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Diagnostic Dilemma of Glandular Odontogenic Cyst-A Case Series and Literature Review

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Abstract

The glandular odontogenic cyst is now a well-known entity comprising < 0.5% of all odontogenic cysts with a recent review tabulating about 200 cases in the English literature. Glandular odontogenic cyst shows epithelial features that mimic glandular differentiation. The importance of glandular odontogenic cyst relates to the fact that it has a high recurrence rate and shares overlapping histologic features with central mucoepidermoid carcinoma. Glandular odontogenic cyst shows no pathognomonic clinico -radiographic characteristics and therefore in many cases it resembles a wide spectrum of jaw cysts and malignancies. Most of the times diagnosis can be difficult due to histopathological similarities with dentigerous cyst, lateral periodontal cyst and central mucoepidermoid carcinoma. Therefore, careful histopathological examination and a long-term follow-up are required to rule out recurrences.

Keywords: Aggressive, Glandular Odontogenic Cyst, Hob Nail, Mucoepidermoid Carcinoma, Plaques, Recurrence.

INTRODUCTION

Glandular odontogenic cyst (GOC) is an uncommon jaw cyst that arises from odontogenic epithelium. It was first described by Gardner *et al*., in 1988 [1]. In 1992, the World Health Organization (WHO) described GOC as "a cyst arising in the tooth-bearing areas of the jaws and 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." [2]. The prevalence of GOC varies from 0.012% to 1.3% of all jaw cysts with a mean of 0.17% [3]. Its clinical importance is due to its high recurrence rate and aggressive growth pattern [4]. In 1987, Padayachee and Van Wyk reported two cases of botryoid odontogenic cyst (BOC) with glandular components, so they proposed a term of sialo-odontogenic cyst [4]. Further evidence supported its odontogenic origin rather than sialogenic origin depending on lack or minimal marker expression.

CASE SERIES

In this article we discuss the variability in clinical, radiological and histological features of 5 cases reported as GOC.

CASE 1

A 29 year old male complains of swelling in the upper right back tooth region since 3 months. On inspection of oral cavity, a well defined solitary round swelling was noted in the right posterior aspect of the palate extending from 14 to 17 region measuring approximately 3x3 cms which was firm in consistency and non tender.

Figure 1: Clinical image shows a well defined solitary round swelling in the posterior aspect of the palate extending from 14 to 17 region

No other history was relevant. CBCT revealed a unilocular radiolucent lesion with well defined borders extending from the 16 to 18 region with elevation of the floor of the maxillary sinus. (FIGURE 2).

Figure 2: Radiographic image shows a unilocular radiolucent lesion with well defined borders involving the maxillary sinus.

On histopathological examination, non-keratinized stratified squamous cystic epithelium exhibiting cuboidal basal cells along with mucous cells, ciliated cells and hobnail cells with apocrine snouts superficially. Microcysts with mucous pools, crypt like formations and papillary archietecture are also evident in the epithelium. Connective tissue showed subepithelial hyalinization at areas.

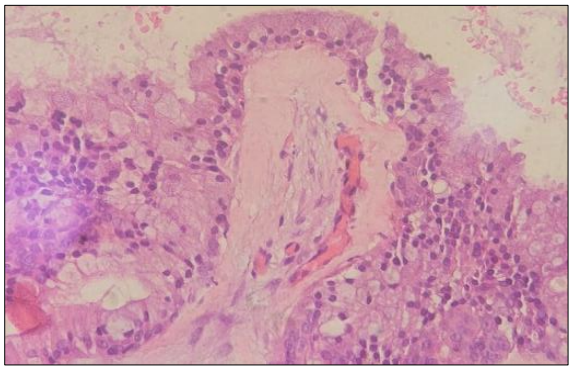

Figure 3A: Histopathological image shows variable epithelial thickness, ciliated cells, mucous cells, clear cells and microcysts (H&E stain, 20x magnification)

