Case study and review

Granular Cell Ameloblastoma Of Mandible with Ghost Cells -A Rare Case Report and Review

ABSTRACT

Ameloblastoma is a benign locally aggressive type of odontogenic tumor derived exclusively from the odontogenic epithelium. Granular cell ameloblastoma, is a rare histopathological subtype of ameloblastoma and accounts for 3-5% of all ameloblastoma cases. This variant of ameloblastoma is aggressive with high recurrence rate of 33.3%. In this presentation a case of granular cell ameloblastoma is reported which occurred in a 28-year-old male, extending from the right angle of mandible to the left angle of mandible. Histopathologically, tumor showed predominantly follicular pattern, with central sheets of giant eosinophilic granular cells and peripheral ameloblast-like cell in conjunction with the presence of ghost cells which is a rare presentation.

KEY WORDS: Ameloblastoma, granular cell, odontogenic tumor, ghost cell .

INTRODUCTION

Ameloblastoma is that the most vital epithelial odontogenic tumor of concern due to its true infiltrative and recurrent neoplastic potential, combined with its varieties of histologic patterns.[1] It was described by Broca in 1868 and constitutes about 1%–2% of all cyst and tumors of the jaw. It is most often seen in the posterior mandible in the region of third molar. There is no definite gender predilection and is seen most commonly in fourth and fifth decades. The most common clinical presentations are painless slow growing swelling, facial deformity, malocclusion, tooth loss, pain and paresthesia of the affected region.[2]

Granular cell ameloblastomas are uncommon lesions accounting for about 3-5% of all histologic subtypes of ameloblastoma. Granular cells are a transitional or matured phase in the life cycle of

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ameloblastomas, starting with normal stellate reticulum like cells, resulting in a production of granules and eventually leading to degeneration and formation of cystic areas [1].

Ghost cells are typical characteristic of many odontogenic and nonodontogenic lesions, but if their presence has any pathognomonic role in the pathogenesis of these lesions is still debatable. In general, Ghost cells are described as pale eosinophilic, balloon shaped, elliptic epithelial cells that have lost their nuclei, leaving only a faint outline, hence the term "ghost." Although the cell outlines are usually well-defined, they will sometimes be blurred giving the group of ghost cells a fused appearance. Ghost cells are seen in odontomas, calcifying odontogenic cyst, ameloblastic fibro-odontomas, keratinizing ameloblastoma but their presence is rarely reported in granular cell ameloblastoma.

Here, we present a rare case of granular cell ameloblastomas in a 28-year-old male with focus on its unique microscopic features.

CASE REPORT

A 28yearold male patient reported to the outpatient department with a swelling in the anterior mandible for past 8-10 months. A swelling appeared insidiously in the lower anterior region 8 months back about the size of a peanut, and thereafter gradually, it has increased

to the present size approximately 12 cm × 6 cm (FIGURE :1). Extraoral examination revealed facial asymmetry, with swelling extending anteroposteriorly from the right angle of mandible to the left angle of the mandible and superoinferiorly from superior border to the inferior border of mandible.

Intraoral examination revealed, the swelling extending from right to left angle of mandible obliterating the buccal vestibule with mobility of lower anteriors. Routine biochemical tests were within normal limits. Panoramic view revealed multilocular radiolucency (honeycomb pattern) involving the body of mandible with bilateral expansion of both the buccal and lingual cortical plates along with root resorption in the posterior teeth (FIGURE :2). The clinical and radiological differential diagnosis were odontogenic keratocyst and ameloblastoma. An excisional biopsy was performed with adequate margins and sent to the department of Oral Pathology for histopathological diagnosis. Grossly, lesion was involving body and ramus of the mandible measuring 8 cm × 7 cm × 5 cm having solid and cystic cut surface (FIGURE: 3). Hematoxylin and eosin stained section revealed the tumor to be composed of islands of epithelial cells interspersed between loose connective tissue stroma. Each island consisted of peripherally

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placed tall columnar cells with reverse polarization and palisading nucleus resembling ameloblasts and centrally placed sheets of large granular cells, having abundant coarse granular eosinophilic cytoplasm (FIGURE: 4). Some of the cells in these areas had lost their nuclei and appeared as pink-staining masses of cytoplasm still retaining their boundaries resulting in formation of ghost cells. Although the cell outlines are usually well-defined, they are blurred giving the group of ghost cells a fused appearance (FIGURE: 5). The connective tissue stroma was loose and well vascularized and showed moderate mononuclear inflammatory infiltrate. Based on clinical, radiographical and histopathological findings, the final diagnosis of Granular cell ameloblastoma was made. Patient is on regular follow-up and is free of disease till date.

