Original Article

Glandular odontogenic cyst: Series of five cases

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Abstract

Introduction: Glandular odontogenic cyst (GOC) is a clinically rare and histopathologically unusual type of developmental odontogenic cyst with unpredictable and potentially aggressive behaviour.

Materials and Methods: Archival data of cases histopathologically identified as GOC were analyzed from the Department of Oral Pathology over the past six years. The clinical, radiographic, histopathological features and treatment were evaluated. Special stains such as periodic acid Schiff, mucicarmine along with immunohistochemical staining for cytokeratin 19 were employed to confirm the histopathological diagnosis.

Results: The study indicated a strong female predilection with slightly more number of cases found in maxilla than mandible. Most cases showed a well defined multilocular radiolucency. The microscopic features which aid in its differentiation from its mimickers such as central mucoepidermoid carcinoma, lateral periodontal cyst, dentigerous cyst and botryoid odontogenic cyst which were observed included presence of variable thickness of the lining epithelium, epithelial plaques and whorls, hobnail cells, ciliated cells, clear cells and goblet cells.

Conclusion: The present case series aims to throw light on the clinical, radiographic and microscopic features of GOC, which may aid in its definitive diagnosis in problematic cases.

Keywords: Central mucoepidermoid carcinoma, cytokeratin 19, glandular odontogenic cyst

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INTRODUCTION

Glandular odontogenic cyst (GOC) is a developmental cyst of the jaw which is a clinically rare and histopathologically unusual cyst with unpredictable and potentially aggressive behavior. In 1987, Padayachee and VanWyk reported two cases that were similar to botryoid odontogenic cyst (BOC) but with a glandular element and proposed the term sialo-odontogenic cyst. Later in 1988, Fowler CB*et al.* described it as a distinct entity due to unusual histological features.[1] Till date, 181 cases of GOC have been reported in English literature.[2]

GOC usually occurs in males over 40 years of age with a predilection for the anterior region of the mandible. Radiographically, it presents as either a unilocular or multilocular well-defined radiolucent lesion. The clinical and radiographic features are nonspecific, and it can mimic any other destructive lesion of the jaw.[3,4] Its importance relates to the fact that the cyst exhibits a propensity for recurrence similar to odontogenic keratocyst, has morphological similarities to lateral periodontal cyst (LPC) or BOC and may mimic central mucoepidermoid carcinoma (CMEC) histologically.[3] The objectives of the present study were to systematically analyze the cases of GOC reported in our department to

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further define the clinical, radiographic and microscopic features of the cyst. An attempt was made to determine which microscopic features may be more specific in the diagnosis of problematic cases and to determine if GOC and CMEC share a histopathological spectrum.

METHODS

Archival data of cases histopathologically identified as GOC were analyzed from the Department of Oral Pathology, Maulana Azad Institute of Dental Sciences in the past 6 years. A total of five cases were retrieved with complete relevant clinical, radiographic and histopathological data. Clinical features such as age, sex, site of lesion and presenting features were analyzed. Orthopantograms were evaluated to assess the locularity of the lesion, presence or absence of scalloping, lesion definition at periphery and effect on associated teeth. Hematoxylin and eosin stained glass slides were reviewed for each case by three oral pathologists. In all cases, special stains such as mucicarmine and periodic acid-Schiff (PAS) were also used. Each oral pathologists recorded the presence or absence of 10 microscopic parameters for each case namely: surface eosinophilic cuboidal cells also called hobnail cells, intraepithelial microcysts, apocrine snouting of hobnail cells, clear or vacuolated cells, variable thickness of the cyst lining, papillary projections or "tufting" into the cyst lumen, mucous goblet cells, epithelial spheres or plaque-like thickenings, cilia and multiple compartments. In all cases, the decision of whether to accept or reject the lesion as GOC was based on interpretation of the diagnostic criteria set forth by Kaplan *et al*.[4,5] Further, immunohistochemical staining for cytokeratin 19 was performed to determine the odontogenic nature of the cyst.

RESULTS

The mean age at diagnosis was 44.4 years with a range of 30–62 years. Out of the five cases, four were females and three presented as maxillary lesions. A strong predilection was noted for the involvement of the anterior segment irrespective of the jaw involved. Most of the patients presented with a chief complaint of painless swelling without expansion, thereby simulating odontogenic keratocyst clinically. Displacement of teeth, mobility and root resorption was noted in two cases. Three out of the five cases showed a well-defined multilocular radiolucency while two showed unilocular radiolucency. Histopathologically, the most common features observed were the presence of variable thickness of the lining epithelium, epithelial plaques, hobnail cells, ciliated cells and goblet cells with mucin material. The clinical and radiographic feature have been summarized in Figures 1, 2 and Table 1 whereas the histological findings have been summarized in Figure 3 and Table 2.

