Case Report

Glandular odontogenic cyst: A diagnostic dilemma

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Abstract

Glandular odontogenic cyst (GOC) is a rare and uncommon jaw bone cyst of odontogenic origin described in 1987 by Gardener *et al*. as a distinct entity. It is a cyst having an unpredictable, potentially aggressive behavior, and has the propensity to grow in large size with relatively high recurrence rate. It poses a diagnostic challenge as it can be clinically and histopathologically confused with lateral periodontal cyst, botryoid odontogenic cyst, radicular and residual cysts with mucous metaplasia, and low-grade mucoepidermoid carcinoma. The present case report describes GOC in both male and female patients with intra-oral swelling following extraction of 36 and 46, respectively. Careful histopathological examination is needed to diagnose GOC, and a careful long-term follow-up is advocated.

Key words: Glandular odontogenic cyst, "hobnail" cells, mucous cells

INTRODUCTION

Glandular odontogenic cyst (GOC), a relatively rare cyst occurring in the tooth -bearing areas, was originally reported by Padayachee and Van Wyk[1] based on the possibility of salivary gland origin and microscopic resemblance to the salivary gland tissue, they proposed the term "Sialo-odontogenic cyst." Shear favored the term "muco-epidermoid cyst," which was advocated by Sadeghi *et al*.[2] However, this term was already used by Hudson[3] to describe radicular, residual, and dentigerous cyst with mucus metaplasia. Other terms such as polymorphous odontogenic cyst have also been suggested. Later Gardner in his report of eight cases in 1988, based on the clinical, radiological, and histological characteristics, suggested this cyst to be odontogenic in origin. The term GOC was first coined by Gardner.[4] It was later in 1992; the World Health Organization (WHO) accepted GOC as a distinct pathological entity and included it in the classification as developmental odontogenic cysts.[5]

In the following years, more evidence supporting its odontogenic rather than sialogenic origin have been reported.[6-8] Several cases of hybrid lesions of GOC with other odontogenic lesions such as ameloblastoma, squamous odontogenic tumor, unicystic ameloblastoma, and many more have been reported. Also, the minimal or lack of expression of markers such as epithelial membrane antigen (EMA) and mammary serine protease inhibitor do not support its sialogenic origin.[4,9-13]

Histologically, it bears a resemblance to lateral periodontal cyst (LPC), botryoid odontogenic cysts (BOCs), radicular and residual cysts with mucous metaplasia, and low-grade mucoepidermoid carcinoma. Thus posing a challenge in making the diagnosis.

Although rare it has been noted that, GOC has an aggressive potential, a high incidence of cortical

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perforation, and a relatively high rate of recurrence, especially in cases treated conservatively. Therefore, the correct diagnosis is a major challenge and is of extreme clinical importance.[14]

The aim of the present paper is to discuss the clinical, radiological, histopathological aspects, and differential diagnosis of the cases reported in our institution.

CASE REPORTS

Case 1

A 25-year-old male patient reported to our institution with a swelling in the lower left posterior region of lower jaw for 2 months that followed the extraction of 36 [Figure 1]. The swelling was gradually increasing in size. Medical history was not significant. Extraoral examination revealed swelling that was bony hard and nontender on palpation. Overlying skin was normal. Submandibular lymph nodes were not palpable. Intraoral examination revealed swelling extending from the left second premolar to the second molar region, causing the expansion of both buccal and lingual aspect of alveolar ridge [Figures 2-4]. Radiographic examination (intraoral periapical radiograph [IOPA and OPG]) revealed well–defined, unilocular radiolucency with sclerotic borders in relation to 35–37 and 36 were missing [Figures 5 and 6]. Based on the clinical and radiographic findings, a provisional diagnosis of residual cyst or odontogenic keratocyst was made. Enucleation of the cyst was done and sent for histopathological examination.

Case 2

A 30-year-old female patient reported to the institute with a complaint of gradually increasing swelling in the lower right back region for 2–3 months following the extraction of carious 46. Medical history was not significant. On intraoral examination, localized swelling was noticed in the edentulous, 46 buccal ridge area approximately measuring about 1.5 cm × 1 cm without the displacement of adjacent teeth. The overlying mucosa was intact and was of normal color. Swelling was non-tender and hard in consistency. IOPA revealed unilocular, well-defined radiolucency in the region of 46 with sclerotic borders. Based on the clinical and radiographic findings, a provisional diagnosis of residual cyst was made. Enucleation of the cyst was done and sent for histopathological examination.