DISCUSSION

Granular cell ameloblastomas are uncommon lesions accounting for about 3-5% of all histologic subtypes of ameloblastoma.[2]

The patient in the present case is 28-year-old, male patient presenting with facial asymmetry due to swelling in the anterior mandibular region. Radiographically GCA has been divided into unilocular & multilocular patterns. However, multilocular pattern is more frequently encountered. In our case, multilocular radiolucency (honeycomb pattern) involving the body of mandible with bilateral expansion of both the buccal and lingual cortical plates were evident.

Histopathologically, GCA is characterized by having numerous large eosinophilic granular cells. These cells usually form the central mass of the epithelial tumor islands and cords with marked transformation of stellate reticulum cells into granular eosinophilic cells, surrounded by tall columnar cells (FIG 6). Sometimes, they extend to include tall columnar and cuboidal cells as well. [3,7,8]

Granular cells change in classic ameloblastoma is well-recognized phenomenon.[9] It was first seen by Krompecher in 1918 and was called pseudoxanthomatous cells. Granular cells are transitional or matured phase in the lifecycle of ameloblastoma, initiating its process from normal stellate reticulum like cells to the production of granules and finally leading to degeneration and formation of cystic areas.[10] The granular cells acquire small pyknotic nuclei

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and bulky cytoplasm filled with coarse eosinophilic granules indicating there is an apoptotic process taking place (FIGURE 7).[11] Some of the cells loose their nuclei and appear as pink-staining masses of cytoplasm still retaining their boundaries. It is thought that this type of change may eventually result in the so-called "ghost" cells.

Nature of granular cells in ameloblastoma has been explained by various theories. Granular cells are epithelial in origin and a number of other ultrastructural and histochemical studies have described granules as lysosomes.[10] Lysosomal aggregation within the cytoplasm is caused by dysfunction of either a lysosomal enzyme or lysosomal associated protein involved in the enzyme activation, enzyme targeting, or lysosomal biogenesis[12].

Highman and Ogden described ghost cells as dyskeratotic viable cells with distinct outline [13]. Praetorius related ghost cells to abnormal sort of keratinization which have affinity for calcification. Similarly, Sedano, Pindborg and Kerebel et al., proposed that the ghost cells represent different stages within the process of ortho-, para- and aberrant keratin formation which they ought to be perceived as a consequence of metaplastic transformation of cells due to the loss of developmental and inductive influences [14,15].The current WHO classification of odontogenic tumors contemplated ghost cells as transient squamous cells at varied stages of differentiation [16]. However, theories proposed regarding the formation of ghost cells are many, yet a transparent, unified stance on its nature and mechanism remains unresolved.

GCA should be differentiated from other odontogenic and nonodontogenic lesions along with granular cells, including granular cell myoblastoma, congenital epulis, and granular cell odontogenic tumor.[12]

Granules of granular cells in granular cell ameloblastoma are positive for cytokeratin, CD68, lysozyme, and alpha-1-antichymotrypsin [20] Granular cell ameloblastoma are easy to rule out with observing follicular, plexiform, and desmoplastic patterns of ameloblastoma within the specimens.[20]

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 inclination for recurrence

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and metastasis. Thus, recognizing this variant of ameloblastoma definitely has an important role in the treatment plan.[21] The recurrence rate of the granular cell variant was 73% in the Armed Forces Institute of Pathology series for all modes of therapy combined.[1] Few cases of metastasis have also been reported in the literature.[22,23,24] Hence, whether granular cell change in ameloblastoma is a degenerative process or a harbinger of a more aggressive course is a matter of debate.[24]

CONCLUSION

Granular cell ameloblastoma is a rare condition with unique histopathological features. Both the ghost cell and the granular cell are believed not to proliferate and are considered as the products of tumor cells or degenerating tumor cells. The diagnosis of odontogenic tumors should be done by the morphology and/or nature of tumor cells themselves, and not by the components undergoing secondary changes like the ghost cell and the granular cells. Granular cell ameloblastoma is a rare condition with unique histopathological features. Early diagnosis and prompt surgical treatment are of prime importance. Patients should be kept under periodic observation because of reports of recurrences even up to 8 years after initial treatment.

