CASE REPORT

Glandular odontogenic cyst: a case report

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Abstract

The glandular odontogenic cyst (GOC) is a rare developmental lesion considered a distinct entity because of its uncommon histopathological characteristics. It has morphological similarities to other lesions, which makes its histopathological diagnosis challenging for some pathologists. This lesion can involve either jaws, but the anterior region of the mandible is the most affected area. It strikes distinct age groups, with an average patient age of 50 years. It can exhibit a tendency towards recurrence when conservative treatment is administered. It is believed that the low prevalence of GOC in the literature is because of not only its rarity, but principally to the fact that its main characteristics are also found in other pathological entities, thereby generating controversial diagnoses. The aim of the present article is to report a case of GOC in a 40-year-old female patient exhibiting an intrabone cyst in the anterior mandibular region. The initial diagnostic hypothesis by means of radiographic imaging was of a traumatic bone cyst. After histological analysis, the lesion was diagnosed as GOC. The specimen was stained with haematoxylin and eosin, and then with the Periodic Acid Schiff (PAS) method. Through immunohistochemical analysis, the cyst tested positively for the Ki-67 and p53 antibodies as well as high molecular pan-cytokeratin.

Introduction

The term glandular odontogenic cyst (GOC) has been proposed as the most appropriate designation for this rare pathological lesion[1]. It was formerly denominated mucous-producing odontogenic cyst and sialo-odontogenic cyst because of a probable origin from the tissue which forms the salivary glands[1,2]. Binda *et al.*[3] stated that a large number of controversies exist regarding the terminology and origin of the GOC. The authors stressed the rarity of the lesion collecting reasonable information from 23 cases of GOC reported in the literature. In 1997, Ramer *et al.*[4] published a new case of GOC, and reviewed 39 reported cases (35 from the English literature and four cases from the German literature). In 2002, Noffke and Raubenheimer[5] reported seven new cases of GOC diagnosed over a 10-year period, and finally, in 2006, Shen *et al.*[6] analysed and published more 12 new cases of GOC including immunohistochemical analysis of them.

Clinically, GOC can involve either jaw, but the anterior region of the mandible is pointed as the most affected area. When in the maxilla, the lesion seems to affect mainly the tuberosity region[5,6]. The limited numbers of reported cases of GOC do not allow the elaboration of trustworthy epidemiological information regarding gender predilection, age or most common location. The main published features include the presence of a radiolucent swelling in the jaws, a tendency towards local recurrence after conservative surgical treatment. Some lesions can grow slowly and remain small, others may reach larger dimension, infiltrate and destroy the bone[2,3,5,7]. Radiography reveals a unilocular or multilocular radiolucent image

with well-defined margins. Other radiographic characteristics which can be presented in GOC include: root displacement and resorption of the teeth involved as well as tapering, erosion and perforation of the cortical bone[8,9].

According to the literature[2,3], GOC's histopathological characteristics comprise: cystic cavity lined with stratified squamous epithelium of variable thickness; the absence of inflammatory infiltrate in the capsular conjunctive tissue; and surface layer of the epithelium may present areas of cuboidal eosinophilic cells, or ciliated cells. Sometimes an irregular papillary surface can be identified. The epithelial cells may form circular proliferations resembling spheres, or spherical nodules, which are a significant characteristic, although not always present. Other characteristics include microcysts or intraepithelial crypts containing mucin, mucous cells and hyaline bodies, within the thickest section of the epithelium and in the lumen of the cyst. An uncommon presence of calcifications, phantom cells, foreign multinuclear giant cells and a chronic inflammatory infiltrate in the wall of the cyst might be also observed. Binda *et al.*[3] and Ferreira Jr *et al.*[10] observed an interesting histological characteristic: epithelial proliferation within the cyst wall, which may suggest a neoplasic potential and a possible association with central mucoepidermoid carcinoma (MEPCa).

A case of GOC is described. The GOC was located in the anterior region of the mandible, mimicking a lesion of an endodontic origin or a pseudocyst. The diagnosis of GOC was confirmed through histopathological examination.