Histopathological examination for both the cases revealed the presence of cystic lumen with epithelial lining and supporting connective tissue capsule. The epithelial lining was 2–3 cell layers thick with a flat epithelio-mesenchymal interface, and at places showed variable thickness with luminal proliferation. The epithelial lining showed few surface cuboidal eosinophilic cells (Hob-nail cells) and few goblet cells. Juxta-epithelial area revealed the hyalinized area suggestive of dentinoid. The connective tissue capsule showed parallelly arranged collagen fibers, few foreign body giant cells, and few blood vessels. Based on these findings, histopathologically it was diagnosed as GOC [Figures 7-10].

DISCUSSION

GOC, accounting for 0.012–1.3% of all jaw cysts, is a recently recognized rare developmental odontogenic cyst with an aggressive behavior and probability of recurrence.[15] Initially reported and coined by Padaychee and Van Wyk in 1987, it was later in 1992, GOC was included in the WHO typing of tumors under the term GOC or sialo-odontogenic cyst. And,

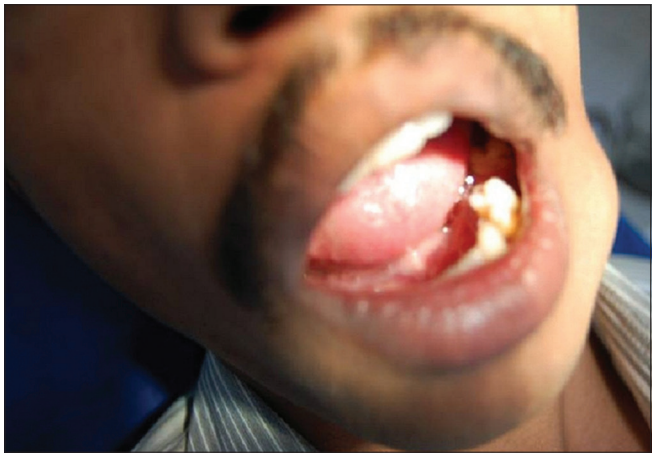

Figure 1: Extra-oral swelling present on the left side of the face. Overlying skin is normal

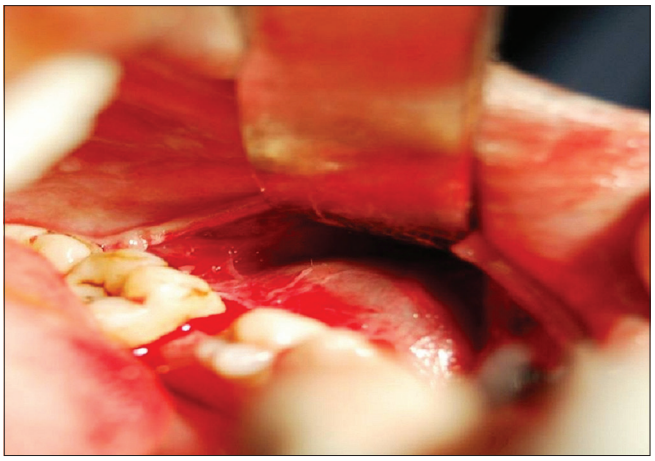

Figure 2: Intra-oral swelling in relation to 35–37. Overlying mucosa appears to be normal, and the expansion of buccal cortical plate can be noted

