

Case Report

Histologic Look- a likes: Glandular Odontogenic Cyst and Odontogenic Cysts with Mucous Metaplasia

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Abstract

Glandular odontogenic cyst (GOC) is among the more aggressive cysts of the jaws.

There is no single microscopic feature that is pathognomonic for GOC, but rather a combination of features would be required for diagnosis, while some of these features may be evident in other odontogenic cysts.

The objective of this short communication is to present a new case of GOC versus a radicular cyst with similarity in clinico-radiographic findings as well as some overlapping microscopic features, with emphasis on the pathway to accurately differentiating GOC from its microscopic look-alikes.

INTRODUCTION

Glandular odontogenic cyst (GOC) is among the more aggressive cysts of the jaws. It is rare, with just under 120 cases published since its description by Gardner in 1988 [1].

GOC may present as unilocular or multilocular radiolucency, usually with well-defined borders. It has been described in association with unerupted teeth (dentigerous position), between roots mimicking lateral periodontal cyst, in a "globulomaxillary" location, or in edentulous areas. GOC involve the mandible more often than the maxilla, and tend to occur in anterior areas in both jaws, frequently crossing the midline [2-6].

It tends to compromise the integrity of the cortical plates or perforate through in more than 50% of the cases, and has a relatively high recurrence rate [2-6].

A variety of microscopic features described in GOC [3,5]. There is no single microscopic feature that is pathognomonic, but rather a combination of features would be required for diagnosis. In most cases only some of these features are present, and there are controversies in the literature as to how many features are required for a diagnosis of GOC, and which individual features are the most typical for GOC [3,5].

Several of the individual microscopic features can also be

found in lateral periodontal or botryoid cyst, and odontogenic cysts with mucous metaplasia [3,4,7]

It is important to make that distinction because GOC has a high tendency to recur after enucleation, and require prolonged follow-up of up to 10 years [2,4,5,8]. In contrast, there is no evidence that simple mucous metaplasia in a cyst has any clinical significance for either treatment or follow-up.

Some microscopic features of GOC may also overlap with central mucoepidermoid carcinoma (MEPCa) [3-5, 12]

In rare cases in which differentiation between GOC and MEPCa is difficult, lack of MAML2 rearrangement, as well as no expression of Mas pin and positive staining for CK19 may help to differentiate GOC from MEPCa [9-12].

The objective of this short communication is to present a new case of GOC versus a case of radicular cyst with similarity in clinico-radiographic findings as well as some overlapping microscopic features, and emphasize the pathway to accurately differentiating GOC from its microscopic look-alikes.

CASE PRESENTATION**Case 1**

A 50 years old male, with a 3 weeks history of swelling and

pain in the right buccal area. The swelling was over 3 cm in diameter, fluctuant, involved the buccal mucosa as well as the maxillary vestibule in the molar-premolar area, and the overlying skin was erythematous. The canine and premolars were non-vital, the first molar was missing and the second molar was vital.

A panoramic radiograph exhibited a large radiolucent area in the right maxilla, with complete lysis of the alveolar crest, encroaching upon the maxillary sinus. (Figure 1, 2). Additional information from the CT scan included perforation of the buccal cortical plate and evidence for displacement of the maxillary sinus floor.

Histopathology showed a cyst lined by multilayered cuboidal epithelium, with a superficial layer of pale eosinophilic cells, resembling "hobnails". A relative uniform epithelial width was observed throughout the lesion (Figure 3a).

PAS (Periodic acid Schiff) and AB (Alcian Blue) stains showed prominent mucous metaplasia of the lining. (Figure3b).

The lesion was signed out as radicular cyst with prominent mucous metaplasia.

Case 2

60 years old male, with a medical history of rheumatoid arthritis, treated with 5 mg of prednisone daily. During dental examination, an asymptomatic soft fluctuant swelling of the right maxillary vestibule was observed.

A panoramic radiograph revealed a well-defined unilocular radiolucent lesion in the edentulous right anterior maxilla (Figure 4a). A cone beam CT scan clearly demonstrated that the cortical plate was perforated. The size of the lesion was 3x1.5 cm (Figure 4b).

Microscopic analysis showed a cyst lined by odontogenic epithelium, demonstrating variations in thickness, with areas of plaque-like or epithelial spheres. Clefts and hob nail cells in the superficial layers were also observed focally (Figure 5 a-c). In some areas intra-epithelial gland-like formation were observed. Other areas showed larger intra-epithelial cysts (Figure 6a), and papillary projections lined by mucous cells (Figure 6b). PAS and AB stains highlighted the mucous cell population, forming both gland-like structures and clefts lines by mucous cells.