Case report

During a routine radiographic exam, a 40-year-old female patient presented an asymptomatic intrabone lesion. It was located in the anterior area of the mandible near the periapical region of the 41, 31 and 32 tooth. The radiography revealed a unilocular radiolucent image with well-defined margins and radiopaque sclerotic edges (Fig. 1). The initial diagnostic hypothesis was of traumatic bone cyst. Involved tooth responded positively to pulp vitality tests. Because it was not a periapical inflammatory lesion of endondontic origin, patient was informed to proceed with surgical removal of the cyst. However, the patient did not return to give continuity to the suggested treatment. Upon returning 4 months after the initial diagnosis, the patient returned with the 41 teeth endodontically treated. The oral surgeon was able to give continuity to the treatment and to perform the

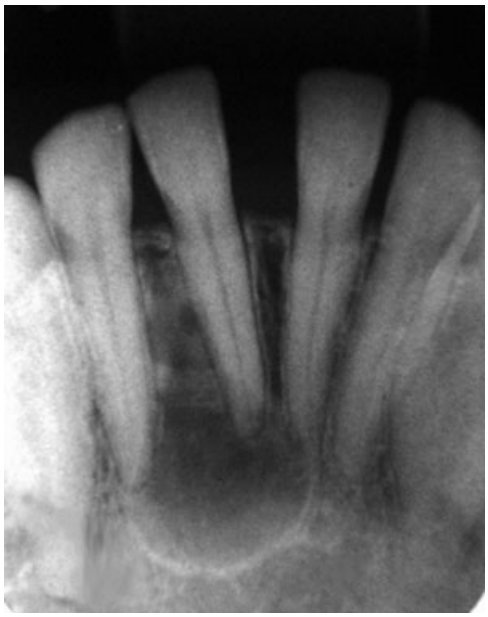

Figure 1 Initial radiographic appearance of the lesion exhibiting a well-defined circumscribed radiolucent image, resulting in root displacement of the 41, 31 and 32 dental elements.

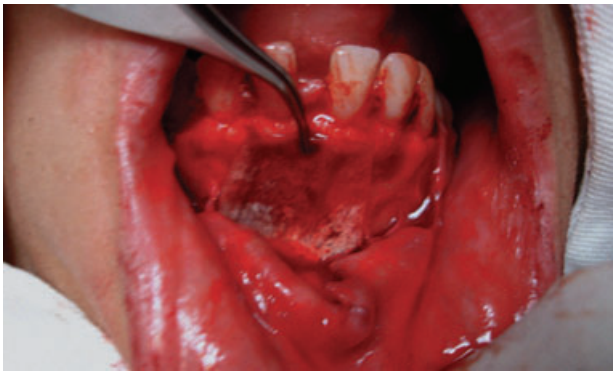

Figure 2 Transurgical findings after specimen removal. Surgeon is replacing a lyophilised bone membrane over the bone defect.

complete surgical removal of the lesion with ample curettage (Fig. 2).

The specimen was formalin fixed and sent to the oral pathology laboratory where the histopathological analysis was performed. The anatomopathological examination revealed fragments of a cystic lesion of odontogenic nature compatible with GOC. The epithelial lining exhibited cuboidal or columnar cells with a stratified aspect in which areas of papillary irregularity could be observed (Fig. 3). Duct-like microcystic spaces were observed bordered by cuboidal cells (Fig. 4). Mucous cells were also seen, as well as

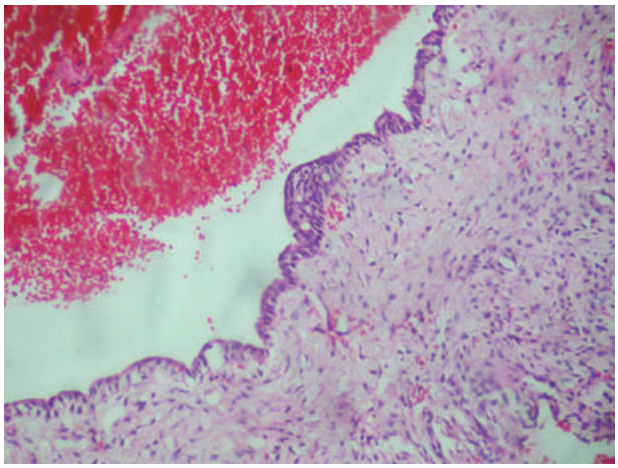

Figure 3 Photomicrography exhibiting a thin epithelial lining with areas of proliferate papillary irregularity. Epithelial cells are predominantly cuboidal shaped (HE–40×).

