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CASE REPORT

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Calcifying odontogenic cyst with AOT-like features: a case report and literature review

Cisto odontogênico calcificante com características adenomatóides: relato de caso e revisão de literatura

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ABSTRACT

Odontogenic lesions are a heterogeneous group of diseases that presents differences in their biological behavior and the occurrence of variable inductive interactions. Calcifying odontogenic cyst (COC), or Gorlin's cyst, is a well-recognized example of these lesions. We describe a case of COC with AOT-like areas and highlights its morphological diversity. A 60-year-old pheoderma man presented with a large swelling in the anterior buccal region of the mandible. Panoramic radiography revealed a well-defined, unilocular, radiolucent lesion associated with important root resorption. Complete enucleation of the lesion was performed and the histopathological findings met the criteria for the diagnosis of COC, although the cyst exhibited unusual AOT-like features. The patient has been recurrence free for 6 months after surgery. COCs with AOT-like features are rare, and reflect the multipotentiality and complexity of the inductive effects of the odontogenic epithelium with the ectomesenchyme. Enucleation seems to be the most indicated treatment, similar to classical COC.

KEYWORDS

Adenomatoid odontogenic tumor; Calcifying odontogenic cyst; Odontogenic cysts; Oral pathology; Oral surgery.

RESUMO

As lesões odontogênicas são um grupo heterogêneo de patologias que apresentam diferenças no seu comportamento biológico, e ocorrência de interações indutivas variáveis. O cisto odontogênico calcificante (COC), ou cisto de Gorlin, é um exemplo bem conhecido destas lesões. Descrevemos um caso de COC com áreas adenomatóides e destacamos a sua diversidade morfológica. Paciente do sexo masculino, 60 anos de idade, apresentou um aumento de volume na região anterior da mandíbula. A radiografia panorâmica revelou uma lesão bem definida, unilocular e radiolúcida associada a uma reabsorção radicular importante. A enucleação completa da lesão foi realizada e os achados histopatológicos preencheram os critérios para o diagnóstico de COC, embora o cisto exibisse características adenomatóides pouco usuais. O paciente permanece livre de recidivas durante 6 meses após a cirurgia. Os COCs com características adenomatóides são raros, e refletem a multipotencialidade e complexidade dos efeitos indutivos do epitélio odontogênico com o ectomesênquima. A enucleação parece ser o tratamento mais indicado, semelhante ao COC clássico.

PALAVRAS-CHAVE

Tumor odontogênico adenomatóide; Cisto odontogênico calcificante; Cistos odontogênicos; Patologia oral; Cirurgia oral.

INTRODUCTION

Calcifying odontogenic cyst (COC), or Gorlin's cyst, is a rare developmental odontogenic cyst characterized histologically by ghost cells, which often calcify [1]. This lesion was first reported in 1962 [2]. However, the World Health Organization (WHO) has changed its classification over the years, and it was called calcifying cystic odontogenic tumor (CCOT) for 12 years, because it was believed in its neoplastic potential [3]. COC accounts for less than 1% of all odontogenic cysts and is part of the group of ghost cell lesions of the jaws [1,4,5].

Clinically, COC usually presents as a slow-growing painless swelling, with a slight predilection for the anterior maxilla [4,6]. Radiographically, COC appears as a well-defined unilocular or multilocular radiolucency that can contain variable amounts and shapes of radiopaque material [4]. In some of cases, the cyst is associated with an impacted tooth, frequently a canine [4].

Histopathologically, COC exhibits a fibrous cystic wall lined with epithelium whose basal cells are columnar or cuboidal. The suprabasal layers resemble the stellate reticulum [5]. Numerous ghost cells and calcifications are identified within the epithelial lining. Masses of ghost cells often pass into the connective tissue of the cyst wall, eliciting a foreign body reaction and inducing dentinoid [1]. Cysts may show intraluminal and/or mural epithelial proliferation producing ameloblastoma-like areas [1,5].