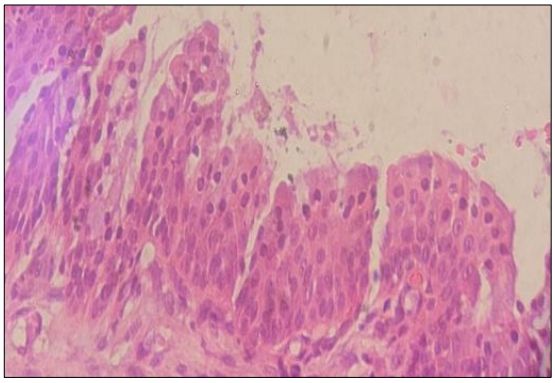

Figure 3B: Histopathological image shows superficial hobnail cells with apocrine snouts (H&E stain, 20x magnification)

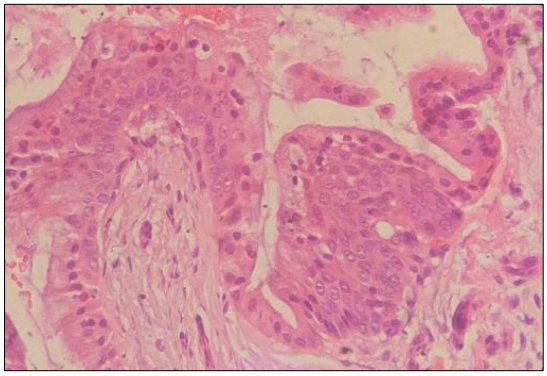

Figure 3C: Histopathological image shows plaque like thickenings, microcysts and crypts (H&E stain, 20x magnification)

CASE 2

A 23 year old male complains of swelling in the lower right back tooth region since 1 year. He had undergone orthodontic treatment 6 years back. On extra oral examination, a diffuse swelling was noted in the right lower 3rd of face, non tender and bony hard in consistency. Intraoral examination also showed a swelling obliterating the mandibular right gingivobuccal sulcus. OPG shows a radiolucent lesion with corticated borders with root resorption of multiple tooth.

Figure 4: Clinical image shows an intraoral swelling obliterating the mandibular right gingivobuccal sulcus

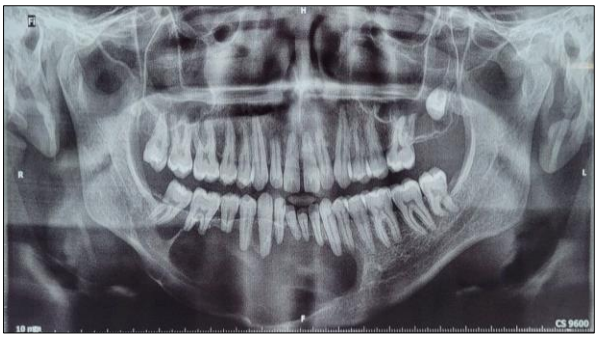

Figure 5: Radiographic image shows a radiolucent lesion with corticated borders and root resorption of multiple tooth

Histological features were similar to that of case 1 except the absence of mucous cells, focal areas of flattened epithelium with parakeratinization, islands of odontogenic epithelium and haemorrhagic areas in the connective tissue.

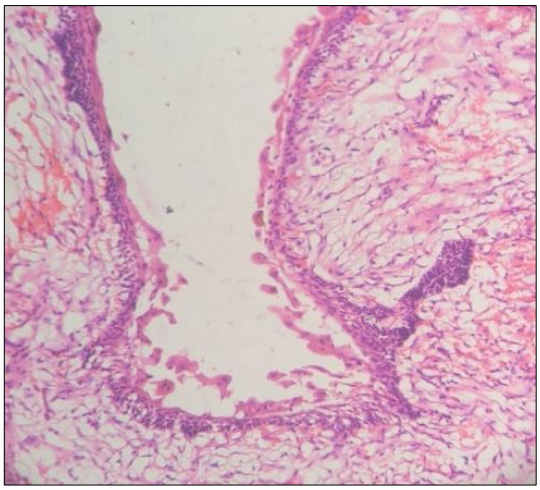

Figure 6A: Histopathological image shows thin squamous epithelium with hobnail cells protruding into the lumen (H&E stain, 4x magnification)