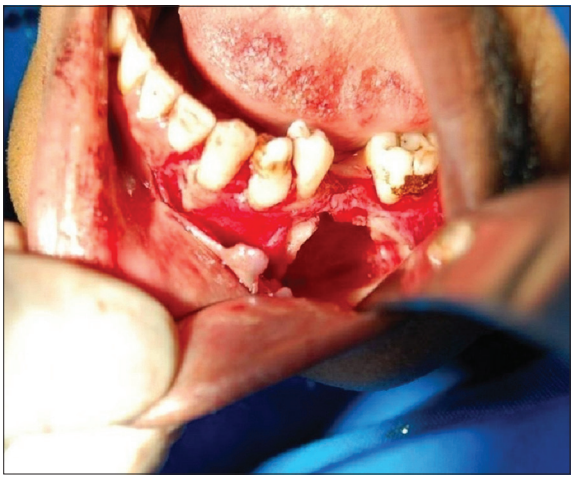

Figure 3: Raised mucosal flap with a defect in the bone

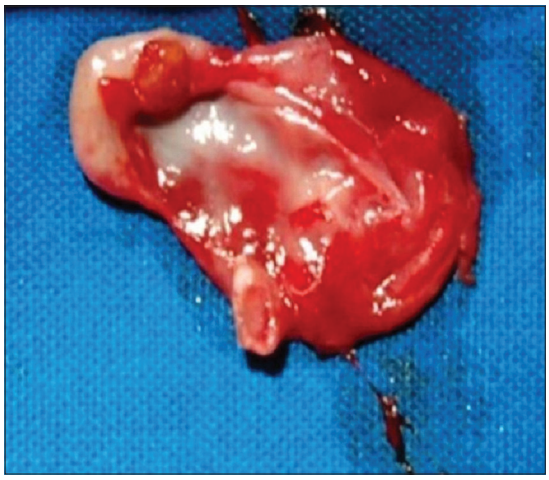

Figure 4: Gross surgical specimen with cystic lumen and well-defined borders

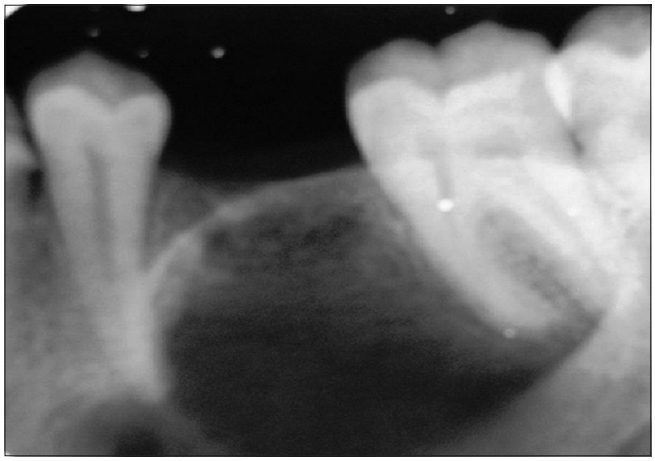

Figure 5: Intraoral periapical radiograph showing unilocular radiolucency with well-defined borders involving 35 and 37. Sclerotic border can be noted, and there is no root resorption. Missing 36 can be noted

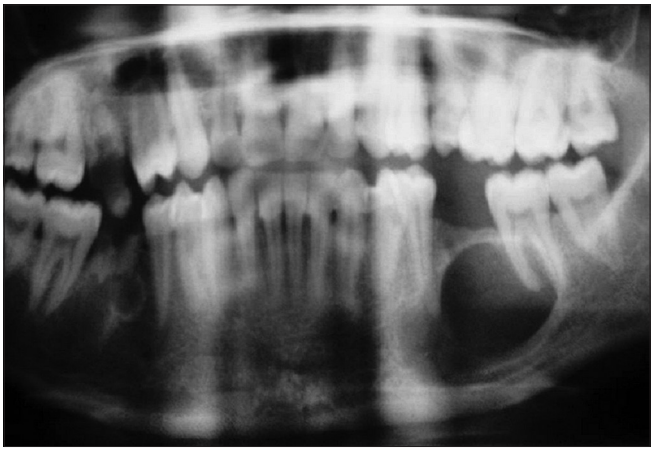

Figure 6: Orthopantomograph showing unilocular radiolucency with well-defined borders involving 35 and 37. Sclerotic border can be noted, and there is no root resorption. Missing 36 can be noted

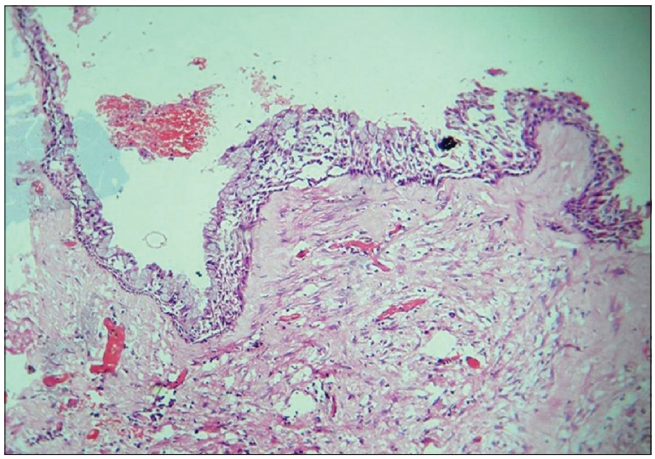

Figure 7: Photomicrograph demonstrating nonkeratinising cystic epithelial lining and supporting connective tissue capsule with flat interphase (H and E, ×4)