Odontogenic lesions mainly develop due to the capacity of the odontogenic epithelium to undergo differentiation and mesenchymal induction, which gives these lesions a wide variety of morphological features [7,8]. Interestingly, COC can occur in association with odontogenic tumors, frequently odontoma [9], ameloblastoma [10], ameloblastic fibroma [11], adenomatoid odontogenic tumor (AOT) [7] or with odontogenic keratocyst (OK) [12].

This study describes a case of COC with AOT-like areas and highlights the great differentiation potential and morphological diversity of this cyst.

CASE REPORT

A 60-year-old pheoderma man, with a one-year history of a large swelling on the left side of the anterior mandible, attended at the Oral and Maxillofacial Surgery and Traumatology Service of Santo Antônio Hospital - Irmã Dulce Social Works (Figure 1A and 1B). The patient had no history of extraoral trauma to the region and reported a history of tobacco and alcohol use. Intraoral examination revealed a large lesion of hardened consistency exhibiting mild pain upon palpation. The mass was covered with intact mucosa and there were no signs of infection (Figure 1C and 1D). Pulp vitality tests showed sensitivity loss in the anterior teeth (3.1 to 3.4). Panoramic radiography revealed a well-defined, unilocular, radiolucent lesion extending from the sagittal midline (Figure 2). The lesion caused important resorption at the roots of the anterior teeth (3.3 and 3.4). Aspiration yielded a serous yellowish fluid and the first hypothesis was unicystic ameloblastoma (UA).

An incisional biopsy was performed and sent to the Surgical Pathology Laboratory of the Federal University of Bahia, where the study was conducted. The report was compatible with a ghost cell odontogenic lesion suggestive of COC. Then, an excisional biopsy was obtained and complete enucleation of the lesion and peripheral ostectomy were performed. During surgery, the surgeon observed the extent of the lesion from the region of the 3.4 to the 4.3. All teeth associated with the lesion were removed.

The specimen was sent for histopathological analysis, which revealed the presence of a cystic fibrous wall lined with ameloblastomatous epithelium (Figure 3A) whose basal columnar cells resembled ameloblasts and exhibited a palisade arrangement and inverted nuclear polarity. The upper epithelial layers resembled the stellate reticulum of the enamel organ (Figure 3B). Ghost cells were found interspersed, with the fusion of these cells forming amorphous acellular eosinophilic material (Figure 3B). The epithelial component together with the ghost cells proliferated into the cystic lumen and toward the fibrous capsule (Figure 3C and 3D). Dentinoid material was also observed amidst the epithelium and capsule (Figure 3E).

These histopathological features were consistent with COC. Interestingly, the epithelium proliferating into the cystic lumen exhibited morphological features not commonly observed