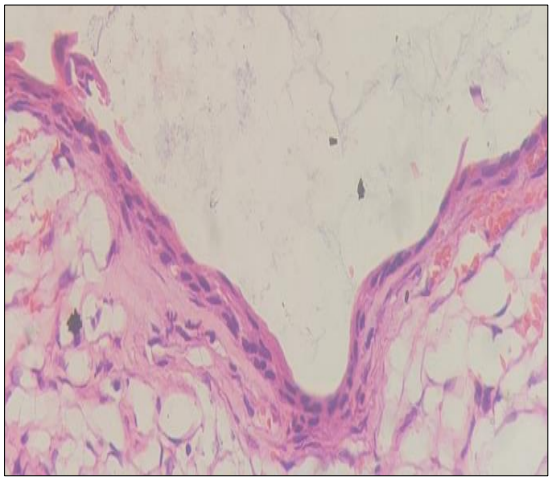

Figure 6B: Histopathological image shows focal areas of parakeratinized epithelium (H&E stain, 20x magnification)

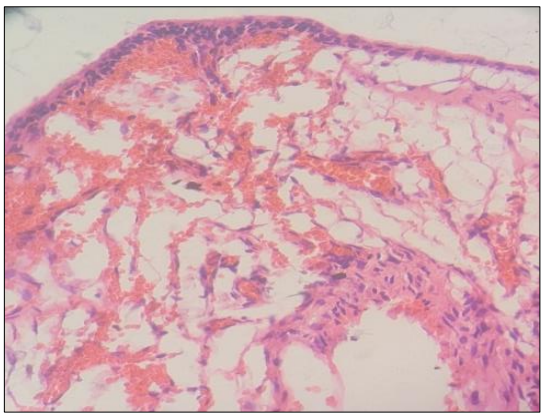

Figure 6C: Histopathological image shows haemorrhagic areas in the connective tissue (H&E stain, 4x magnification)

CASE 3

A 20 year old male was referred from a private clinic for complaint of pain in the lower left back tooth region since 2 weeks. No other relevant history.

Figure 7: CBCT revealed a well defined radiolucency with corticated borders involving the root apices of retained E and 36.

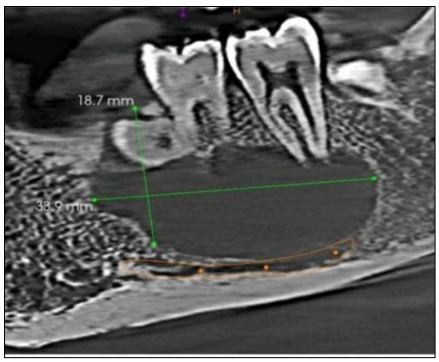

Figure 8: Radiographic image shows a well defined radiolucency with corticated borders involving the root apices of retained E and 36.

Histological features were similar to that of case 1 except that mucous cells were absent.

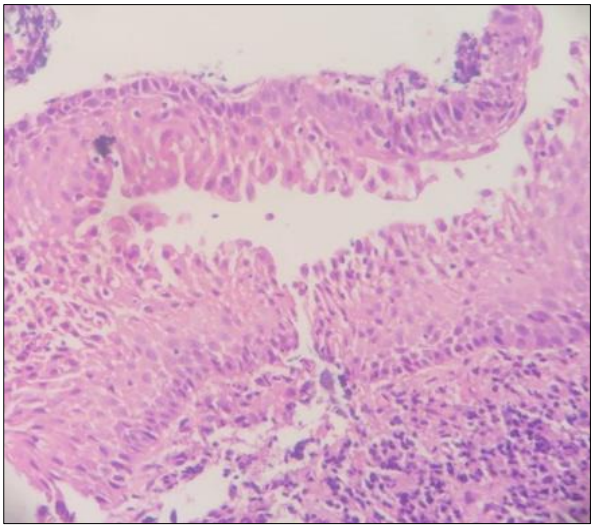

Figure 9: Histopathological image shows epithelium of variable thickness, superficial hobnail cells and clear cells in the spinous layer(H&E stain, 20x magnification)

CASE 4

A 20 year old male complains of swelling in the upper right back tooth region since 1 and ½ years. Patient gives a history of pus discharge 4-5 episodes since 6 months. Bilateral submandibular lymph nodes were palpable, mobile and non tender. Extraorally, facial asymmetry and intraorally, irregular lobular shaped swelling was evident extending from 15 to 18 region with buccal cortical expansion.