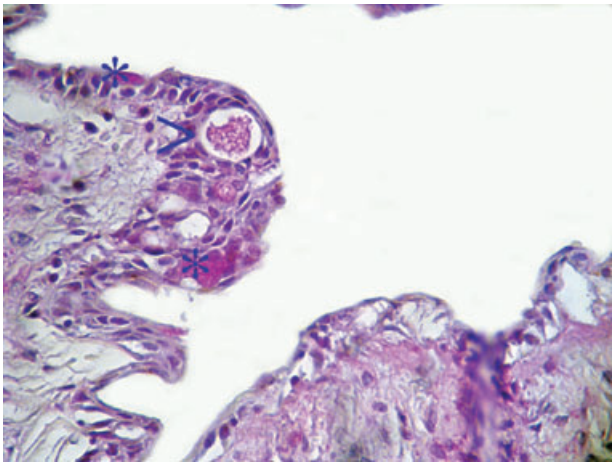

Figure 5 Photomicrography exhibiting PAS-positive eosinophilic material in the interior of the microcystic structures (arrow). Some PAS-positive mucous cells are also present (asterisk) (HE–100×).

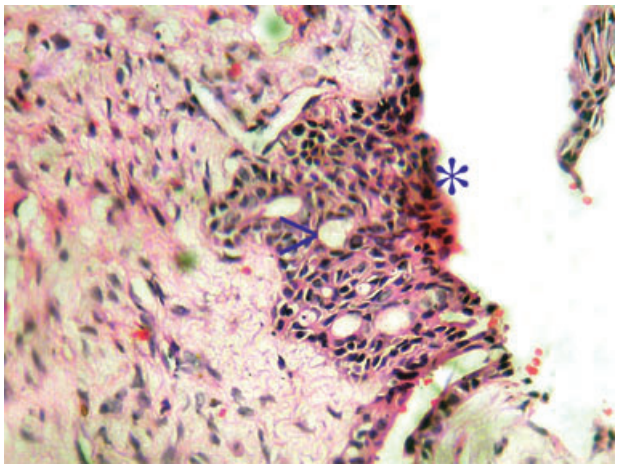

Figure 4 Duct-like microcystic spaces are observed bordered by cuboidal cells (arrow). Some mucous cells are also present, as well as occasional columnar shaped cells (asterisk) (HE–100×).

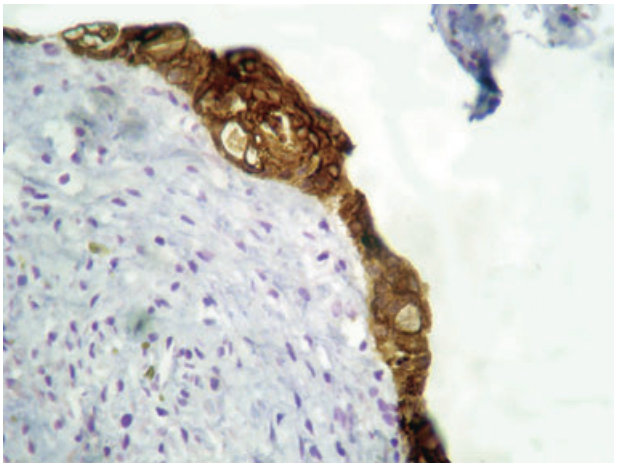

Figure 6 Photomicrography exhibiting the strong positive immunoreaction to the AE1/AE3 (SBP–200×).

occasional eosinophilic material in the interior of the microcystic structures. The cyst sac was composed of richly cellularised and vascularised fibrous conjunctive tissue containing occasional islands of inactive odontogenic epithelia. Special methods using PAS and immunohistochemistry were performed for the proteins p53, Ki-67 and pan-cytokeratin. The PAS staining revealed positive mucous cells and occasional cystic spaces containing positive PAS material (Fig. 5).