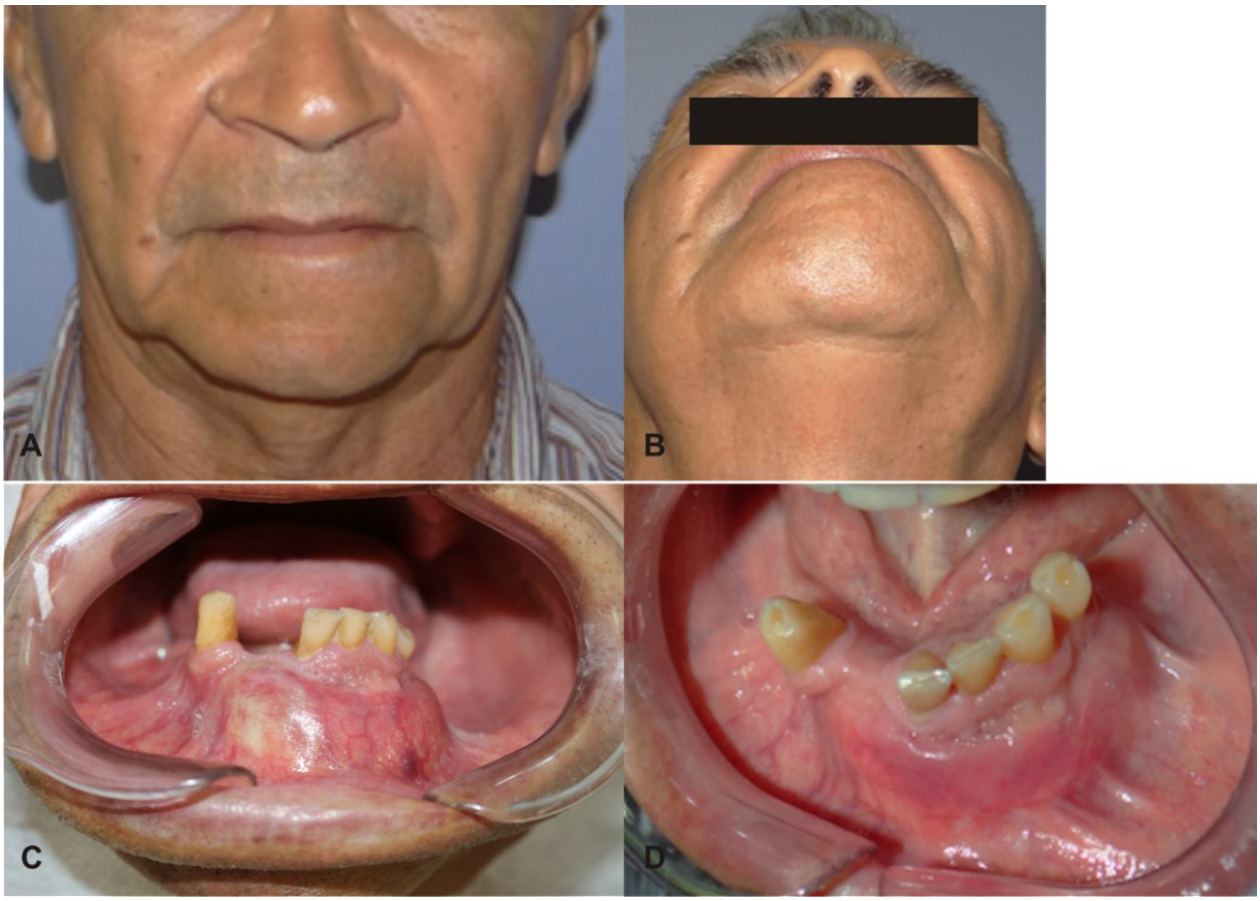

Figure 1 - Extraoral and intraoral views. (A and B) Note large swelling on the left side of the anterior mandible; (C and D) Large lesion covered with intact mucosa.

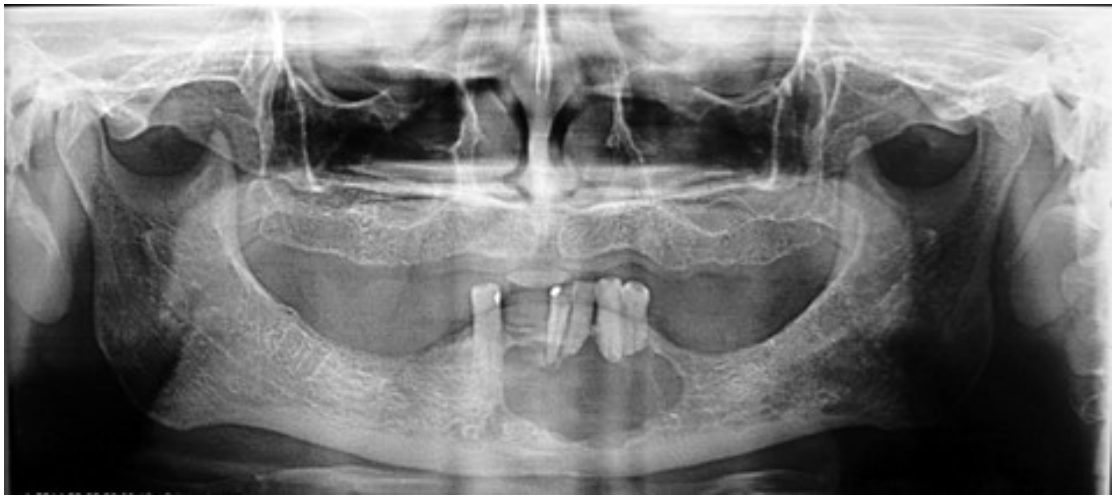

Figure 2 - Panoramic radiograph. Note large circumscribed radiolucent image extending from the sagittal midline and resorption in the roots of the teeth 3.3 and 3.4.

in COC. They were represented by numerous spindle-shaped and oval epithelial cells. Narrow strands of epithelial cells were also found (Figure 4A). Duct-like structures of variable size were observed amidst this proliferation, and were lined with a single layer of cells which exhibited AOT-like features, as it showed terminal bar (Figure 4B and C).