Disclaimer regarding Consent and Ethical Approval:

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

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FIGURE : 1

Swelling in the lower anterior region with a necrotic ulcer in the labial alveolar mucosa extending from left angle of mandible to the right angle of mandible

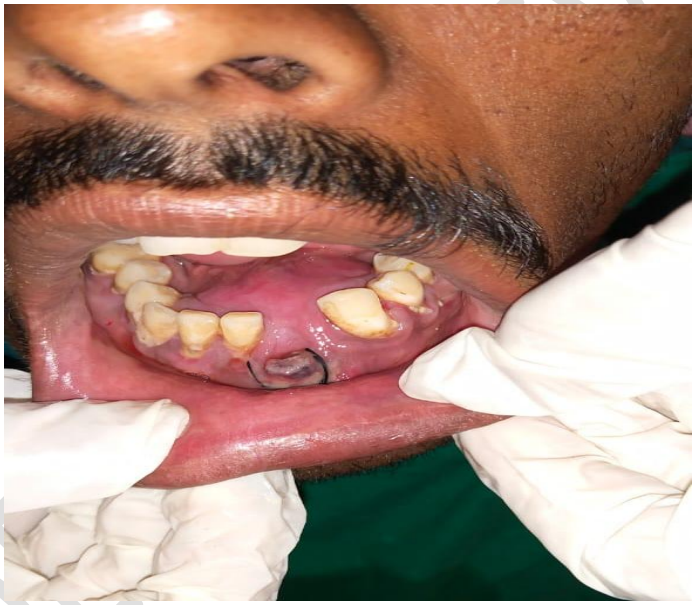

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FIGURE :2

Panoramic view revealed multilocular radiolucency (honeycomb pattern) involving the body of mandible with bilateral expansion of both the buccal and lingual cortical plates along with root resorption in the posterior teeth

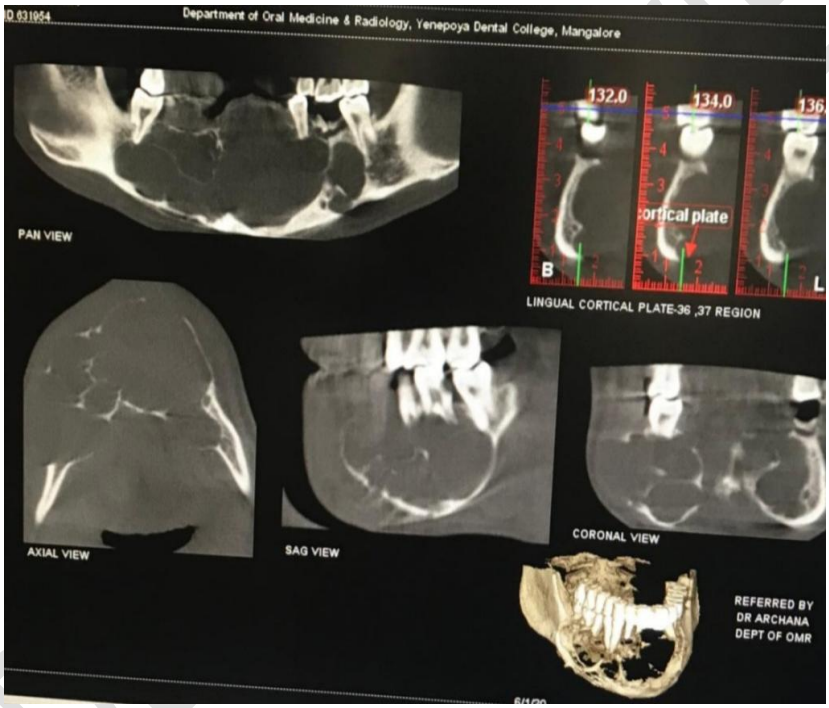

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FIGURE :3

Grossly, lesion was involving body and ramus of the mandible measuring 8 cm × 7 cm × 5 cm having solid and cystic surface

