

Ghost Cell Presenting Odontogenic Lesions- “ A Comprehensive Description Of The Enigma”

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ABSTRACT:

Ghost cell have always been a topic behind the shadow and a controversy for years. Many research have made an attempt to explain the nature of ghost cells by using special histochemical methods, transmission electron microscopy, and scanning electron microscopy. Ghost cell is a enlarged epithelial cell with eosinophilic cytoplasm, but without a nucleus. In routine H and E staining these cells give a shadowy appearance. Hence these cells are also called as shadow cells or translucent cells. The appearance of these cells varies from lesion to lesion involving odontogenic and nonodontogenic lesions. The purpose of this article is to unravel some of the facts regarding ghost cells with emphasis on their histogenesis, a comprehensive review of available literature on ghost cells and ghost cell containing odontogenic lesions.

KEY WORDS: *Ghost cells, ghost cell odontogenic lesions, odontogenic tumors.*

INTRODUCTION:

According to several literatures, 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 may sometimes be blurred giving the group of ghost cells a fused appearance.¹ These groups of ghost cells are noticed particularly in the thicker areas of the epithelial lining. The spinous cells may be widely separated by intercellular edema and the epithelium around the ghost cell is often complex. They are characterized by the tendency for granuloma formation, potential to calcify and resistance to resorption.²

HISTORY AND THEORIES BEHIND GHOST CELL APPEARANCE:

In the literature the First ever description of ghost cells has been reported by Highman and Ogden during the illustration of pilomatricomas in the year 1944. They described ghost cells as dyskeratotic viable cells with distinct outline³. And they related ghost cells to abnormal type of keratinization which have affinity for calcification. However, the nature of ghost cells has been illusional and many hypotheses have been proposed and debated upon. Ghost cells are believed to be transformed odontogenic epithelial cells, the mechanism of which is still unclear. Gorlin et al. believed that ghost cells represent normal or abnormal keratinization. He also suggested that they represent squamous metaplasia with subsequent calcification caused by ischemia.⁴ Sedano and Pindborg thought the ghost cells represented different stages of normal and aberrant keratin formation, and they were derived from the metaplastic transformation of odontogenic epithelium⁵. Other investigations suggest that ghost cells may represent the product of abortive enamel matrix in odontogenic epithelium. Hong, Ellis and Hartman in 1991 proposed that ghost cells might be the result of coagulative necrosis as they express little or no cytokeratin reactivity in contrast to marked reaction of adjacent odontogenic epithelium suggesting altered keratin antigen expression in ghost cells.^{6,7} Kim et al. performed an immunohistochemical study for ghost cells using

cytokeratins, involucrin, and apoptosis-related proteins such as Bcl-2, Bcl-XL, and Bax. Their study demonstrated expression of cytokeratins and involucrins in the nucleated cells adjacent to the ghost cells, whereas the ghost cells showed no reaction; but, they exhibited Bax proteins, which made them conclude that ghost cells undergo abnormal terminal differentiation.⁸ Ghost cells whether odontogenic or non-odontogenic are always epithelial in origin. The illusionary nature of ghost cells can be reflected in various confusing terminologies such as a form of true keratinization, prekeratin, stages in the process of ortho, para and aberrant keratin formation, abnormal/aberrant keratinization, highly keratinized epithelial cells, and cells which have lost their developmental and inductive effect.¹

GHOST CELL PRESENTING LESION:

As described earlier, Ghost cells generally lack nuclear and cytoplasmic details and are characteristically seen in :

- CCOT,
- craniopharyngiomas and pilomatricomas
- odontomas,
- dentinogenic ghost cell tumor,
- dentinogenic ghost cell carcinoma,
- ameloblastoma,
- ameloblastic fibroma.

CLASSIFICATION OF ODONTOGENIC GHOST CELL LESIONS:

Praetorius in the year 2006 classified odontogenic ghost cell lesions into four groups

Group 1 : Simple cyst (Calcifying odontogenic cyst, COC)

Group 2 : Cysts associated with odontogenic hamartomas or benign neoplasms (Calcifying cystic odontogenic tumours, CCOT)

Group 3 : Solid benign odontogenic neoplasms with similar cell morphology to that in COC and with dentinoid formation (Dentinogenic ghost cell tumour)

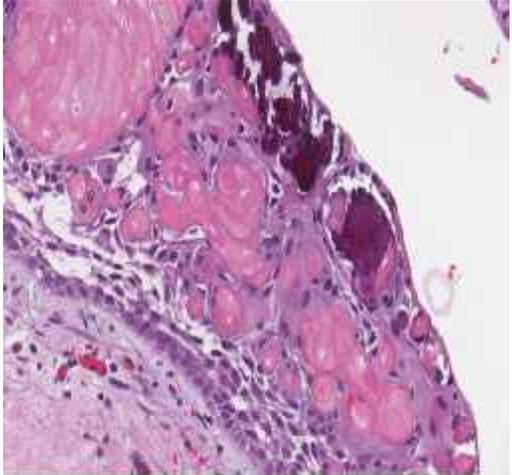
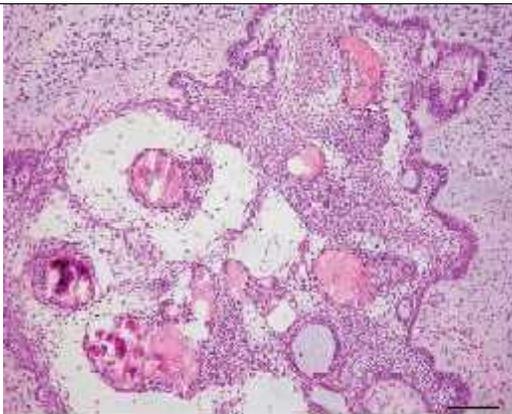
Group 4 : Malignant odontogenic neoplasms with features similar to those of the dentinogenic ghost cell tumour (Ghost cell odontogenic carcinoma)⁹.