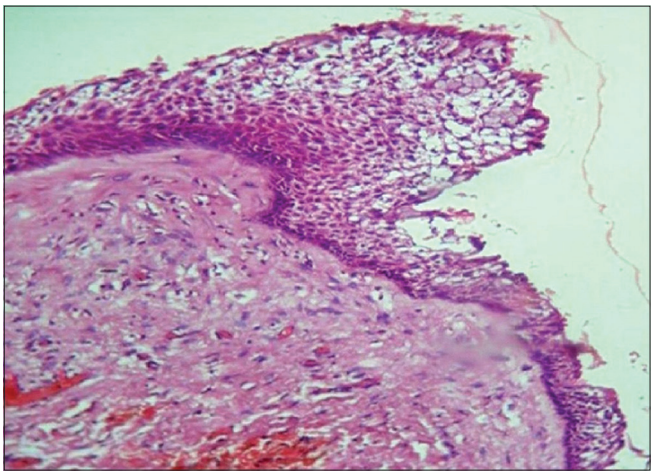

Figure 8: Cystic epithelial lining showing epithelial "plaques" with luminal proliferation and the presence of microcystic spaces (H and E, ×10)

was recognized by WHO as a "cyst arising in the tooth-bearing areas of the jaws characterized by an epithelial lining with cuboidal or columnar cells both at the surface and lining crypts or cyst-like spaces within the thickness of the epithelium."[16]

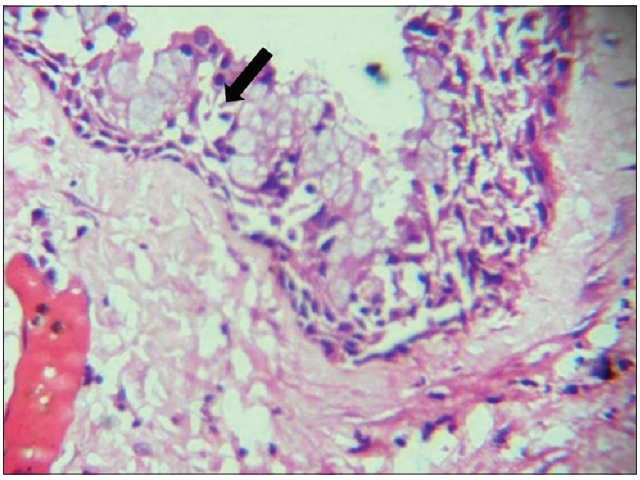

Figure 9: Photomicrograph showing numerous mucous cells and cubaoidal cells (arrow) at the surface microcystic spaces in the eptithelial lining (H and E, ×40)

GOC usually presents as a slow-growing, asymptomatic swelling generally affecting the anterior parts of jaws, particularly the mandible. Few cases of bilateral occurrences have also been reported.[15,17]

Radiographically, GOC is localized intraosseously and may appear as multilocular or unilocular radiolucent lesion with well-defined borders. Many times, it may present with scalloping and peripheral osteosclerotic border. Root resorption and displacement of the teeth are occasionally noted. Thus, the clinical and radiographic findings are varied and pathognomonic.[18]

On aspiration, clear and low viscosity fluid content may be a helpful clinical indication of GOC. The fluid may be brownish-red, which can be attributed to blood, perhaps because of previous surgery or secondary inflammation.[19]

According to Kaplan *et al*. histopathologically it exhibits:[14]

Major criteria

- Non-keratinized squamous epithelial lining with a flat interface
- Presence of "spherules"/knobs or "whorls" or focal luminal proliferations
- Epithelial lining exhibits surface cuboidal eosinophilic cells or "hob-nail" cells
- Mucous/goblet cells with intraepithelial mucous pools with or without crypts lined by mucous producing cells
- Intraepithelial glandular microcystic or duct-like (pseudoglandular) structures.

Minor criteria include

- Papillary proliferation
- Ciliated cells

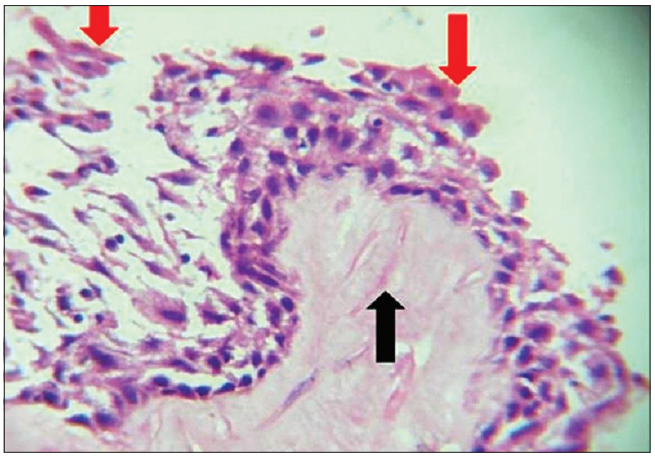

Figure 10: Photomicrograph showing the presence of "hobnail" cells (red arrows) in the epithelial lining and "dentinoid" (black arrow) (H and E, ×40)

- Multicystic or multiluminal architecture
- Clear or vacuolated cells in basal or spinous layer.