These histopathological characteristics were consistent with COC with AOT-like features.

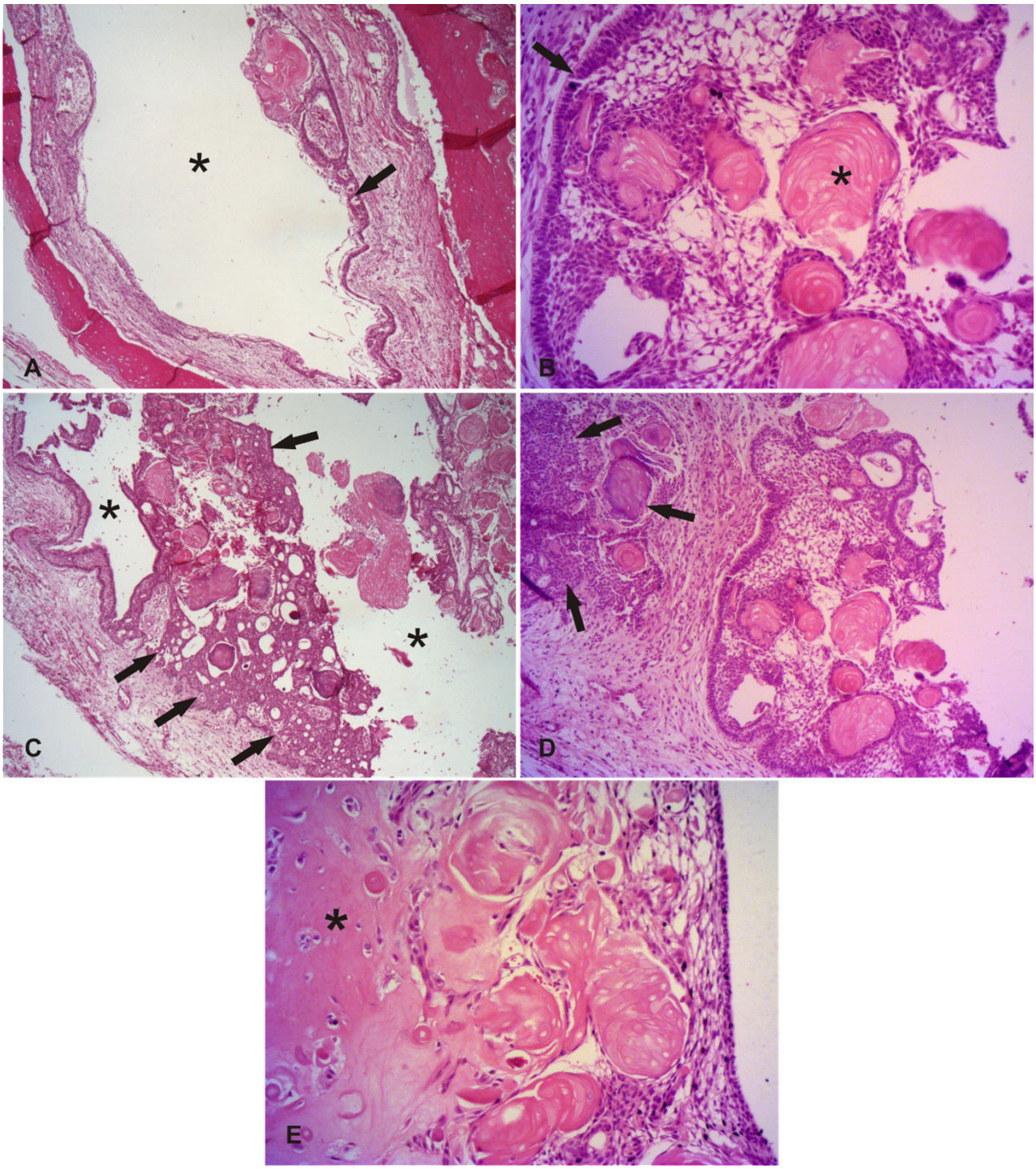

Figure 3 - Histological sections of COC stained with hematoxylin-eosin. (A) Note cystic lumen (asterisk) and fibrous wall lined with ameloblastomatous epithelium (arrow) (*40x*); (B) Detail of the basal columnar cells with a palisade arrangement and inverted nuclear polarity (arrow). The upper epithelial layers resembled the stellate reticulum of the enamel organ. Note clusters of ghost cells forming amorphous acellular eosinophilic material (asterisk) (*200x*); (C) Proliferation of epithelial component and ghost cells (arrows) into the cystic lumen (asterisk) (*40x*); (D) Epithelial and ghost cells in the fibrous capsule (arrows) (*100x*); (E) Detail of the dentinoid material in the fibrous capsule (asterisk) (*200x*).

The patient continues under clinical and radiographic follow-up and has shown no signs of recurrence after 6 months of follow-up (Figure 5).

To support the discussion of the case presented, a literature review was carried out in the Medline databases. The descriptors "calcifying odontogenic cyst", "adenomatoid odontogenic tumor", "AOT-like", "calcifying cystic odontogenic tumor" and "hybrid" were used to search for case reports published in English in all years.