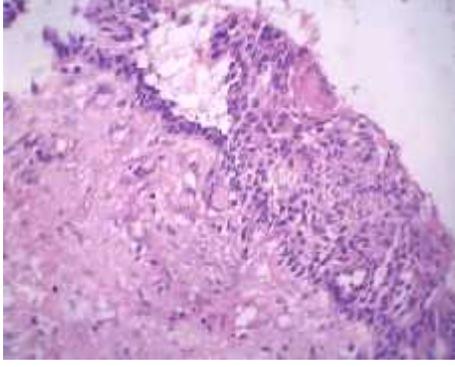
ENUMERATION OF GHOST CELL LESIONS:

ODONTOGENIC CYST	Eruption cyst <ul style="list-style-type: none"> • Glandular odontogenic cyst • Calcifying epithelial odontogenic cyst
TUMORS OF ODONTOGENIC ORIGIN	<ul style="list-style-type: none"> • Calcifying cystic odontogenic tumor • Ameloblastic fibroma • Odontoameloblastoma/ Dentinoameloblastoma • Odontoma (complex and compound)

	<ul style="list-style-type: none"> • Ghost cell odontogenic carcinoma
OTHERS (NON- ODONTOGENIC LESIONS)	<ul style="list-style-type: none"> • Cutaneous calcifying epithelioma of Malherbe / Pilomatrixoma (in skin) • Craniopharyngioma (in pituitary gland)

GHOST CELL PRESENTING ODONTOGENIC LESION:

<p>CALCIFYING CYSTIC ODONTOGENIC TUMOR</p>	<p>-previously named as calcifying odontogenic cyst (COC).</p> <p>-Gorlin et al. discussed the development of CCOT and ghost cells in 1962.</p> <p>- According to Abrams and Howell , the theory states that during the development of CCOT, the transformation of an odontogenic epithelial cell into a ghost cell firstly starts by enlargement of mural cells, followed by other epithelial cells in cystic lining into abnormally keratinized cells. The basal cells transform toward the end, and this transformation leads to loss of distinction between epithelium and connective tissue. Since ghost cells are abnormally keratinized, they are considered as foreign bodies if they reach the connective tissue.¹⁰</p>	 <p>Ghost cells seen in calcifying odontogenic tumor</p>
<p>AMELOBLASTIC FIBROMA</p>	<p>-Ameloblastic fibroma containing ghost cells such as those seen in CCOT , but are reported less in number.</p> <p>-Ghost cells were seen in neoplastic epithelial nests. They tend to gather in small groups, and the calcification seemed to occur in the ghost cell background.</p> <p>-Lining epithelium show ghost cell differentiation and calcification.</p> <p>-Groups of ghost cells were also seen within ameloblastic epithelium in the area of ameloblastic fibroma.¹¹</p>	 <p>Ameloblastic fibroma containing ghost cells</p>

<p>DENTINOGENIC GHOST CELL TUMOR</p>	<p>-Presence of ghost cells in dentinogenic ghost cell tumor was first observed by confocal laser scanning microscopy in 2007.</p> <p>- Three different maturative stages of ghost cells were observed with varying extents of keratin expression, indicating accumulation of hard keratin in their cytoplasm during the pathological transformation process, thus indicating that ghost cells might represent differentiation into hair.¹²</p>	 <p>Presence of ghost cells in dentinogenic ghost cell tumor</p>
<p>ODONTOMA</p>	<p>-Ghost cells seen in odontomas have resemblance to poorly decalcified osteodentin.</p> <p>- Pindborg suggested that ghost cells were found within odontogenic epithelium, generally near or at the surface of enamel matrix, entrapped within calcified tissue corresponding to either enamel or dentinal matrix and/or isolated within connective tissue.</p> <p>- In a study by levy et al. suggests that ghost cells are formed due to cell death from local anoxia. Some found that these cells are probably a special form of degeneration with a marked aberrant keratinization.^{13,14}</p>	 <p>Ghost cells seen in odontomas have resemblance to poorly decalcified</p>
<p>GHOST CELL ODONTOGENIC CARCINOMA</p>	<p>-Ghost cell odontogenic carcinoma (GCOC) is an exceptionally rare and malignant odontogenic tumor with aggressive growth characteristics. GCOC has a low incidence.</p> <p>-Ward and Cohen suggested three possible explanations for the histogenesis of a cyst with lining epithelium and its associated carcinoma in jaws.</p> <ol style="list-style-type: none"> 1) carcinomas and cysts have different origins, the former possibly originating from adjacent epithelium or by distant metastasis of a primary tumor. 2) the primary lesion was a carcinoma, which partially underwent cystic degeneration. 3) the primary lesion was a cyst, and the 	 <p>Cluster of ghost cells diffusely distributed in the tumor nest</p>

	<p>lining epithelium subsequently underwent malignant transformation.</p> <p>-Histopathological the tumor shows composed epithelial cell nests. The neoplastic cells shows cytological atypia, manifested mainly as hyperchromatic cells with variably sized nuclei, raised nuclear-cytoplasmic ratio and an increased number of mitotic ares. Clusters of ghost cells are diffusely distributed in the tumor nests.¹⁵</p>	
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CONCLUSION:

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. True nature of ghost cells remains elusive and controversial, though their most accepted nature is aberrant keratinization. Recent studies are directed toward the role of Wnt and Notch signaling pathways in tumorigenesis and assigning cells to particular fate. However, further extensive studies on these aspects will give us the possible clue in determining the role of these 'shadow cells' in many odontogenic as well as nonodontogenic lesions

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