

A Contemporary Approach to Classify Ghost Cells Comprising Oral Lesions

ACHLA BHARTI YADAV¹, SUMIT KUMAR YADAV², ANJALI NARWAL³, ANJU DEVI⁴

ABSTRACT

Ghost cells are swollen eosinophilic epithelial cells that have lost their nuclei but retain the cellular and nuclear outline. Pathologic ghost cell formation could be the process of aberrant keratinization or the result of coagulative necrosis. Ghost cells have been described in several odontogenic lesions, which include calcifying epithelial odontogenic cysts or tumours like odontomas, ameloblastic fibro-odontomas, and ameloblastomas. This article present a view on the formation of ghost cells with proposal/introduction of a classification for ghost cell lesions of the oral cavity in an attempt to organize these lesions for the better understanding and academic purpose.

Keywords: Classification, Keratinization, Odontogenic lesions, Swollen epithelial cells

INTRODUCTION

Ghost cells can be defined as translucent epithelial cells which are pale and eosinophilic, with swollen cytoplasm and absence of nucleus. A few of them may contain nuclear remnants but they are in various stages of degeneration and in majority all traces of chromatin have disappeared leaving only a obscure outline of the indigenous nucleus. Sometimes, a faint nuclear membrane outlines can be recognized [1,2]. The cell outlines are usually well-defined, or may be blurred and the cells appear fused [3] [Table/Fig-1]. In haematoxylin-eosin stained sections, the hazy and indistinct appearance of these structures originate the term “ghost cells”. They are characterized by the tendency for granuloma formation, potential to calcify and resistance to resorption [4]. Ghost cells are found in groups particularly in the thicker areas of the epithelial lining. In such situations the spinous cells may be widely placed due to intercellular edema and the epithelium around the ghost cells is usually intricate [2]. Ghost cells with similar histomorphologic

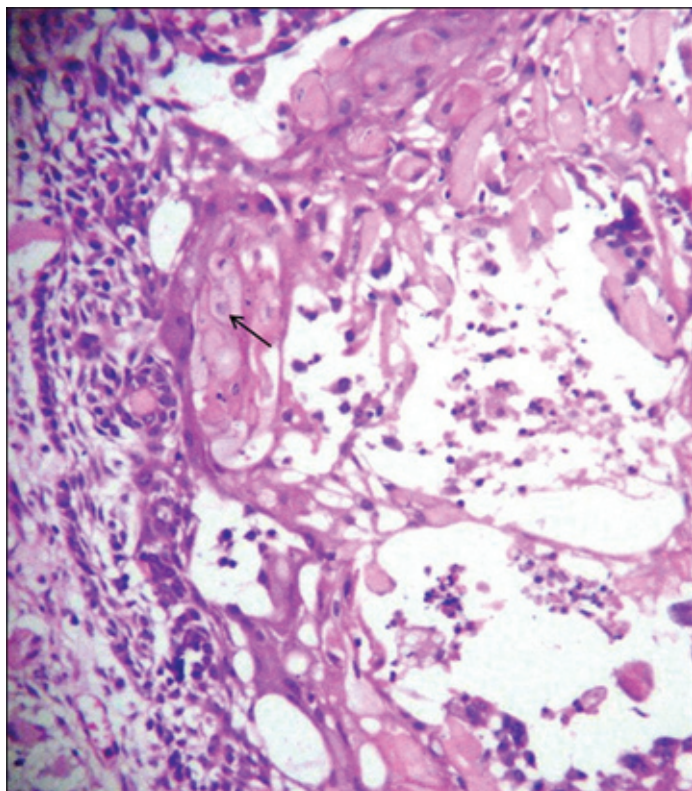
impressions as found in cutaneous epithelioma of Malherbe and craniopharyngiomas are also seen in the inner enamel epithelium of a normal developing human tooth and other oral pathological lesions. These include calcifying odontogenic cysts or tumour, solid/ multicystic ameloblastomas, odontomas, ameloblastic fibro-odontomas [3,4].

Theories/ Hypothesis of ghost cell formation

In the literature the foremost description of ghost cells has been quoted by Highman and Ogden during the illustration of pilomatricomas. They described ghost cells as dyskeratotic viable cells with distinct outline [4]. Praetorius related ghost cells to abnormal type of keratinization which have affinity for calcification. Similar histological reaction of ghost cells as that of keratin i.e. a yellow fluorescence with rhodamine B is also reported by Shear [2]. Levy in odontomas suggested that ghost cells represent squamous metaplasia with subsequent calcification caused by ischemia [5]. Similarly, Sedano, Pindborg and Kerebel et al., proposed that the ghost cells represent different stages in the process of ortho-, para- and aberrant keratin formation and that they should be perceived as a consequence of metaplastic transformation of cells due to the loss of developmental and inductive influences [6,7]. Laba et al., demonstrated that the histochemical reaction for keratin and the immunohistochemical reaction for epithelial membrane antigen and cytokeratin were positive in ghost cells, suggesting their epithelial origin [8].

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 [3,4]. Similarly, Takata et al., found that ghost cells in calcifying odontogenic cysts showed only faint or no positivity for a wide spectrum of cytokeratins, while adjacent non ghost epithelial cells were evidently positive, which entailed that aberrant keratinization make only a minor contribution to the formation of ghost cells and their biologic properties are inconsistent to keratinocytes [3]. In an immunohistochemical review of odontogenic ghost cell carcinoma by Kim et al., using cytokeratins, involucrin and apoptosis-related proteins (Bcl-2, Bcl-XL and Bax) 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 positivity for Bax, suggesting their formation to be an apoptotic process as they undergo abnormal terminal differentiation [9].

