

MULTINUCLEATED GIANT CELLS IN AMELOBLASTOMA: AN UNCOMMON FINDING

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ABSTRACT

Ameloblastoma is a benign, slow growing and locally aggressive odontogenic tumor. Typical histopathological findings include islands, strands, sheets, cords of variable size with core of loosely arranged cells in reticular pattern and peripheral layer of palisading cuboidal to columnar cells. An uncommon event in this is presence of multinucleated giant cells. These cells are formed by the fusion of cells usually of monocyte or macrophage lineage and presence of these cells is indicative of the disease process. This case series affirms the presence of multinucleated giant cells in the different histopathological patterns of ameloblastoma. These cells may be related to the aggressive nature of the pathology. However, the origin and nature of the giant cells in the present case series could not be established. Further evaluation of more cases and investigations needs to be done to identify the nature and origin of these cells.

KEY WORDS

Ameloblastoma, Multinucleated giant cells, Monocyte, Macrophage, Odontogenic tumors,



Ameloblastoma is one of the common benign odontogenic tumors of epithelial origin. The word Ameloblastoma was suggested by Ivey and Churchill in 1934 that is derived from English word “amel” which means enamel and the Greek word “blastos” meaning germ.^{1,2} It may arise from the remnants of dental lamina, cell rests of enamel organ, epithelial lining of odontogenic cysts or basal epithelial cells of oral mucosa.¹ According to WHO it is a benign but locally aggressive tumor with high tendency to recur which may be attributed to MMP-9 expression by ameloblastoma leading to degradation of basement membrane, extracellular matrix and pathological bone resorption.^{3,4} It accounts for about 1% of all oral tumors and about 9-10% of odontogenic tumor.⁵ Studies show that most of the cases are located primarily in the posterior mandibular region.^{1,5}

Typical histological findings include islands, strands, cords of variable size consisting of core of loosely arranged cells in reticular pattern and peripheral layer of palisading cuboidal to columnar cells along with histopathological variations.⁶ Multinucleated giant cells have been reported in ameloblastoma. These cells are formed by the union of cells usually of monocyte or macrophage lineage and presence of these cells is indicative of the disease process.⁷

Here we present a case series of ameloblastoma with presence of numerous multinucleated giant cells.

CASE PRESENTATION

Case I

- Age/gender: 26 y/F
- Site: Right body of mandible
- Radiographic presentation: Multilocular radiolucency from 43 - 48
- Histopathological diagnosis: Follicular ameloblastoma

Case II

- Age/gender: 30 y/M
- Site: Posterior mandible on right side
- Radiographic presentation: Multilocular radiolucency involving angle, ramus, neck of condyle and coronoid process
- Histopathological diagnosis: Plexiform ameloblastoma

Case III

- Age/gender: 60 y/M
- Site: Posterior mandible on right side
- Radiographic presentation: Multilocular radiolucency extending from 46 till retromolar area
- Histological diagnosis: Plexiform ameloblastoma

Case IV

- Age/gender: 20 y/F
 - Site: Posterior mandible on right side
 - Radiographic presentation: Mixed radiolucency and opacity apical to 46-47 till ramus
- Histopathological diagnosis:
Unicystic ameloblastoma

On routine histopathological evaluation of the cases confirmed three different patterns of ameloblastoma; follicular, plexiform and unicystic pattern. Follicular pattern revealed numerous islands of odontogenic tumors (Figure 1a) lined by basal cell layer composed of columnar cells displaying hyperchromatic, palisaded nuclei with reverse polarity of the nuclei. Numerous multinucleated giant cells (Figure 1b) along with other fibroblasts and chronic inflammatory cells were present in the fibro-cellular stroma. Long anastomosing cords and large sheets of odontogenic epithelium bounded by basal columnar cells with central stellate reticulum like cells along with few areas of cystic degeneration (Figure 2a) and squamous metaplasia (Figure 3a) was suggestive of plexiform pattern. The underlying connective tissue stroma showed accumulation of sparse multinucleated giant cells (Figure 2b)(Figure 3b) with chronic inflammatory cells and numerous small endothelial lined blood vessels. Unicystic variety showed basal cuboidal cells with hyperchromatic nuclei showing reverse polarity along with loosely cohesive upper epithelial cells resembling stellate reticulum. Nodules of tumor cells were evident within the cystic lumen (Figure 4a) and the underlying connective tissue revealed numerous multinucleated giant cells (Figure 4b).