Figure 10: Clinical image shows facial asymmetry of right side

Figure 11A: Clinical image shows irregular lobular shaped swelling extending from 15 to 18 region

Figure 11B: On radiographic examination,a multilocular radiolucent lesion was evident in the occlusal radiograph7.

Figure 12: Histological findings were similar to that of case 1 except that most of the areas showed thin epithelium. Multicystic archiectecure was very prominent.

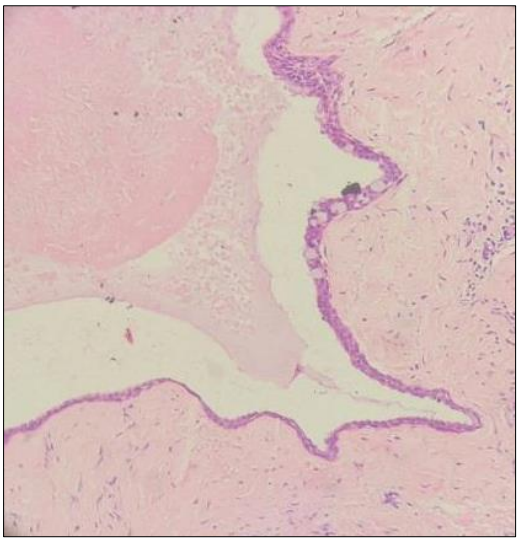

Figure 13A: Histopathological image shows thin epithelium with mucous cells and mucous pool in the cystic lumen(H&E stain, 4x magnification)

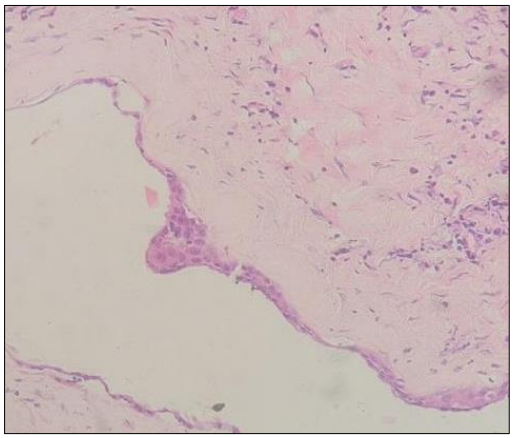

Figure 13B: Histopathological image shows epithelial plaques(H&E stain, 4x magnification)

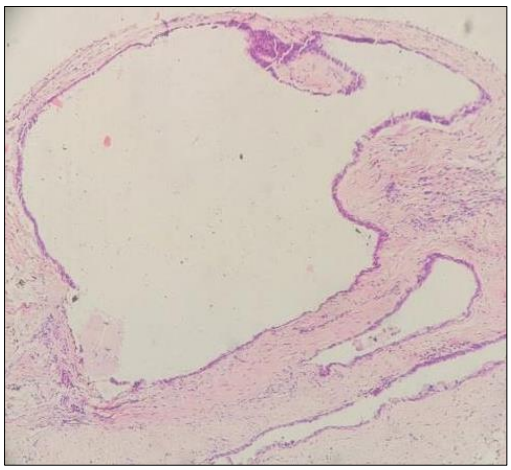

Figure 13C: Histopathological image shows multicystic archietecture of epithelium (H&E stain, 4x magnification)

CASE 5

A 58 year old male complains of pain and swelling in the lower left back tooth region since 1 month.Extraorally,a diffuse palapable swelling of size 3x2.5 cms was noted in the left lower 3rd of face which was non tender and bony hard in consistency. Vestibular obliteration and buccal cortical expansion was evident intraorally with Grade I mobility of 36,37 and 38.

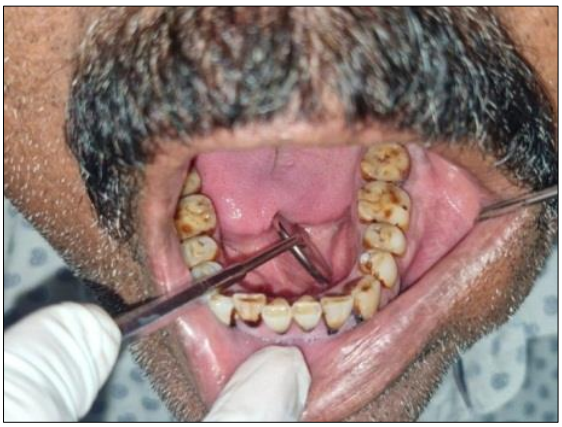

Figure 14: Clinical image shows vestibular obliteration and buccal cortical expansion evident intraorally

OPG shows a multilocular radiolucency with corticated borders with root resorption of multiple tooth. Histological features were similar to that of case 1 except focal areas of parakeratinized epithelium and sub epithelial dystrophic calcifications.

