Research Article
A Comparative Histochemical Study of Mucous Cells in Odontogenic Cysts

Ridwaana Carim and Farzana Mahomed

Department of Oral Pathology, School of Oral Health Sciences, Faculty of Health Sciences, University of the Witwatersrand, Private Bag 3, Wits, Johannesburg 2050, South Africa

Correspondence should be addressed to Farzana Mahomed; farzana.mahomed@nhls.ac.za

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The diagnosis of a glandular odontogenic cyst (GOC) on an incisional biopsy continues to remain a diagnostic challenge for the histopathologist. A marker for distinguishing GOC from odontogenic cysts with mucous metaplasia is thus needed in routine pathology practice. This study aimed to determine the histochemical composition of the mucous cells in the GOC and to compare the findings with the mucous cells in odontogenic cysts that show overlapping histomorphological features with the GOC. GOCs (n=10), dentigerous cysts (DCs) (n=9), and radicular cysts (RCs) (n=8) with mucous metaplasia were stained using the combined alcian blue (pH 2.5)-PAS histochemical technique. The cysts were evaluated for the frequencies of acidic-(type I), neutral-(type II) and mixed- (acidic and neutral (type III)) mucin containing cells. Significant differences were found between the levels of type I, type II, and type III mucous cells within the 3 cyst types, GOC (P=0.006), DC (P=0.0004), and RC (P=0.0017), which all showed a predominance of type III mucous cells. There were, however, no significant differences for each mucous cell type between the 3 cyst types. GOC thus appears to share the same histochemical mucin phenotype with the mucous cells in DC and RC.

1. Introduction

The occurrence of mucous cells in odontogenic lesions is a rare but well-recognised phenomenon [1–5]. Those odontogenic cysts that have a tendency for showing mucous cells in their cyst linings include dentigerous cysts (DC), radicular cysts and residual radicular cysts (RC), and, by definition, glandular odontogenic cysts (GOC) [1–4, 6]. The pathological basis for the transition from the usually nonmucinous odontogenic epithelium to cells that produce mucin is poorly understood. On the basis of the presence of clear or vacuolated cells that are occasionally observed near the mucous cells in the epithelial linings of these cysts, it has been suggested that the mucous cells arise as a consequence of a metaplastic process in these cysts [4]. Other theories include grafting of mucous cells from a contiguous epithelium such as the maxillary sinus or from embryological pluripotential cells in the epithelial residues from which these cysts arise [1, 2]. Although the histogenesis of GOCs remains uncertain, it is widely believed that these cysts originate from odontogenic epithelium [7]. This is borne out to a considerable extent by many histomorphological characteristics of the GOC that are reminiscent of odontogenic lesions [8]. The presence of duct—like structures and mucous—producing cells is, however, not unique to the GOC as these features overlap with such lesions as intraosseous mucoepidermoid carcinoma, DCs and RCs with mucous metaplasia [9]. A definitive histological diagnosis of GOC can hence often be difficult to make. While Kaplan et al. [10] reported a strict set of criteria for the diagnosis of GOC, according to MacDonald-Jankowski [11] and Araújo de Morais et al. [9], histopathology alone may be considered to be insufficiently specific in each and every case of GOC. Furthermore, in small biopsy specimens not all the required criteria may be evident.

Previous diagnostic studies on the GOC have largely focused on the application of immunohistochemistry for differentiating it from central mucoepidermoid carcinoma [12, 13]. Differentiation of GOC from DCs and RCs with mucous metaplasia also bears treatment and prognostic implications. While simple enucleation or curettage usually suffices in the management of DCs and RCs, for the GOC complete local excision is mandatory and careful follow-up for at least 3 years...
is recommended, as most of the recurrences, the frequency of which is estimated to be 21%, appear after the third year [14]. A marker for distinguishing GOC from odontogenic cysts with mucous metaplasia remains to be identified.

Since studies on the histochemical composition of the mucous cells in the GOC and its clinically more indolent histological mimics are lacking, this study sought to determine the histochemical composition of mucous cells in the glan-
dular odontogenic cyst (GOC) and to compare these findings with the mucous cells of DCs and RCs in order to determine whether significant differences exist.

2. Material and Methods

2.1. Tissue Samples. Twenty-seven odontogenic cysts comprising 10 GOCs, 9 DCs showing mucous metaplasia, and 8 RCs (3 radicular cysts and 5 residual radicular cysts) showing mucous metaplasia were selected from the University of the Witwatersrand Oral Pathology archived data retrieval base. The corresponding hematoxylin and eosin, periodic acid-Schiff (PAS), PAS-diastase, and/or mucicarmine stained slides were reviewed to confirm the initial diagnosis and the presence of mucous cells within the cyst linings. The odontogenic cysts were purposely chosen from the mandible in order to negate the possibility that the origin of the mucous cells may be the result of migration or grafting of such cells from the antral or nasal cavities. This criterion also avoided the inclusion of nonodontogenic cysts found in the maxilla and normally lined, at least in part, by mucous cells. The GOC and DC which were selected were devoid of inflammatory infiltrate in the cyst wall. Varying amounts of inflammation were invariably present in RC. The study had approval from the University of the Witwatersrand Human Research Ethics Committee for research conducted on archived paraffin wax embedded tissue blocks (no.: M0808500).