The immunohistochemistry study was performed using the avidinbiotin complex method (ABComplex/HRP Duet, Mouse/Rabbit Dako A/S, Glostrup Denmark). The following primary antibodies at various working dilutions were Ki-67 1:100 (Mib-1, Dako), p53 1:100 (DO7, Dako) and pan-cytokeratin 1:500 (AE1/AE3, Dako). Microwave antigen retrieval and overnight incubation were performed for primary antibodies. Diaminobenzidine tetrahydrochloride was used as a chromogen.

The AE1/AE3 antibody was positive (Fig. 6), and the proteins p53 and Ki-67 were strongly expressed throughout the length of the epithelia, respectively confirming the deregulation of the tumour suppression mechanism (Fig. 7) and the presence of mitotic activity (Fig. 8). The patient's follow up has been carried out for 18 months and she has not presented any recurrences

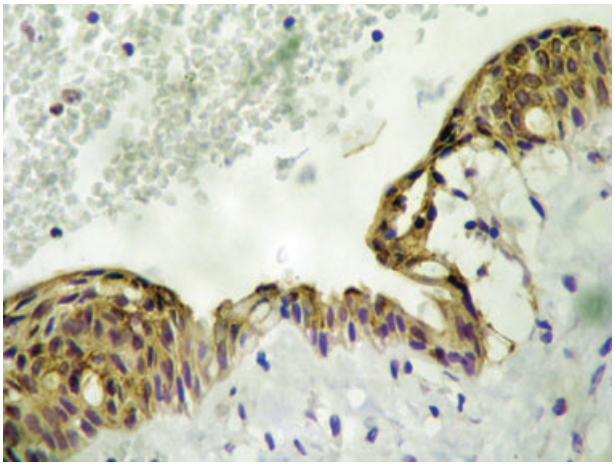

Figure 7 Photomicrography exhibiting the strong positive immunoreaction to the p53 protein (SBP–200×).

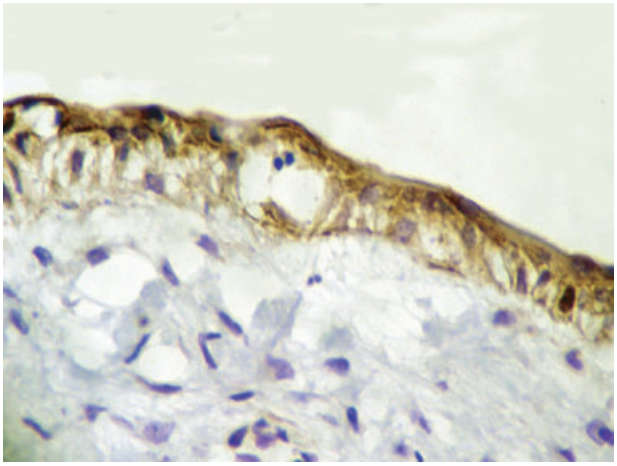

Figure 8 Photomicrography exhibiting the strong positive immunoreaction to the Ki-67 protein (SBP–200×).

thus far. Figure 9 shows the initial bone regeneration after 1 year from the surgical treatment.

Discussion

The few cases of GOC reported in the literature impede any reliable information regarding predilection for gender, age or most common localisation. Moreover, there remains a lack of clarification on some issues, such as histogenesis, biological behaviour and the appropriate treatment of these lesions. The present case report is in agreement with most cases cited in the literature[2,5,8], which consider the anterior region of the mandible the most affected area. Contrarily, Qin *et al.*[9] reported a series of cases with a greater prevalence of lesions in the anterior region of the maxillary.

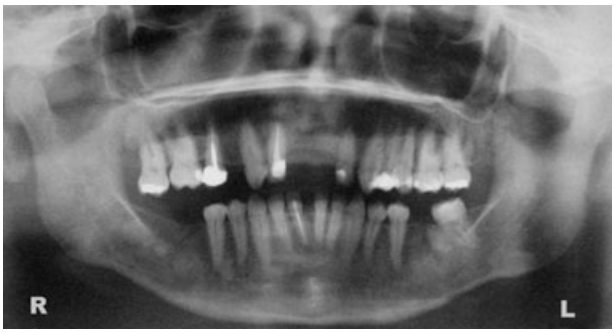

Figure 9 Final radiographic appearance of the lesion 9 months after total excision. It can be observed as initial bone regeneration. Note the endodontic treatment performed on the right lower incisor before the surgical treatment.