Figure 15: Radiographic image shows multilocular radiolucent lesion with root resorption of multiple tooth

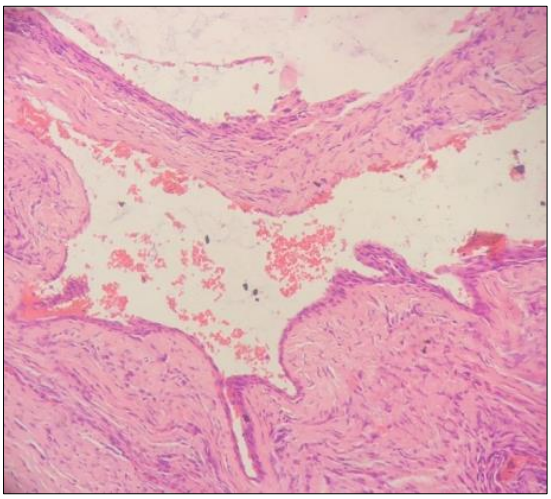

Figure 16A: Histopathological image shows epithelial plaques and crypts (H&E stain, 4x magnification)

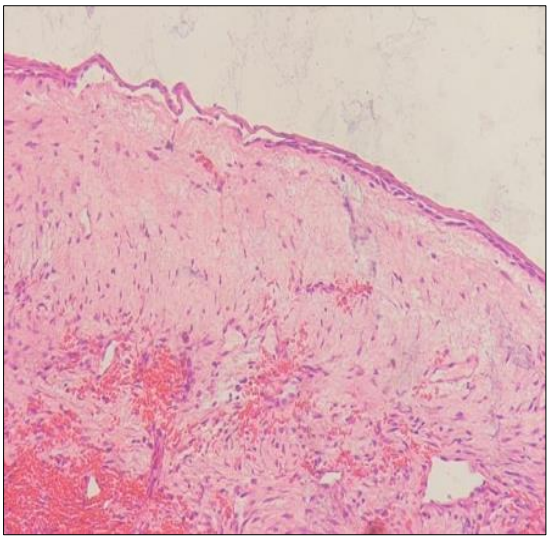

Figure 16B: Histopathological image shows focal areas of parakeratinized epithelium(H&E stain, 4x magnification)

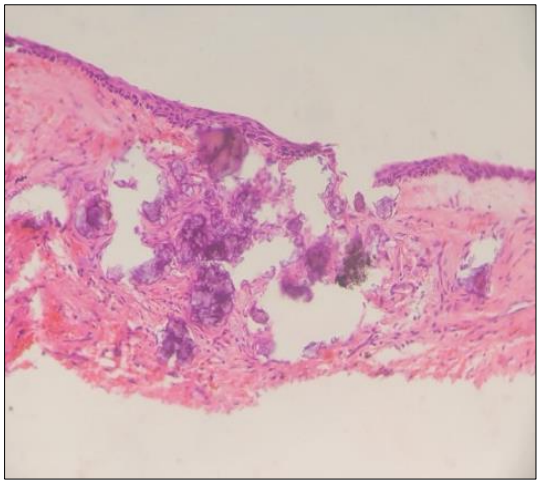

Figure 16C: Histopathological image shows dystrophic calcifications in the connective tissue(H&E stain, 4x magnification)

DISCUSSION

GOCs is a rare odontogenic lesion comprising approximately < 0.5% of all odontogenic cysts [1]. WHO 2022 defines GOC as developmental cyst in which epithelial lining resembles glandular tissue [5]. It is seen in adults with mean age of about 50 years and peak in 6th decade, however, there are also reports in paediatric patients [6]. There was a greater degree of variation in the age of patients in our cases as 4 out of 5 cases occurred in the 2nd and 3rd decade. Over 70% occur in the mandible with a predilection for anterior or premolar area. In contrast to this, 2 out of our 5 cases occurred in the maxilla. Lesions are commonly associated with swelling/expansion in 43.5 % to 87% which is the most common presenting complaint, although about 75% are asymptomatic [7]. All our patients had a complaint of swelling while presenting.