DISCUSSION

GOC is an uncommon developmental cyst with a frequency of 0.012%–1.3% of all the jaw cysts and its prevalence is 0.17%.[6] Although over 180 cases have been reported in the literature, the GOC may still prove to be a diagnostic challenge due to its myriad histopathological presentation. The current case series is a step further to elucidate its clinical, radiographic and histopathological features which may aid in its accurate diagnosis.

The mean age at diagnosis in the current series was 40 years which was in agreement with previous literature.[1,2,4] There was disagreement with regard to site prevalence and sex predilection as reported in the earlier literature. Previous studies point toward a male predilection with a ratio of 1.3:1, though a strong female predilection was noted in the present study. The most common site of its occurrence is the mandible (85%), especially in the anterior region, followed by the anterior maxilla.[2,6] In the present study, slightly higher predilection for the maxilla was recorded, though the majority of the cases involved the anterior segment irrespective of the jaw involved. Clinically, most patients presented as a painless swelling, with displacement and mobility of the involved teeth reported in two cases. GOC does not display specific radiographic findings. It may present either as a unilocular or multilocular radiolucency with well-defined borders. Most of our cases presented as multilocular lesions.

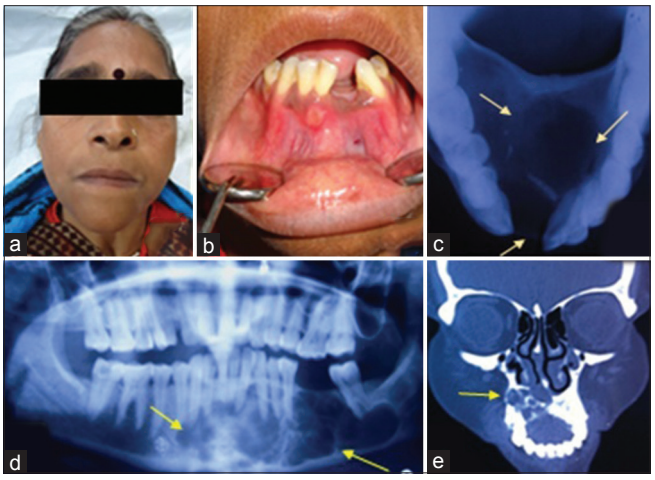

Figure 1: Clinical and radiographic features of glandular odontogenic cyst. (a and b) Extraoral and intraoral photograph of Case #4 showing bony hard swelling in anterior mandible. (c) Occlusal radiograph of Case #4 showing well-defined unilocular radiolucency. (d) OPG of Case #2 showing well-defined multilocular radiolucency in the mandible. (e) CT scan of Case #3 showing expansile lytic multilocular lesion in the anterior maxilla

Table 1: Clinical and radiographic details of the cases

Age (years)	Sex	Site	Radiodensity	Locularity
40	Female	Anterior maxilla (crossing midline)	RL	ML
30	Female	Posterior mandible	RL	ML
40	Female	Anterior maxilla (crossing midline)	RL	UL
50	Female	Anterior mandible (crossing midline)	RL	ML
62	Male	Anterior maxilla	RL	UL

RL: Radiolucency, UL: Unilocular, ML: Multilocular

Table 2: Histopathological findings of the cases

Squamous epithelial lining with flat interface	Variable thickness of lining	Epithelial plaques	Hobnail cells	Goblet cells	Micro cysts	Papillary proliferation of lining epithelium	Ciliated cells	Multicystic architecture	Clear cells
+	+	+	–	+	–	–	–	+	–
+	+	+	+	+	+	+	+	–	+
+	+	+	+	+	+	–	–	+	+
+	+	+	+	+	+	+	+	+	+
+	+	+	–	+	–	–	+	–	+