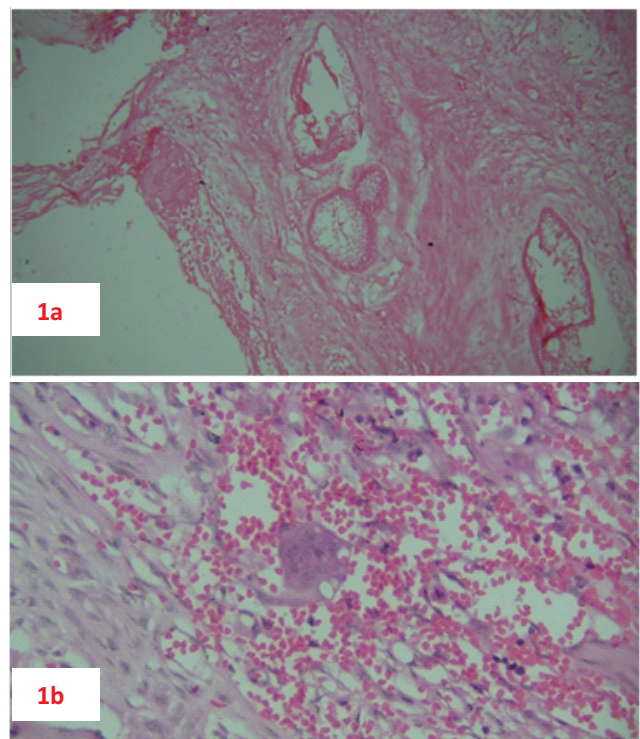
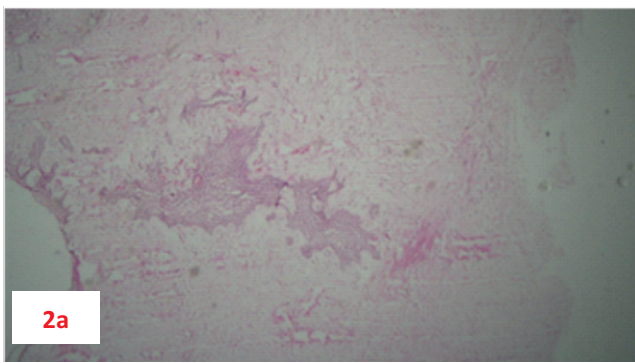
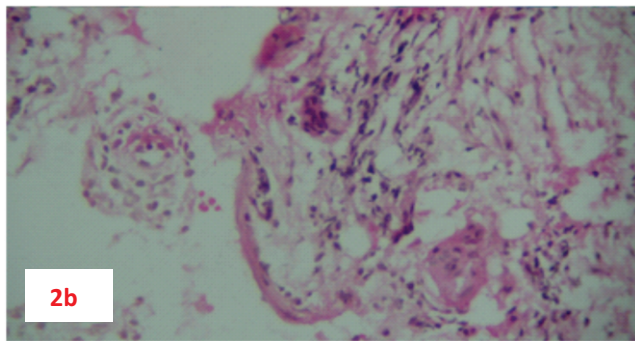


Figure 1: Follicular pattern of ameloblastoma
a) Islands of odontogenic tumor;
b) Multinucleated giant cell

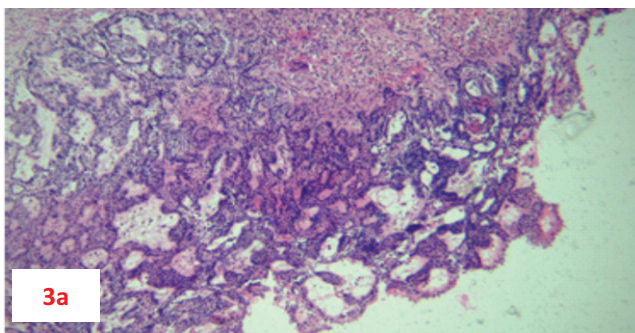


2a

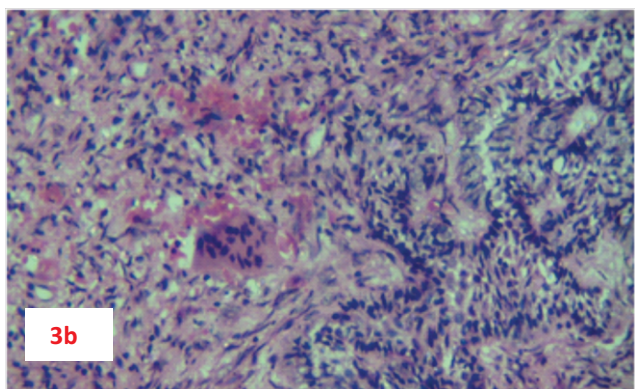


2b

Figure 2: Plexiform pattern a) Sheets of odontogenic tumor; b) Multinucleated giant cells