2.2. Laboratory Method. The formalin fixed and paraffin embedded (FFPE) tissue sections of the 27 odontogenic cysts were dewaxed and rinsed with distilled water. Sections were then treated with alcin blue solution for 5 minutes and washed in distilled water for 2 minutes. 1% aqueous periodic acid was applied for 5 minutes and then rinsed well in distilled water. Schiff’s reagent was applied for 15 minutes and washed in running tap water for 5 minutes. Nuclei were stained with hematoxylin. Sections were then washed in water, rinsed in absolute alcohol, cleared in xylene, and mounted as usual. Cervix was used as control tissue.

2.3. Interpretation of Histochemical Staining. The combined alcian blue pH 2.5-periodic acid-Schiff (AB-PAS) technique distinguishes between acidic mucins that are stained blue and neutral mucins that are stained magenta with this stain. Mucous cells that contain mixtures of neutral and acidic mucin stain purple with the combined AB-PAS stain. Based on this staining reaction pattern the mucous cells in this study were denoted as type I (cells containing only acidic mucin), type II (cells containing only neutral mucin), and type III (cells containing both acidic and neutral mucin) mucous cells.

2.4. Data Analysis. The total number of mucous cells present in the linings of the odontogenic cysts studied was manually counted thereby yielding continuous data. The frequencies of types I, II and III mucous cells both within and between the odontogenic cysts studied were statistically compared using the Kruskal-Wallis test. Interobserver reliability was established with a dual-headed microscope that enabled both observers to count the data simultaneously by consensus. Every second specimen was then subjected to a recount, on a separate occasion to establish reliability of the recorded data. The Wilcoxon matched pairs test was carried out, which showed no significant difference between the count-recount data. Data analysis was carried out in Statistica; StatSoft, Inc. version 7.1. The 0.05 significance level was used for all statistical tests.

3. Results

There were significant differences between the levels of type I, type II, and type III mucous cells within the GOC ($P = 0.006$), DC ($P = 0.0004$), and RC ($P = 0.0017$) (Figure 1). No significant differences were, however, found for type I mucous cells ($P = 0.54$), type II mucous cells ($P = 0.73$), and type III mucous cells ($P = 0.97$) between the 3 cyst types (Figures 2, 3, 4, and 5). The mucin phenotype of the GOC is thus shared by DC and RC with mucous metaplasia.

4. Discussion

Studies on mucin histochemistry of odontogenic cysts with mucous cells are few [1–4], while studies on the histochemical composition of the mucous cells in the GOC are lacking in the literature. The aims of the present study were therefore to histochemically characterise the mucin of the GOC and other odontogenic cysts with mucous cells in order to determine
whether there are any significant variations in the mucin content between these cysts. As far as we are aware, this is the first histochemical study undertaken to analyse the mucous cell phenotype of the GOC.

The mucous cell types within the GOC, DC, and RC were found to be similar within all 3 cyst types, which were characterised by a type I < type II < type III mucous cell phenotype. Notably the mucous cell phenotype of the odontogenic cysts studied, irrespective of them being of developmental (glandular odontogenic cyst, dentigerous cyst) or inflammatory (radicular or residual radicular cyst) origin, was the same. The overlapping mucin phenotype of the GOC, DC, and RC unfortunately, however, does not support the use of the combined AB (pH 2.5)-PAS stain as a marker to distinguish between the GOC and other odontogenic cysts that may show mucous cells within their cyst linings. Within the limitations of the staining reaction employed our findings may admittedly still be recorded as preliminary data only. Nevertheless, the findings are novel and intriguing and provide direction for future studies aimed at identifying a discriminatory mucous cell marker for distinguishing between GOC and other odontogenic cysts with mucous cells.

The study findings also allow us to speculate on the histogenesis of the mucous cells in odontogenic cysts. Immunohistochemical studies on the GOC strongly suggest an odontogenic origin for this lesion [7, 13, 15]. While the findings of this study suggest that the mucous cell phenotype of the GOC is shared by other odontogenic cysts with mucous cells, it further appears that the mucous cell phenotype of odontogenic cysts overlaps with the submandibular and sublingual salivary glands. In the study by Eversole [16] mucous cells harbouring mixtures of acidic and neutral mucins, denoted as type III mucous cells in this study, were found to be the predominant mucous cell type in the major salivary glands. The failure of development or hypofunction of ectodermally derived tissues in conditions characterised by major salivary gland aplasia suggests that the ectodermal germ layer is the most likely developmental source of origin of the major salivary glands [17]. Since odontogenic epithelium is embryologically also of ectodermal derivation [18], similarities in the mucin profiles of the mucous cells in odontogenic cysts and those of salivary glands may be reflective of the common origin of odontogenic and salivary gland epithelia [17]. Recent studies have shown distinct profiles of immunohistochemical expression of mucin core proteins (MUC) for a variety of epithelial cells including the salivary glands [19]. Consequently, a comparative analysis on MUC expression in salivary glands and a larger sample of odontogenic lesions with mucous cells remain an avenue for further research to improve our understanding of mucous cell differentiation in odontogenic lesions.