The size of the lesions ranged from 5 mm to 120 mm. The lesion typically presents radiographically as a unilocular radiolucency in 53.6 % to 61.5% of cases or multilocular radiolucency in 30.4 % to 46.4% of cases with a well-defined corticated rim 94.5% of the lesions which may have a scalloped border [8]. Crossing the midline is characteristic [4]. GOC is typically associated with the roots of multiple teeth, and tooth displacement or tooth resorption is common. Root resorption has been reported in 13.9 % to 30% of lesions and tooth displacement in 24.4 % to 50% of lesions [7]. All these features were appreciated in our cases also. The aggressive potential of GOC is often seen in either cortical thinning or perforation. As the clinical and radiological features are not pathognomonic and recurrence rate is 22%, histopathological correlation is mandatory for final diagnosis and management [4].

The histogenesis of GOC was initially proposed to be from intraosseous salivary gland tissue but now believed to be a developmental odontogenic cyst that arises from cell rests of the dental lamina [9].

Kaplan *et al*., were the first to describe the number of microscopic features that are diagnostic of GOC. The group listed major and minor microscopic criteria for GOC based on the occurance of each feature in previously reported cases from the literature. Based on their analysis, it was suggested that the presence of each of the major criteria must be present for diagnosis and the presence of minor criteria supports the diagnosis but are not mandatory.

Kaplan's Criteria

Table 1: Major and minor criteria given by Kaplan for GOC [3]

Major criteria	Minor criteria
1. Squamous epithelial lining, with a flat interface with the connective tissue wall, lacking basal palisading.	1. Papillary proliferation of the lining epithelium.
2. Epithelium exhibiting variations in thickness along the cystic lining with or without epithelial "spheres" or "whorls" or focal luminal proliferation.	2. Ciliated cells.
3. Cuboidal eosinophilic cells or "hobnail" cells	3. Multicystic or multiluminal architecture.
4. Mucous (goblet) pools, with or without crypts lined by mucous-producing cells.	4. Clear or vacuolated cells in the basal or spinous layers.
5. Intraepithelial glandular, microcystic, or duct-like structures.	

A significant problem with this criteria is that if a major feature is missing the diagnosis cannot be made. Fowler *et al*., analysed 46 cases and also showed that not all features were present in all cysts. A common diagnostic error is to exclude the diagnosis of GOC if mucous cells are not seen. It must be noted that even though mucous cells are characteristic they are not essential for diagnosis. Upto 30% cases may not contain mucous cells.3 out of 5 cases showed absence of mucous cells. For these cases, Fowler's criteria was followed for diagnosis. Fowler *et al*., (2011) thus adopted a more pragmatic approach to diagnosis and suggested the presence of 6 or more out of 10 features for the diagnosis of GOC.

Fowler's Criteria

Table 2: Histological parameters and description listed by Fowler and colleagues [8]

Histological parameters	Histological description
Surface eosinophilic cuboidal cells	Also called "hobnail cells". These cells are present on the surface of the cyst lining and resemble cuboidal cells of the reduced enamel epithelium that lines dental follicles and dentigerous cysts.
Intraepithelial microcysts or duct-like spaces lined by a single layer of cuboidal to columnar cells similar to surface cells	Sometimes the microcysts are lined by mucous goblet cells. These microcysts may contain mucous pools, eosinophilic material, or may appear to be empty. In areas, the microcysts may open onto the surface of the lining epithelium.
Apocrine snouting of hobnail cells	Sometimes the hobnail cells demonstrate "pinching off" of the surface similar to decapitation secretion seen in cells that line apocrine gland ducts.
Clear or vacuolated cells	These cells contain clear cytoplasm and may be present in the basal and/or parabasal layers. The clear cytoplasm is due to glycogen in some cases. In areas of attenuated cyst lining, clear basal cells may be directly subjacent to the surface eosinophilic cuboidal cells.
Variable thickness of the cyst lining	This was recorded as positive only if marked variability in the thickness of the cyst lining was present.
Papillary projections or "tufting" into the cyst lumen	These papillary projections sometimes are formed by several microcysts opening onto the surface of the cyst lining, but may also be formed independent of microcysts.
Mucous goblet cells	These cells may be present singly or in small clusters on the surface or within the cyst lining. They may also line microcysts.
Epithelial spheres or plaque-like thickenings	These are identical to those seen in lateral periodontal cysts or botryoid odontogenic cysts. Sometimes the epithelium in these plaques exhibits swirling or spherule formation.
Multiple compartments	Multiple cystic spaces similar to those seen in botryoid odontogenic cysts.
Cilia	These are true cilia on the surface of eosinophilic cuboidal cells, and are distinct from apocrine snouting.