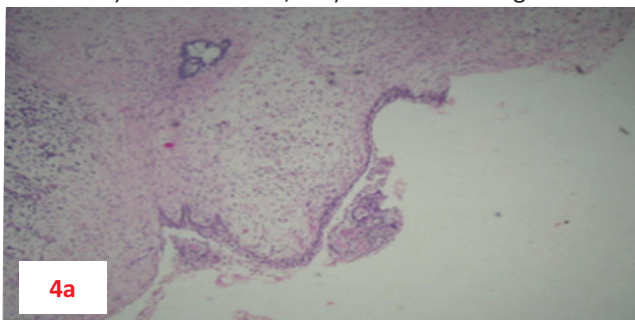


3a

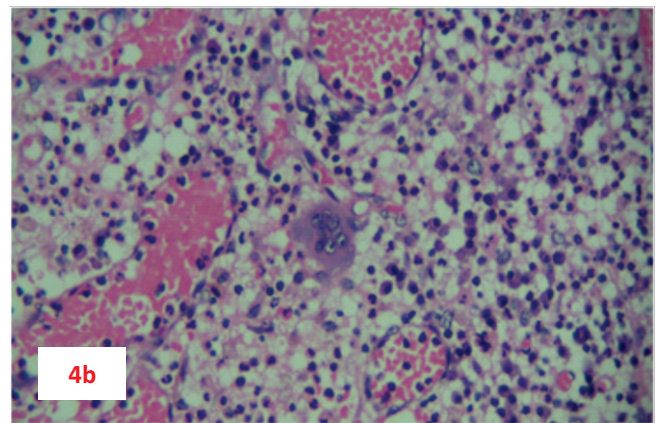


3b

Figure 3: Plexiform pattern a) Cords of tumor; b) Multinucleated giant cell



4a



4b

Figure 4: Unicystic pattern a) Cystic lining with tumor nodule; b) Multinucleated giant cell

DISCUSSION

Multinucleated giant cells associated ameloblastoma are an uncommon presentation. In the last five years, out of 42 cases of ameloblastoma only four presented with multinucleated cells in our laboratory. The multinucleated giant cell associated with benign tumors usually affects young adults, mostly occur around second to fourth decade of life with majority of giant cells tumor noted among female.⁸ Similarly, in our case three out of four cases are of below 30 years with equal prevalence in either gender.

Multinucleated giant cells associated ameloblastoma have been reported however discussion is limited. Boss JH proposed three types of giant cells based on different types of giant cell reaction on stromal connective tissue.⁵ Later Kawakami et al. debated that hematoxylin-eosin staining only cannot determine cytologic nature of these giant cells and histochemical, immunohistochemical and ultrastructural examination is needed for confirmation.⁹ According to Kawakami et al. non-neoplastic giant cells mainly arise from stromal elements reactive to malignant epithelial elements which act as a foreign body. The giant cells showed strong acid phosphatase activity and was positive for α -1-antichymotrypsin. Ultrastructurally, smooth border with oval to markedly irregular nuclei with one or two prominent nucleoli and multiple mitochondria in cytoplasm could be appreciated concluding that these giant cells were of histiocytic in origin.⁹ Similarly Richard et al reported that most of the giant cells expressed CD68 and HLA DR indicating characteristics of macrophage polykaryons and linked to focal areas of woven bone were osteoclastic in nature.¹⁰ Case reported by Sekhar et al. of unicystic ameloblastoma showed positivity of giant cells for CD68 suggesting they were of macrophagic or histiocytic origin. The giant cells were in close proximity to unusual calcification suggesting that they were formed by fusion of macrophages and in the process of removal of calcifications, probably indicating foreign-body giant cell.¹¹

Routaryet al. suggested that giant cells in their case of multicystic ameloblastoma was strongly positive for tartrate resistant acid phosphatase (TRAP) that is associated with

initiation of osteoblastic differentiation, migration, activation, and proliferation and diffusely positive for calcitonin receptors concluding the osteoclastic nature of giant cells.¹²

The primary function of multinucleated giant cells is to degrade and reabsorb a substrate and help in progression of tumor.¹³ They have been associated with the aggressive nature of tumor by synthesizing MMP-9. Literatures have shown these giant cells cause inflammatory tissue damage leading to granuloma formation thereby releasing MMP-9.¹² The expression of MMP-9 is known for mediating degeneration of basement membrane, remodeling of ECM and angiogenesis.¹⁴ MMP-9 secreted by the giant cells play an important role in the vascular invasion of the tumor tissue by breaking down the framework of basement membranes composed of type IV collagen and it also has an important role in tumor growth and progression.¹⁵ MMP-9 expression is also related to the extent of bone resorption and bone destruction and local recurrence which leads to the conclusion that it may be linked to prognostic indication

of the possible aggressive behavior of the underlying pathology.^{12,14}

CONCLUSION

This case series provides evidence of presence of multinucleated giant cells in different histological patterns of ameloblastoma. The giant cells may be related to the aggressive nature of the pathology. However, the origin and nature of the giant cells in the present case series could not be established. Thorough evaluation of more cases and further investigations needs to be done to understand the nature and origin of these giant cells and its clinical implication.

PATIENT CONSENT

The written consent was obtained from the patient.

CONFLICTS OF INTEREST

None

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