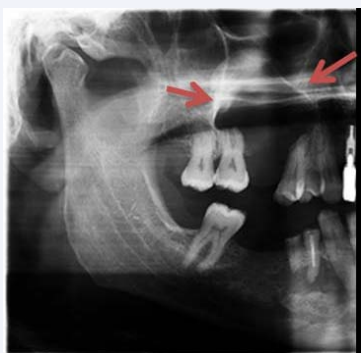


Figure 1 Cropped panoramic radiograph showing a well-defined radiolucent lesion in premolar maxillary area. The crestal alveolar bone is completely resorbed. (case1).



Figure 2 A CT scan axial image exhibits perforation of the anterior plate, as well as encroachment of the maxillary sinus. (same case).

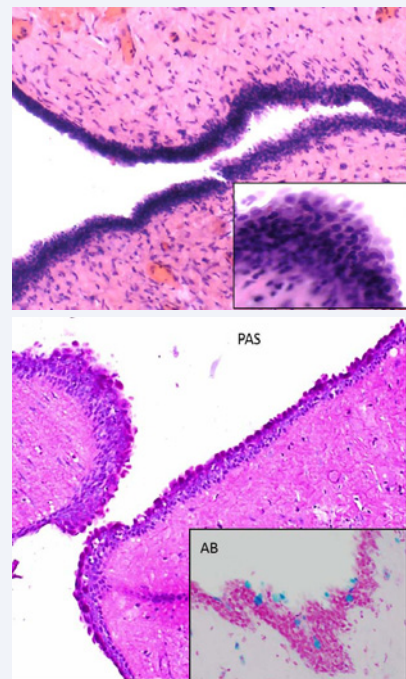


Figure 3 a: The microscopic slide shows a cyst lined by a uniform layer of stratified epithelium with prominent mucous cells at the superficial layers. Hob-nail cells can also be observed. (Hematoxylin& Eosin, original magnification, X 40 main image, X 200 inset)

b: Periodic Acid Schiff (PAS) stain highlighted the mucous cells in the superficial layers of the lining. Inset shows some but not all these cells stained positive with Alcian Blue (AB) as well. (Original magnification X 40)

The combination of a number of these microscopic features was considered sufficient for the diagnosis of GOC.

DISCUSSION

The individual features described in GOC include variation in the width of the epithelial lining in different areas, epithelial plaque-like thickening, papillary projections, intra-epithelial gland-like or microcystic structures, mucous goblet cells, intra-epithelial cleft-like structures lined by mucous cells, hob-nail cells sometime demonstrating apocrine like snouting, ciliated cells and clear cells. Multiple compartments have also been described [3,5].

The comparison of the present two cases shows significant

similarity in radiographic and clinical features: both lesions were located in anterior maxilla, both were radiolucent with well-defined borders, both cases demonstrated perforation of cortical plates and significant osteolysis.

Thus, in both cases GOC should be included in the differential

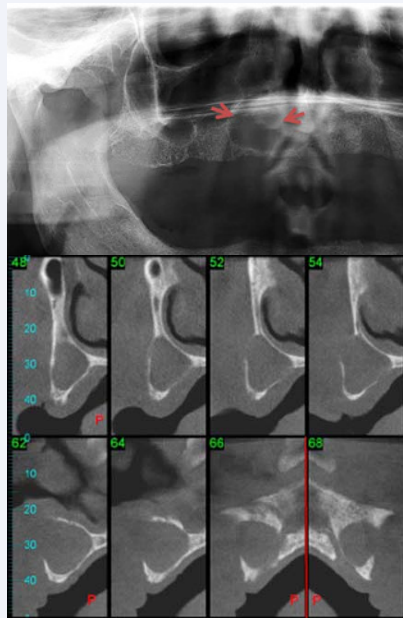


Figure 4 a. Cropped panoramic radiograph shows a well-defined radiolucent lesion in the edentulous premolar maxilla. (Case 2)
b. Several sections of a cone beam CT scan demonstrate persistent large perforation of the buccal plate. (Same case).