The high degree of multilocularity in GOC in comparison to other odontogenic cysts and its tendency towards the expansion of the cortical bone underline the local aggressive potential. Data collected in a study by Manor *et al.*[8] indicated that GOC exhibited aggressive behaviour, with expansion and perforation in a significant number of cases. Such aspects were not observed in the case reported herein.

Because of the location of the cyst near the apices of elements 41, 31 and 32, it mimicked an inflammatory endodontic lesion. Therefore, pulp vitality testing was essential in order to exclude the possibility of a periapical lesion of an endodontic origin. Consequently, the most adequate clinical diagnostic hypothesis was that of a traumatic bone cyst. The unnecessary endodontic treatment carried out on the teeth directly related to the cyst was because of the patient's seeking another dental health-care professional after the initial diagnosis of traumatic bone cyst. This fact reveals the importance of knowledge regarding the intrabone lesions that share the differential diagnosis with GOC. According to Tran *et al.*[11], the radiographic characteristics observed in GOC can lead to a diagnosis of keratocystic odontogenic tumour, ameloblastoma, central lesion of giant cells, lateral periodontal cyst, root cyst, simple bone cyst, aneurysmatic bone cyst, periapical cementum dysplasia, ossifying fibroma, odontogenic myxoma and central low-grade MEPCa.

The patient ultimately sought the assistance of the oral surgeon once again and the correct treatment was performed, namely, the complete excision of the cyst with ample curettage. The recurrence mechanism may be partially related to the thinness of the cyst wall and the presence of microcysts that hamper the complete

removal of the lesion, as well as the surgical technique employed for treatment[9,12]. The aggressive nature of GOC is also cited as a possible cause of recurrence[10]. As a result, a local block excision is suggested as the best treatment option[9]. In our case, based on the patient's decision, the surgeon opted for conservative surgery with curettage, follow up and a commitment to rigorous radiographic control.

The definitive diagnosis of GOC cannot be performed by radiographic exams because of the similarities with the various intrabone pathologies mentioned above[8]. Thus, the majority of the authors[1,2,6,8,9] stress the importance of a histological evaluation of all cases. In fact, lateral periodontal cysts may also present histological findings described as 'circular nodules' on epithelial layer surface[11], but the later should not reach bigger dimensions or provoke clinical swellings. Thus, ultimate diagnosis should be achieved by a complete observation of all possible characteristics: clinical, radiographic and histopathological.

Attention to some microscopic details should help in separating low-grade MEPCa from GOC. To help in the differentiation from MEPCa, the lesion should be screened for presence of hobnail or cuboidal eosinophilic cells in the superficial layer of the lining epithelium, and for small intraepithelial glandular microcysts or duct-like structures which are not typical for MEPCa. The epidermoid component in MEPCa is usually seen at the periphery of the cystic spaces, and not as epithelial spherules or whorls protruding into the lumen which is characteristic of GOC[13].

In a study by Kaplan *et al.*[12], immunohistochemical findings revealed that GOC positively marks the proteins p53 and Ki-67, which was corroborated by our findings. The authors also affirm that the immunoreaction for these antibodies in GOC is stronger when compared with that of MEPCa, and these markers may be considered an auxiliary aide in the differential histopathological diagnosis between these lesions.

The presence of p53-positive and Ki-67-positive cells in GOC should not be taken as an indication of malignancy or malignant potential. In fact, it requires further investigation because it may reflect a disrupted cell proliferation and thereby the aggressive behaviour of the lesion[12,13].

We stress the importance of a prolonged post-surgery follow-up period for approximately 3–5 years. As Ferreira Jr *et al.*[10] state, GOC has an aggressive nature, with a considerable chance of recurrence. The authors report a case of GOC that recurred four times following unsuccessful surgical treatment. The present case has been followed up for 18 months and there have been no signs of recurrence thus far. The presentation of this case can contribute to the previously presented data in the world literature and add further information so that this thus far little understood entity can be better clarified statistically.

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