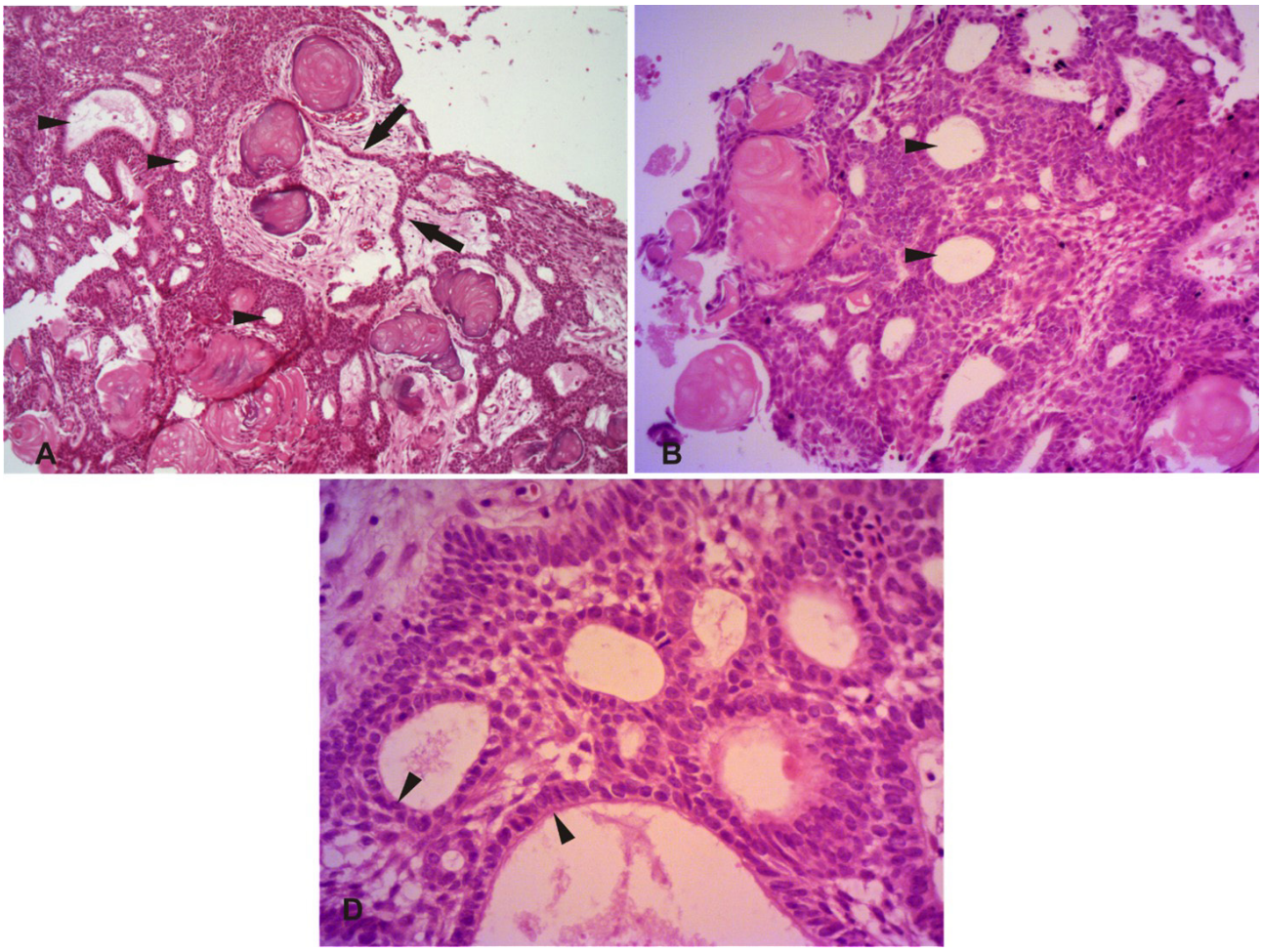

Figure 4 - Histological sections of COC stained with hematoxylin-eosin. (A) Note narrow strands of epithelial cells (arrows) and duct-like structures of variable size (arrowhead) (*100x*); (B) AOT-like area demonstrating the presence of duct-like structures lined with a single layer of cells (arrowhead) (*200x*); (C) Detail of the terminal bar in duct-like structures (arrowhead) (*400x*).