Common errors in diagnosis are due to overlapping features with Central Mucoepidermoid Carcinoma and botryoid odontogenic cyst. Multilocularity in radiographs, multicystic appearance in histology and typical plaque like thickenings are features that mimic GOC with botryoid odontogenic cyst however, GOC also shows microcysts, hobnail cells, apocrine secretion and mucous cells which are not features of botryoid odontogenic cyst. Also, epithelial plaques are more prominent in GOC and may form bulbous papillary processes which is rare in botryoid cysts. Botryoid odontogenic cysts lie lateral to the teeth and are rarely greater than 40 mm whereas size ranging between 5 mm to 120 mm and crossing the midline is characteristic of GOC [4].

Central Mucoepidermoid Carcinoma (CMEC), a rare malignant intraosseous neoplasm in contrast to the typical presentation of GOCs usually present as painful swellings in the mandibular posterior body-ramus region, in association with impacted teeth. Few authors speculate that these 2 entities represent a biological spectrum of the same disease. CMEC are almost always multicystic whereas GOCs are multicystic in only 60% of the cases. Mucous cells, duct-like structures and clear cells in GOC are seen within the lining of the cyst where as CMEC shows more solid islands or sheets of tumor infiltrating into the underlying connective tissue or adjacent bone from the cyst lining with an admixture of epidermoid cells, intermediate cells and mucous cells or clear cells. Ciliated cells, apocrine secretion, superficial hobnail cells, plaque like thickenings, whorling and papillary projections are features of GOC that are rarely or never seen in CMEC [4]. CMEC has a t(11;19)(q21;p13) translocation which results in fusion of MECT1-MAML2 gene whereas GOCs lack the MAML2 gene rearrangements [10]. Pires *et al*., investigated expression of cytokeratin 18 and 19 (CKs 18 and 19) in GOC and CMEC. It has been suggested that CKs 18 and 19 could be useful in differentiating between the two entities. The group concluded that all CMEC expressed CKs 18 whereas GOCs expressed CKs 19

consisting with previous studies [4]. Because of the similar histological features between GOC and CMEC, literature review speculates that CMECs may arise from GOCs, but its considered as a rare event [4].

Most cases of GOCs have been treated by conservative procedures such as enucleation or curettage. GOC shows a high recurrence rate which is correlated to its size, multilocular appearance and the amount of thinning of cortical plates. Marsupialization and decompression may be performed for larger lesions to promote shrinkage prior to enucleation or curettage. Lesions have been reported to recur after three years, eight years and ten years. Long-term follow-up is advocated and some authors suggest at least 3-year follow-up, and preferably 7 years for GOCs. Because of its local aggressive behaviour and tendency for recurrence, some authors have advocated block resection, particularly for larger or multilocular lesions [8].

Though rare, the cyst is now relatively well known among oral and head and neck pathologists. Diagnosis can be extremely difficult due to the variable histological features presented by the cyst in different cases and also histopathological similarities with dentigerous cyst, lateral periodontal cyst and central mucoepidermoid carcinoma. Therefore a careful histopathological examination and a long-term follow-up - preferably seven years are required to rule out recurrences.

Declaration of Patient Consent

I have obtained all appropriate patient consent forms including their images and other clinical information to be reported in the journal. Patients were assured that their names and initials will not be published anywhere and due efforts will be made to conceal their identity.

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