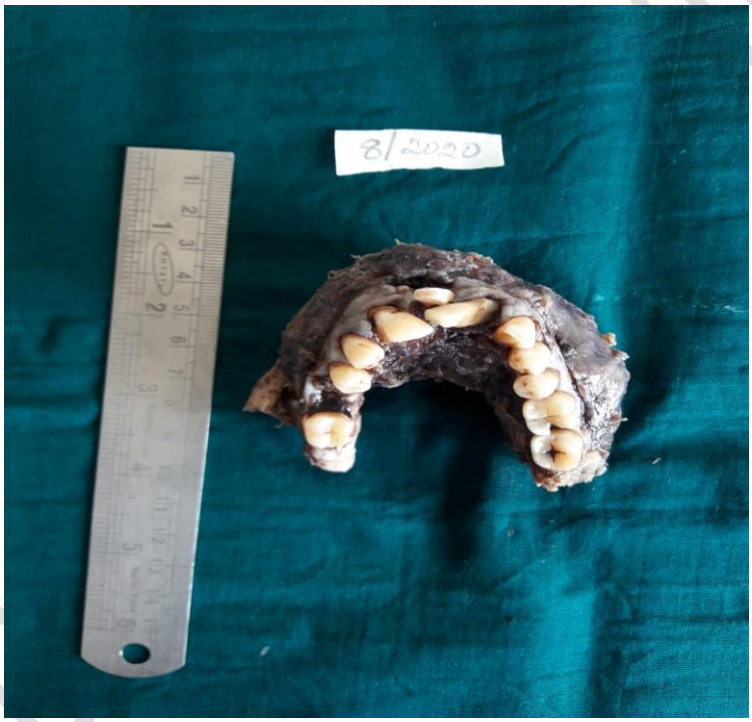

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FIGURE :4

Hematoxylin and eosin stained section revealed the tumor to be composed of islands of epithelial cells interspersed between loose connective tissue stroma. Each island consisted of peripherally placed tall columnar cells with reverse polarization and palisading nucleus resembling ameloblasts and centrally placed sheets of large granular cells, having abundant coarse granular eosinophilic cytoplasm (4 X Magnification)