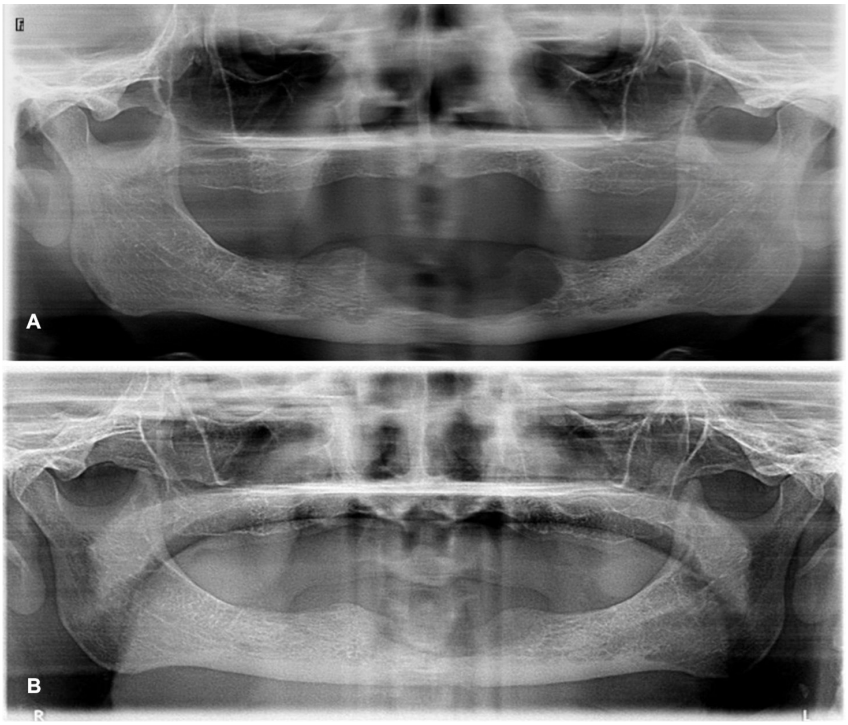

Figure 5 - Panoramic radiograph. Osseo repair after two months (A) and six months (B) of lesion removal.

DISCUSSION

This study reported the case of a 60-year-old man with COC involving the anterior mandible that exhibited unusual features. The histopathological diagnosis of COC at this site is not surprising since other odontogenic cysts have been described in this region, including COC with AOT-like areas [13].