The current WHO classification of odontogenic tumors contemplated ghost cells as transient squamous cells at varied stages of differentiation [10]. However, theories proposed regarding the



[Table/Fig-1]: Photomicrograph of COC showing balloon shaped ghost cells (arrow) with pale eosinophilic cytoplasm, well-defined cellular outline and faint nuclear outline (H&E, 10X) (obtained from the archives of Department of Oral Pathology, PGIDS, Rohtak)

formation of ghost cells are many, yet a clear, unified stance on its nature and mechanism remains unresolved.

Classification

Only one classification for ghost cell odontogenic lesions (Praetorius, 2006) is available in the English literature [11]. So, an attempt has been made to organize these lesions for better understanding and academic purpose.

Basis of The Classification

The two characteristics used here to define the fundamental groups are the nature of the lesion and the histological cell of origin.

Old Classification

Praetorius (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) [11].

Revised Classification

- I. Developmental [4]
 - A. Inner enamel epithelium of developing teeth
- II. Odontogenic cysts [4,10,11]
 - A. Eruption cyst
 - B. Glandular odontogenic cyst
 - C. Calcifying epithelial odontogenic cyst
- III. Tumours of odontogenic origin [5,7,10,11]
 - A. Ameloblastoma (granular cell type)
 - B. Ameloblastic fibroma

- C. Ameloblastic fibro-odontoma
- D. Odontoameloblastoma/ Dentinoameloblastoma
- E. Odontoma (complex and compound)
- F. Ghost cell odontogenic carcinoma
- IV. Others (non-odontogenic lesions) [3,4,10,11]
 - A. Cutaneous calcifying epithelioma of Malherbe / Pilomatrixoma (in skin)
 - B. Craniopharyngioma (in pituitary gland)

CONCLUSION

Ghost cells in certain tissues might be the part of embryologic development or result of any pathology. The distinction among these necessitates the system which clearly defines and classifies ghost cell lesions. An attempt is made to introduce the new classification which could assist the clinicians and researchers in the categorization of ghost cell lesions according to its biological behavior to widen the horizons of oral and maxillofacial pathology.

REFERENCES

- [1] Neville BW, Damm DD, Allen CM. Odontogenic cyst and tumours. In: Gnepp DR (editor). Diagnostic surgical pathology of the head and neck. Philadelphia: WB Saunders Company; 2000;pp 605-43.
- [2] Shear M, Speight P. Calcifying odontogenic cyst. In: Cysts of the oral and maxillofacial regions, 4th ed. Oxford, UK: Blackwell Publishing Ltd; 2007; pp 101-07.
- [3] Halappa TS, George J, Shukla A. Odontogenic ghost cells: Realities behind the shadow. *Journal of oral research and review*. 2014;6(1):40-43.
- [4] Mehendiratta M, Bishen KA, Boaz K, Mathias Y. Ghost cells: a journey in the dark. *Dental Research Journal*. 2012;9 (7)(Issue1):S1-8.
- [5] Levy BA. Ghost cell and odontomas. *Oral Surg Oral Med Oral Pathol*. 1973;36:851-55.
- [6] Sedano HO, Pindborg JJ. Ghost cell epithelium in odontomas. *J Oral Pathol*. 1975;4:27-30.
- [7] Kerebel B, Kerebel LM. Ghost cells in complex odontoma: a light microscopic and SEM study. *Oral Surg Oral Med Oral Pathol*. 1985;59:371-78.
- [8] Laba E, Dumitrescu G, Ardeleanu C, Gogalniceanu D, Laba CD. Calcifying odontogenic cyst: report of two cases and review of literature. *Rom J MorpholEmbryol*. 1997;43(3-4):205-12.
- [9] Kim J, Lee EH, Yook JI, Han JY, Yoon JH, Ellis GL. Odontogenic ghost cell carcinoma: A case report with reference to the relation between apoptosis and ghost cells. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000;90:630-35.
- [10] Reichart PA, Phillipsen HP. Odontogenic Tumors and Allied Lesions. London: Quintessence Publishing Co. Ltd.; 2004.
- [11] Ahn SG, Kim SA, Kim SG, Lee SH, Kim J, Yoon JH. β -catenin gene alterations in a variety of so called Calcifying Odontogenic Cysts. *APMIS*. 2008;116:206-11.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Oral Pathology, Post Graduate Institute of Dental Sciences, Pt. B. D Sharma University of Health Sciences, Rohtak, Haryana, India.
2. Reader, Department of Orthodontics & Dentofacial Orthopedics, Mithila Minority Dental College & Hospital, Darbhanga, Bihar, India.
3. Associate Professor, Department of Oral Pathology, Post Graduate Institute of Dental Sciences, Pt. B. D Sharma University of Health Sciences, Rohtak, Haryana, India.
4. Assistant Professor, Department of Oral Pathology, Post Graduate Institute of Dental Sciences, Pt. B. D Sharma University of Health Sciences, Rohtak, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Achla Bharti Yadav,
Assistant Professor, Department of Oral Pathology, Post Graduate Institute of Dental Sciences, Rohtak, Haryana, India.
E-mail: drachlabharti@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 09, 2015**
Date of Peer Review: **May 25, 2015**
Date of Acceptance: **Jul 02, 2015**
Date of Publishing: **Sep 01, 2015**