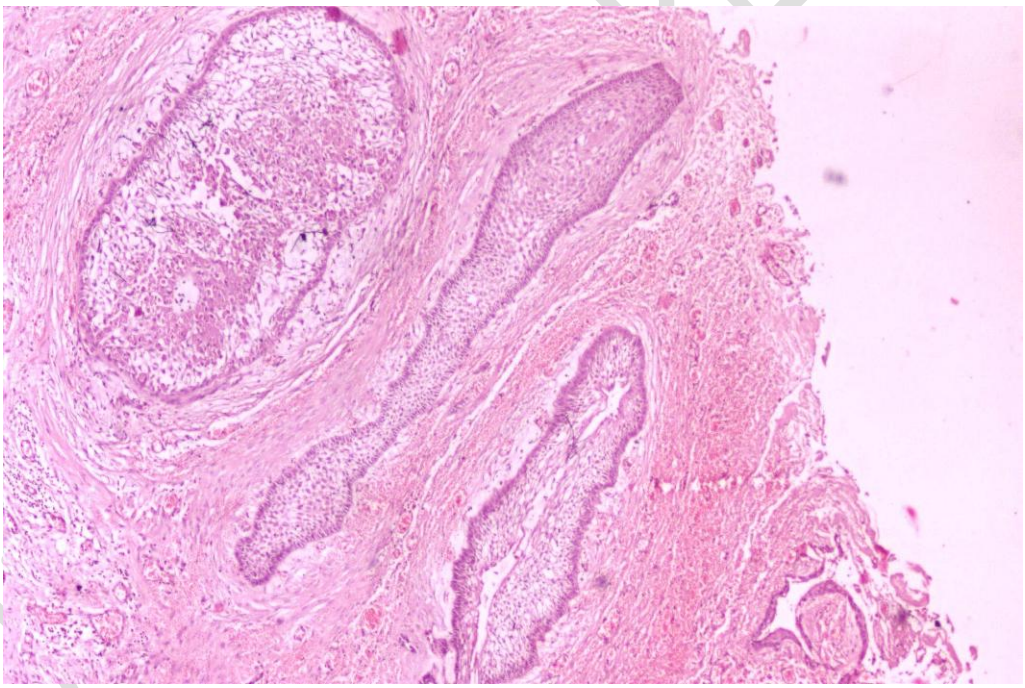

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FIGURE :5

Hematoxylin and eosin-stained section revealed that some of the tumor cells had lost their nuclei and appeared as pink-staining masses of cytoplasm still retaining their boundaries resulting in formation of ghost cells. Although the cell outlines are usually well-defined, they are blurred giving the group of ghost cells a fused appearance (20x magnification)