+: Indicates present, -: Indicates absent

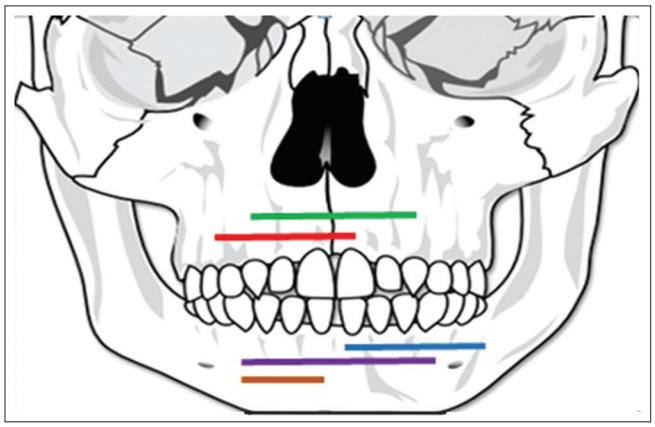

Figure 2: Site involvement of cases of glandular odontogenic cyst. — Case #1, — Case #2, — Case #3, — Case #4, — Case #5

GOC shows certain histological characteristics, which have been divided into major and minor categories by Kaplan *et al*.[4,5] Major criteria include squamous epithelial lining with flat interface with the connective tissue wall, lacking basal palisading, variations in thickness of the lining with or without epithelial spheres or whorls, cuboidal eosinophilic cells or hobnail cells, mucous goblet cells with interepithelial mucous pools with or without crypts lined by mucous-producing cells, interepithelial glandular microcystic or duct-like structures. Minor criteria comprise papillary projections, ciliated cells, multicystic or multiluminal architecture, clear or vacuolated cells in basal or spinous layer. The cases presented in the present study displayed most of these features such as the presence of variable thickness of the lining epithelium, epithelial plaques and whorls, hobnail cells, ciliated cells, clear cells and goblet cells. The presence of mucin was confirmed by PAS without diastase and mucicarmine staining.

Histopathologically, GOC should be differentiated from LPC, BOC and CMEC as they exhibit a considerable overlap of histological features.[7] LPC, a developmental odontogenic cyst lined by thin nonkeratinized epithelium, is a commonly considered mimicker of GOC as it also exhibits focal epithelial thickenings and glycogen-rich epithelial cells, similar to those found in GOC. BOC is a locally aggressive polycystic variant of LPC, showing similar histomorphic features as GOC, like epithelial plaques and areas of glycogen-rich clear cells. However, the identification of ciliated epithelium and duct-like spaces with mucous cells specifically differentiate GOC from LPC and BOC.[4,8]

Low-grade variant of CMEC is the most important histological differential diagnosis of GOC. In our cases, characteristics common with low-grade CMEC were the presence of mucous and clear cells along with cystic spaces filled with mucin.

The cases were diagnosed as GOC as they fulfilled the criteria given by Kaplan *et al*.[4,5] Distinguishing features of GOC were typical thin lining without any solid epithelial proliferation, the presence of swirling spherical aggregates or epithelial plaques and absence of cellular atypia as seen in CMEC.

Another close differential diagnosis to be considered in reporting GOC, especially in cases of incisional biopsy is dentigerous cyst. Areas of GOC exhibiting thin reduced enamel like epithelium, therefore, should cautiously be investigated as they can be misinterpreted as dentigerous cyst with mucous metaplasia.

The morphology of epithelium of GOC suggests its odontogenic origin, especially from the remains of dental lamina. The thin cuboidal epithelium resembles the reduced enamel epithelium. The epithelial thickenings seen in the epithelium may be comparable to the