**Conflict of Interests**

The authors declare no conflict of interests.
References

[1] R. J. Gorlin, “Potentialities of oral epithelium manifest by mandibular dentigerous cysts,” *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, vol. 10, no. 3, pp. 271–284, 1957.

[2] R. M. Browne, “Metaplasia and degeneration in odontogenic cysts in man,” *Journal of Oral Pathology*, vol. 1, no. 4, pp. 145–158, 1972.

[3] Y. Takeda, Y. Oikawa, I. Furuya, M. Satoh, and H. Yamamoto, “Mucous and ciliated cell metaplasia in epithelial linings of odontogenic inflammatory and developmental cysts,” *Journal of Oral Science*, vol. 47, no. 2, pp. 77–81, 2005.

[4] H. Slabbert, M. Shear, and M. Altini, “Vacuolated cells and mucous metaplasia in the epithelial linings of radicular and residual cysts,” *Journal of Oral Pathology & Medicine*, vol. 24, no. 7, pp. 309–312, 1995.

[5] A. V. Punnya and K. Rekha, “‘Ameloblastoma with mucous cells’: review of literature and presentation of 2 cases,” *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*, vol. 106, no. 6, pp. e20–e26, 2008.

[6] D. G. Gardner, H. P. Kessler, R. Morency, and D. L. Schaffner, “The glandular odontogenic cyst: an apparent entity,” *Journal of Oral Pathology*, vol. 17, no. 8, pp. 359–366, 1988.

[7] J. Shen, M. Fan, X. Chen, S. Wang, L. Wang, and Y. Li, “Glandular odontogenic cyst in China: report of 12 cases and immunohistochemical study,” *Journal of Oral Pathology & Medicine*, vol. 35, no. 3, pp. 175–182, 2006.

[8] K. I. Tosios, E. Kakarantza-Angelopoulou, and N. Kapranos, “Immunohistochemical study of bcl-2 protein, Ki-67 antigen and p53 protein in epithelium of glandular odontogenic cysts and dentigerous cysts,” *Journal of Oral Pathology & Medicine*, vol. 29, no. 3, pp. 139–144, 2000.

[9] H. H. Araújo de Morais, R. José de Holanda Vasconcellos, T. de Santana Santos, L. M. Guedes Queiroz, and É. J. Dantas da Silveira, “Glandular odontogenic cyst: case report and review of diagnostic criteria,” *Journal of Cranio-Maxillofacial Surgery*, vol. 40, no. 2, pp. e46–e50, 2012.

[10] I. Kaplan, Y. Anavi, and A. Hirshberg, “Glandular odontogenic cyst: a challenge in diagnosis and treatment,” *Oral Diseases*, vol. 14, no. 7, pp. 575–581, 2008.

[11] D. S. MacDonald-Jankowski, “Glandular odontogenic cyst: systematic review,” *Dentomaxillofacial Radiology*, vol. 39, no. 3, pp. 127–139, 2010.

[12] M. Vered, I. Allon, A. Buchner, and D. Dayan, “Is maspin immunolocalization a tool to differentiate central low-grade mucoepidermoid carcinoma from glandular odontogenic cyst?” *Acta Histochemica*, vol. 112, no. 2, pp. 161–168, 2010.

[13] F. R. Pires, S. Y. Chen, D. E. da Cruz Perez, O. P. de Almeida, and L. P. Kowalski, “Cytokeratin expression in central mucoepidermoid carcinoma and glandular odontogenic cyst,” *Oral Oncology*, vol. 40, no. 5, pp. 545–551, 2004.

[14] P. Economopoulou and A. Patrikiou, “Glandular odontogenic cyst of the maxilla: report of case,” *Journal of Oral and Maxillofacial Surgery*, vol. 53, no. 7, pp. 834–837, 1995.

[15] I. Semb, M. Kitan, T. Mimura, S. Sonoda, and A. Miyawaki, “Glandular odontogenic cyst: analysis of cytokeratin expression and clinicopathological features,” *Journal of Oral Pathology & Medicine*, vol. 23, no. 8, pp. 377–382, 1994.

[16] L. R. Eversole, “The mucoprotein histochemistry of human mucous acinar cell containing salivary glands: submandibular and sublingual glands,” *Archives of Oral Biology*, vol. 17, no. 1, pp. 43–53, 1972.