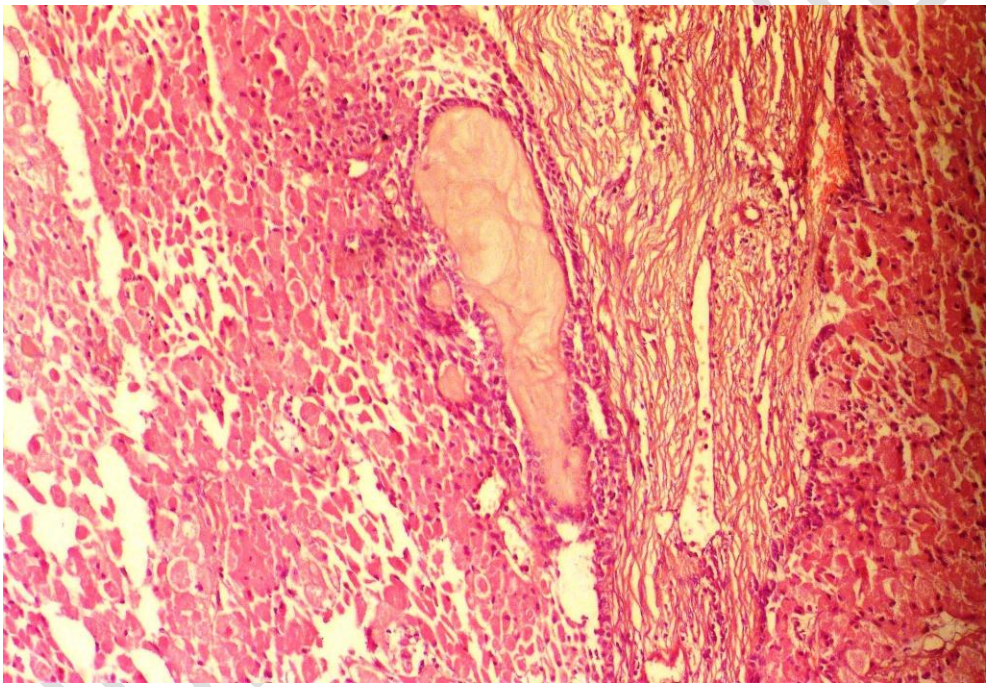

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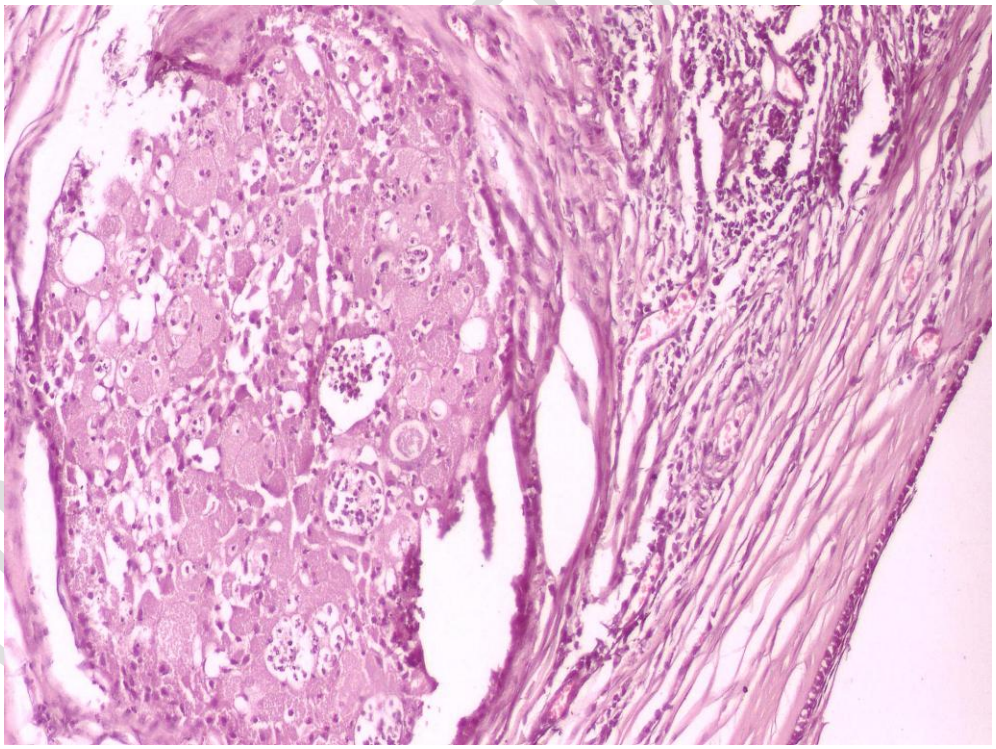
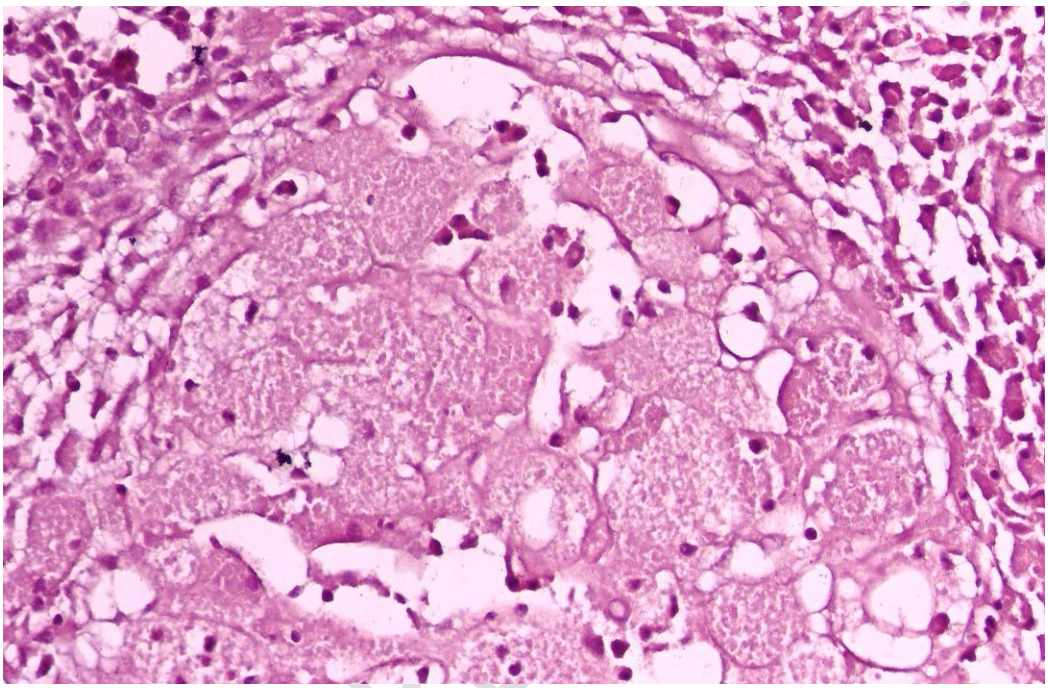
FIGURE :6

Hematoxylin and eosin stained section revealed numerous large eosinophilic granular cells form the central mass of the epithelial tumor islands and cords(20X magnification)





Hematoxylin and eosin stained section revealed the granular cells acquire small pyknotic nuclei and bulky cytoplasm filled with coarse eosinophilic granules indicating there is an apoptotic process taking place(40X magnification)

FIGURE :7

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