As a guideline, they suggested that at least the focal presence of each of the major criteria is mandatory, whereas the minor criteria need not be present for the diagnosis but may just support it.

The mucous cells in the present case reports are stained positively by Periodic acid–Schiff (PAS) stain and is considered to be a result of metaplasia. These metaplastic mucous cells are generally seen in many other odontogenic cysts; however, in GOCs they are seen in abundance. The vacuolated and clear cells observed near the mucous cells may represent an initial stage in the histogenesis of mucus cell metaplasia.[15]

Epithelial plaques or whorls which are a prominent feature of LPC and BOC, also seen in GOC suggest the odontogenic origin of GOC. These epithelial proliferations may be comparable to the proliferative changes seen in the dental lamina.[20]

Histologically, GOC needs to be differentiated from LPC and BOC as there is considerable overlap of clinical, radiological, and histopathological features. LPC is a developmental odontogenic cyst lined with thin non-keratinized epithelium, focal epithelial proliferations, and glycogen-rich clear cells, similar to those seen in GOC. BOC is a polycystic variant of LPC with similar features. However, the identification of ciliated epithelium and duct-like spaces with mucous cells clearly differentiates LPC and BOC, and favors the diagnosis of GOC.[15]

The differentiation of low-grade central mucoepidermoid carcinoma (CMEC) from GOC is more challenging as

there is significant overlap. The presence of superficial cuboidal cells, epithelial whorls, ciliated cells, and intraepithelial microcysts or duct-like structures is suggestive of GOC.[20]

Immunohistochemical studies demonstrating positivity for cytokeratin-7, 13, 14, and 19; the identification of osteodentin and negative reaction for EMA in the areas of glandular structures strongly suggests the odontogenic nature of GOC, and thereby rejecting the theory of glandular origin. GOC exhibited decreased p-53 positivity and increased ki-67 index as compared to CMEC suggesting that GOC lining displays increased proliferation but not malignant transformation potential.[21] Tosios *et al*. demonstrated increased B-cell lymphoma 2—an antiapoptotic protein suggesting that the biological behavior of GOC is associated with dysregulation of cell death in the lining epithelium.[22]

Several studies support the aggressive behavior and a tendency for recurrence; this might be associated with the cell kinetics in the lining epithelium. The high recurrence rate is possibly explained by the multilocular nature, and the tendency of the thin epithelium to separate from the underlying connective tissue capsule thus making the removal difficult at the time of surgery. Another factor responsible for increased recurrence rate is the conservative treatment method. Multicystic lesions treated by curettage or enucleation demonstrated increased recurrence rate of 55% with an average of 4.9 years.[21,23]

Histochemical stains (special stains) used for GOC are Alcian blue, PAS, and mucicarmine.[23] In certain planes of section, these microcysts may be seen to open onto the surface of the epithelium through openings or crypts, giving the epithelium a papillary or corrugated surface. They are sometimes empty and sometimes contain a structureless eosinophilic material which gives a positive mucicarmine reaction.[5]

The treatment of choice is still controversial and ranges from curettage, enucleation, *en bloc,* and partial osteotomy.[24] The present case underwent enucleation due to its clinical and pathologically benign behavior. A follow-up of 18 months is uneventful. Thereafter, the patient was lost for further follow-up. In the light of the present data, we suggest a more aggressive approach in treating GOC, and a careful long-term follow-up is mandatory.

CONCLUSION

To summarize, GOC's are comparatively rare, developmental odontogenic cysts, common in middle age group, with mandibular predilection, with overlapping clinical and radiological findings, and specific histopathogical criteria. The increased recurrence rates can be due to the multilocularity of the cyst, the cell kinetics of the lining epithelium, thin lining is often detached from the connective tissue capsule and thereby making the surgical removal incomplete.

Clinical significance

Careful histopathological examination is needed to diagnose GOC as the clinical and radiological findings are overlapping with lateral periodontal, BOC, residual, and radicular cyst. Aggressive behavior and the tendency for recurrence have been mentioned in the literature so careful, long-term follow-up is advocated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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