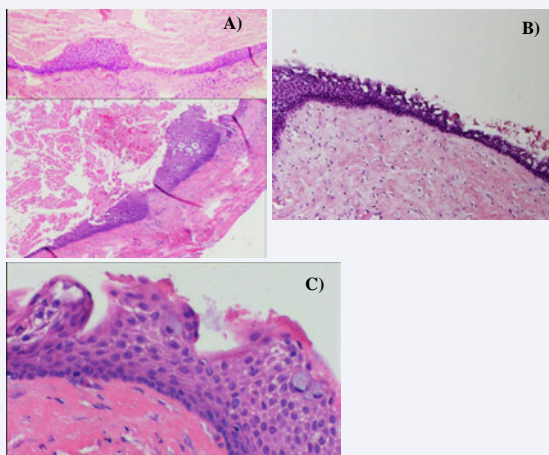


Figure 5 a. Microscopic sections exhibit variations in the thickness of the epithelial lining, with plaque-like projection (upper panel). The lower panel shows a different area of the lining with clear gland-like formation in the center of an epithelial plaque-like projection. (Hematoxylin & Eosin, original magnification X40).
b. Micro-papillary projections as well as pale mucous cells are apparent in the lining. (Hematoxylin & Eosin, original magnification X40)
c. Different areas show clefts in the lining, as well as mucous cells and eosinophilic hob-nail cells protruding towards the lumen. (Hematoxylin & Eosin, original magnification X200)

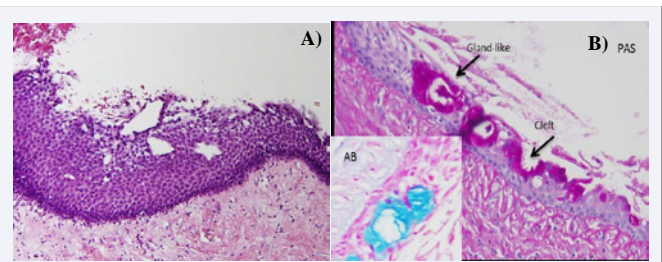


Figure 6 a. Large intra-epithelial cysts are observed within the lining. (Hematoxylin & Eosin, original magnification X100).
b. PAS stain highlights both gland-like formation and clefts lined by mucous cells. Inset shows positive staining in Alcian Blue in the gland-like structures. (Original magnification X200).

diagnosis, alongside other possible diagnoses such as radicular or residual cyst, and odontogenic keratocyst.

The lesions also shared two microscopic features- both had a prominent population of mucous cells, and some "hob-nail" cells. However, whereas in case 1 the lining was uniform in width, in case 2 there was considerable variations in width, with the typical epithelial spheres. In addition, other features consistent with GOC were observed such as the formation of intra-epithelial cysts, groups of mucous cells arranged in a gland like configuration, clefts lined by mucous cells and papillary projections protruding towards the lumen.

In case 2 both mucous cells and "hobnail" cells have been identified, and although these types of cells have been described in 100% of GOC cases in some series [5], relative uniform epithelial width throughout the lesion and absence of intra-epithelial gland-like or microcyst formation were strong indicators that this odontogenic cyst is not GOC, in spite of its radiographic signs of aggressive behavior.

Variation in the width of the epithelial lining in different areas with epithelial plaque-like thickening, and occasional clear cells are typical findings in lateral periodontal cyst and botryoid cysts, but these lesions do not present any of the other features of GOC [3,4]

Mucous cells representing mucous metaplasia may be found in up to 20% of odontogenic cysts, such as radicular or dentigerous cysts, more frequently in the maxilla than in the mandible, and in about half of these cases ciliated cells are also present alongside mucous cells [7]. When prominent mucous metaplasia is present, differentiation from GOC becomes relevant. However, if these features are not associated with the remaining characteristics of GOC, a population of mucous and ciliated cells is not sufficient for a diagnosis of GOC.

A population of mucous cells and cystic formation are some of the microscopic features of observed in low-grade central mucoepidermoid carcinoma (MEPCa). Although significantly less frequent than GOC, this possibility may need to be considered as a differential diagnosis in selected cases. In rare cases in which differentiation between GOC and MEPCa is difficult, lack of MAML2 rearrangement, as well as no expression of Maspin and positive staining for CK19 may help to differentiate GOC from MEPCa [9-12].

Lack of podoplanin expression in GOC has been shown to help in differentiation of GOC from other inflammatory and developmental cysts, which do express this marker in the majority of cases [13].

According to Fowler et al., cysts with 5 or less of the classical characteristics for GOC are inconsistent with GOC (as represented in case 1), whereas the presence of 6 or more of these features (preferably 7-8), strongly support the diagnosis GOC (as in case 2) [5].

It is important to make that distinction, because GOC has a high tendency to recur, enucleation with peripheral ostectomy and in selected cases marginal resection are recommended as treatment. The patients require prolonged follow-up of up to 10 years, due to reports of late recurrence [2,4,5,8]. In contrast, there is no evidence that simple mucous metaplasia in a cyst has any clinical significance for either treatment or follow-up.

For the pathologist, familiarity with the individual microscopic features within the spectrum of GOC, as well as the requirement for a combination of several features to qualify for the diagnosis of GOC are key for accurate diagnosis. This set of criteria can also aid in recognition of other lesions which mimic GOC but have a significantly different biologic behavior.

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