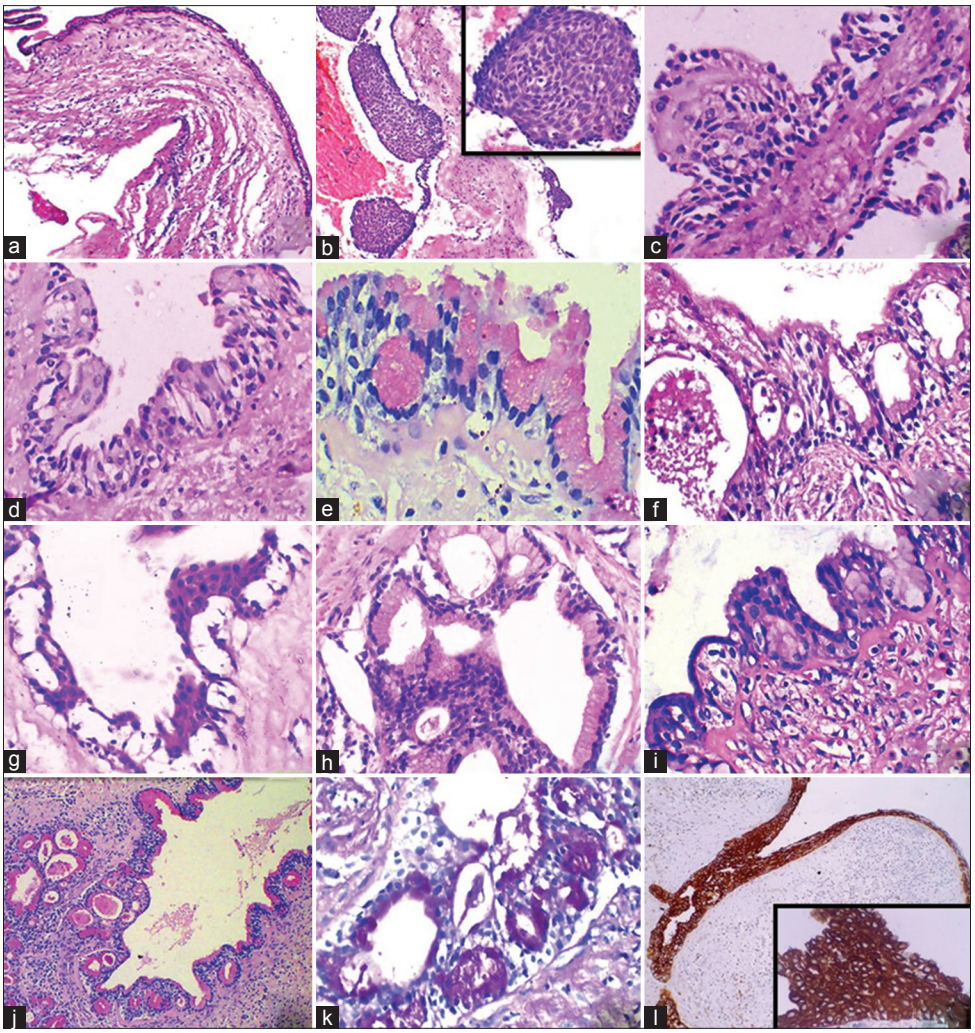

Figure 3: Histopathological features of various cases. (a: H & E, ×10) Squamous epithelial lining with flat interface with the connective tissue. (b and c: H & E, ×40) Cystic lining with epithelial whorls or spheres.(d: H & E, ×40) Cuboidal eosinophilic cells or hobnail cells along with vacuolated cells in basal layer.(e: H & E, ×40) Crypts lined by mucous producing cells.(f-h: H & E, ×40) Intraepithelial glandular and microcysts.(i: H & E, ×40) Papillary proliferation of the lining epithelium with ciliated cells.(j: Mucicarmine, ×10, k: PAS, ×10) Multicystic architecture. (l: CK, 19 ×10) Positivity in the epithelial lining with cytokeratin 19

proliferative changes seen in epithelial cells of dental lamina. Immunohistochemical staining with CK19 revealed strong positivity in all layers of epithelium confirming its odontogenic nature. The identification of osteodentin and the negative reaction for epithelial membrane antigen in the glandular structures suggest a nonglandular origin which has been proposed by various authors.[3,6]

Treatment choice varies from conservative approach such as enucleation, marsupialization and curettage with or without peripheral ostectomy to marginal or segmental resection. Some surgeons prefer marginal or segmental resection due to the tendency of GOC to recur after conservative treatment.[8-10] The rate of recurrence has been found to vary with its radiographic complexity. Patients with large multilocular lesions and cortical perforation show tendency for recurrence. All the cases in the present study were treated conservatively by enucleation or marsupialization. None of the cases in our study reported recurrence after a follow-up ranging from 1 to 5 years.

In conclusion, this case series on GOC is an attempt to add to the existing knowledge of this cyst. The study revealed predominance of GOC in middle age group mostly presenting as a painless swelling with a predilection in anterior region of either jaw mostly in females. It shows varying clinical and radiographic findings, and its diagnosis depends on its microscopic features. Histopathologically, it may prove to be a diagnostic dilemma due to its close resemblance to LPC, BOC, dentigerous cyst and most importantly CMEC. It is mandatory to differentiate GOC from the much more aggressive lesions like CMEC, and we recommend the use of cytokeratin 19 antibody to establish odontogenic origin when in doubt.

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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Nil.

Conflicts of interest

There are no conflicts of interest.

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