COC was first described by Gorlin et al. [2] in 1962. In 2005, in view of the complexity of clinical and histopathological characteristics presented by this group of lesions, the WHO classified COC as a benign cystic neoplastic variant of odontogenic origin, and renamed it CCOT [3]. Additionally, the lesions with invasive biological behavior and tumor growth have been described as dentinogenic ghost cell tumor (DGCT) and, together with ghost cell odontogenic carcinoma (GCOC), the three entities form the group of ghost cell lesions of the jaws [3]. Over the years, some classifications were proposed, and a very useful and comprehensive classification that includes all cystic and solid subtypes of COC has been suggested by Ledesma-Montes et al. [6]. Recently, based on its behavior and clinicopathological features, the WHO renamed the CCOT as COC, a developmental cyst that originates from dental lamina [5].

Finally in 2022, the classification of the COC as a development odontogenic cyst was consolidated. The scientific evidence confirms the cystic nature and indolent behavior of the lesion and therefore no change occurred in its nomenclature and classification [14].

COC have been found in association with odontogenic tumors such as odontoma [9], ameloblastoma [10], ameloblastic fibroma [11], and AOT [7], or with OK [12]. COC associated exclusively with AOT is rare [6-8,13,15]. The mechanism that causes the occurrence of two odontogenic lesions together is not well known. However, several theories have been proposed to explain the phenomenon, including a transformation of one lesion into another, a collision of two separate lesions, and an inductive effect of one lesion into another [11]. Thus, although extremely rare, it is not unexpected that COC gives rise to AOT because of the multipotentiality of the odontogenic epithelium [7,8].

The histopathological findings of the present case meet the criteria for the diagnosis of COC [4,5]. However, part of the cystic epithelium that proliferated into the lumen exhibited some features resembling those seen in AOT, such as spindle-shaped and oval cells forming duct-like structures with an evident terminal bar. It is important to state that terminal bar is not present in microcysts and this aspect is important to the differential diagnosis. Additionally, cells clustered in a cord-like arrangement were observed in focal areas.

It should be noted that there was no collision of two odontogenic lesions, COC and AOT, in the present case. Furthermore, other features necessary for the characterization of AOT, such as the presence of rosette-like structures, were absent. Thus, there are not sufficient criteria to classify this case as a hybrid odontogenic lesion. The morphological features observed suggest an unusual pattern of differentiation of part of the epithelial component of COC, since the odontogenic epithelium has a diverse differentiation potential under the influence of ectomesenchyme and also due to its multipotentiality. The multipotentiality of odontogenic tissues favors the biological event of transdifferentiation in some odontogenic cysts and tumors, without influencing the biological behavior of the lesions. The present case therefore meets the histopathological criteria for COC with AOT-like features.

Although previous studies [6-8,13,15] have reported an association between COC and AOT, we highlight some differences and similarities compared to the present case. The microscopic findings described by Zeitoun et al. [13] are very similar to our case in which the AOT-like component appeared to arise from the epithelial component that proliferated into the cystic lumen, but differed by the presence of epithelial rosettes. Also, in contrast to the present case, Soares et al. [7] detected an AOT with evident features such as the presence of epithelial cells with secretory activity forming solid nodules, which contained some rosettes and several duct-like structures adjacent to the COC.

Balaji and Rooban [8] published a case of COC with unusual features, including AOT-like areas. The authors attributed this morphological diversity to the pluripotent cells present in the epithelial lining of COC, which could give origin to

odontogenic tumors. Narrow anastomosed cords alongside duct-like structures were observed, in agreement with the present case. However, the rosette-like pattern was also described. As in our case, the authors of the latter study did not consider the lesion to be a hybrid and called it COC with AOT-like areas. According to Balaji and Rooban [8], if the case had been diagnosed at a later stage, it is likely that a COC and an AOT would have been clearly found.

