the plexiform variant. The first documented case of plexiform ameloblastoma with granular cell transformation was reported by Suchitra et al., who described a lesion exhibiting multiple histological subtypes.[2] Similarly, Mathew et al. identified granular cell transformation within plexiform ameloblastoma in their review study.[17] These findings suggest that while granular cell changes predominantly occur in follicular ameloblastoma, their occurrence in the plexiform variant is exceedingly rare. The exact nature of granular cell transformation in ameloblastoma remains controversial. Histochemical and ultrastructural studies suggest that granular cells are lysosome-rich epithelial cells, and various theories have been proposed to explain their origin. Tandler and Rossi (1977) speculated that lysosomal granules may develop due to genetic alterations.[2] Suchitra et al. proposed that tumor cells accumulate cellular components with aging due to reduced lysosomal degradation, leading to granular cytoplasm.[2] Kumamoto et al. suggested that cytoplasmic granularity may result from increased apoptosis of neoplastic granular cells, followed by their phagocytosis by adjacent cells.[20, 22] More recently, Ara Sathi et al. hypothesized that granular cells in ameloblastoma show upregulated synthesis of signaling molecules like β-catenin and Wnt-5a, but impaired secretion leads to their accumulation within autophagosomes.[21] These molecular insights provide a deeper understanding of granular cell transformation in ameloblastoma and raise questions regarding its role in tumor progression. Although traditionally considered an aggressive variant, recent findings challenge the notion that granular cell ameloblastoma exhibits a more aggressive biological behavior. Immunohistochemical studies indicate that the proliferative index of granular cells in GCA is lower than that of other ameloblastoma variants, suggesting reduced tumorigenic potential.[22, 23] a review of documented cases, including those analyzed in this study (Table 1), reveals that most did not show recurrence, contradicting the assumption of increased aggressiveness. Interestingly, in some documented cases—including those reported by Suchitra et al.,[2] and in the present case—granular transformation appeared only after recurrence. This suggests that granularity may not indicate inherent aggressiveness but could represent a later stage in tumor evolution, possibly associated with cellular degeneration rather than increased proliferative activity. Our findings align with emerging evidence that challenges the widely held belief regarding the aggressiveness of granular cell ameloblastoma. Given the rarity of granular transformation in the plexiform variant, this case expands the histologic spectrum of ameloblastoma and underscores the importance of recognizing such variations to avoid diagnostic confusion. Further studies, particularly those incorporating immunohistochemical and molecular analyses, are necessary to fully understand the biological significance of granular cell transformation in ameloblastoma and its implications for prognosis and management.

Table 1. Summary of Reported Cases of Granular Cell Ameloblastoma.

Author/Year	Age	Sex	Site	Recurrence
Rattanakuntee et al. 2023[1]	75	F	Maxilla	Not Detected
Gupta at al. 2012[2]	50	M	Mandible	Not Detected
Sriram et al. 2024[3]	46	F	Mandible	Not Documented
Sukumaran et al. 2011[4]	34	M	Mandible	Not documented
Motahhary et al. 2014[5]	57	F	Mandible	Not Detected
Nikitakis et al. 2012[10]	65	M	Mandible	Not Detected
Arora et al. 2015[11]	29	M	Mandible	Not Detected
Martin et al. 2017[12]	42	F	Mandible	Not documented
Kulkarni et al. 2018[13]	50	F	Mandible	Not Detected

Reddy et al. 2018[14]	32	M	Mandible	Not Detected
Jahanshahi et al. 2018[15]	47	M	Mandible	Not Documented
Cadavid et al. 2018[16]	35-64	M	Mandible	Not Detected
Mathew et al. 2020[17]	35	F	Mandible	Not Documented
Banerjee et al. 2024[18]	75	M	Mandible	Not Documented
Babu at al. 2025[19]	45	M	Mandible	Not Detected

4. Conclusion

Granular cell ameloblastoma remains a rare histologic variant, and its occurrence within the plexiform pattern is even more uncommon, with only a few documented cases. While traditionally considered aggressive, emerging evidence suggests that granularity may represent a transitional or degenerative phase rather than a marker of increased aggressiveness. Granular transformation may signify a transitional phase in the tumor's evolution rather than an inherently aggressive feature. Whether this represents progression or degeneration remains a subject of debate. This case adds to the limited literature, emphasizing the need for further studies to better understand the biological behavior of granular transformation, particularly in the plexiform subtype.

Conflict of Interest

The authors declared that there is no conflict of interest.

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