The present case concurs in some aspects with previous studies on COC. According to Ledesma-Montes et al. [6] and literature review of Arruda et al. [4], there is a male predilection and COC occurs over a broad age range. Concerning localization, there is no consensus, but the anterior maxilla seems to be the site of greatest occurrence, and the cyst commonly manifests as a painless swelling with a mean size ranging from 3 to 4 cm [4,6]. In the present case, the cyst occurred in a 60-year-old male patient, was located in the anterior mandible, and was of large size.

A search of the English-language literature for cases of COC with AOT-like areas identified five case reports [6-8,13,15]. These cases are summarized in Table I.

Most authors classified the cyst as a hybrid odontogenic lesion and only one case was called COC with unusual features [8], similar to the present case. These aspects were a limitation of the literature review carried out. Analysis of the clinical data (Table I) showed male-to-female ratio: 1.5:1, the mean age was 22.8 years (range, 2-43 years), with 3 cases in the maxilla and 2 in the mandible, and there appeared to be a preference for the anterior region.

Radiographically, COC appears as a well-defined unilocular or multilocular radiolucency that can contain variable amounts and shapes of radiopaque material. The cyst may be associated with an impacted tooth and root resorption and divergence of adjacent roots are frequent [6]. The present case manifested as an extensive radiolucent, unilocular lesion associated with important root resorption and root divergence. Foci of radiopaque material and impacted teeth were absent.

The clinical and radiographic features of the present case can mimic other odontogenic lesions, including glandular odontogenic cyst, UA, OK and residual radicular cyst. Although UA is more common in young patients and is generally associated with an impacted tooth, it was the first hypothesis because it is the most frequent and because the unilocular radiographic image favored this clinical hypothesis [1]. Analyzing the radiographic features of COC with AOT-like areas (Table I), similar to the present case, all cysts had a unilocular appearance and only one case was associated with root resorption [13]. Few cases exhibited radiopaque foci [7,13] or were associated with an impacted tooth [7].

COC is considered a cyst of non-invasive biological behavior and enucleation has been the treatment of choice [5], including cases with AOT-like areas (Table I). In this case report, the patient showed significant resolution of the mandibular radiolucency and no signs of recurrence 6 months after surgery. According to

Table I - Epidemiological data of COC with AOT-like areas published in English language

Age, years	Sex	Location	Clinical Diagnosis	Size, cm	Radiopaque clusters	Treatment	Reference
15	Female	Posterior Mandible	X	X	No	Enucleation with curettage	Freedman et al. [15]
35	Male	Anterior Mandible	CCOT	5	Yes	Enucleation with apicetomy of adjacente teeth	Zeitoun et al. [13]
19	Male	Posterior Maxilla	X	4	X	X	Ledesma-Montes et al. [6]
2	Female	Anterior Maxilla	AFO	3	Yes	Enucleation without associated tooth	Soares et al. [7]
43	Male	Anterior Maxilla	PG	1.7	No	Enucleation	Balaji and Rooban [8]
60	Male	Anterior Mandible	UA	5	No	Enucleation with curettage	Present

X - Not avaliable; CCOT - Calcifying Cystic Odontogenic Tumor; AFO - Ameloblastic Fibro-Odontoma; PG - Periapical Granuloma; UA - Unicystic Ameloblastoma.

Ledesma-Montes et al. [6], cases of isolated or combined COC are indeed associated with low recurrence.

This study reported a case of COC with AOT-like features, highlighting the morphological diversity of odontogenic lesions. These cysts are uncommon and we believe that each case is indeed unique and has its particularities, since the inductive effects between odontogenic epithelium and ectomesenchyme are complex. In addition, the multipotentiality of the odontogenic epithelium favors a diversified potential for differentiation. Finally, COC with AOT-like features does not seem to differ about the biological behavior from that of classical COC when the period of follow-up of the present case is considered.

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Author's Contributions

LVS: Investigation, Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing, Visualization. IJVAC: Writing – Original Draft Preparation, Writing – Review & Editing, Visualization. LMGF: Conceptualization, Investigation. BCJ: Conceptualization, Investigation. JNS: Investigation, Writing – Review & Editing. ACGH: Conceptualization, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing.

Conflict of Interest

The authors declare no conflict of interest.

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Regulatory Statement

A signed consent form was obtained from the patient to disclose the case.

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