RESEARCH

Calcifying odontogenic cysts: A 20-year retrospective clinical and radiological review

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Abstract

Objective: Calcifying odontogenic cysts (COCs) exhibit diverse clinical behaviours, and may be associated with other benign odontogenic tumours. In this study, the clinical and radiological features of COCs were analysed according to subtypes based on the classification by Praetorius *et al*. Emphasis was placed on cases exhibiting atypical or aggressive radiological appearances. This information may assist the clinician to better understand the radiological spectrum of COCs.

Methods: Histologically confirmed cases of COCs were retrospectively reviewed in a 20-year period from three tertiary institutions. The following clinical information was reviewed: patient demographics, main complaint, clinical duration, anatomical site and detailed radiological features.

Results: Twenty-seven cases of COCs were included in the study. Asymptomatic swelling was the main clinical presentation with infrequent reports of associated pain. COCs had an anterior mandibular predilection. Well-demarcated borders were seen in all cases with isolated cases showing focal areas with loss of demarcation. Unilocular lesions were more common than multilocular

variants. Internal calcifications were frequent and six cases presented with associated odontomas. Maxillary COCs resulted in the displacement of the maxillary sinus and/or nasal cavity walls. Radiological signs of aggression, including cortical destruction, were noted in a few cases.

Conclusion: Given the fact that COCs can present with a spectrum of clinical behaviours and radiological presentations, the academic debate regarding the cystic versus neoplastic nature of the entity is justifiable. The cases in the current sample presented with diverse clinical behaviours and radiological presentations, ranging from indolent to lesions with significant growth and aggression.

Keywords: Calcifying odontogenic cysts, Odontogenic cysts, Odontogenic tumours, Maxillofacial radiology

Introduction

Calcifying odontogenic cysts (COCs) are defined as developmental cysts lined by ameloblastoma-like epithelium containing focal accumulations of ghost cells that frequently undergo dystrophic calcification.[1] Most authors recognise that the entity was first described in 1962 by Gorlin *et al*, and was subsequently given the eponym Gorlin cyst.[2] However, documented cases preceding this initial description have been discovered, linking the first reported case to Thoma *et al* in 1917.[3] Since then, reports of COCs exhibiting diverse clinical behaviour and histopathological presentations have been published.[4] Subsequently, a debate ensued whether these lesions are cystic or neoplastic in nature, with some cases showing an indolent growth and others being more aggressive. This, in part, led to the 2005 World Health Organisation (WHO) classification categorising these lesions as benign cystic neoplasms, termed calcifying cystic odontogenic tumours (CCOT).[5] This resulted in divergent opinions amongst academics as not all lesions exhibited neoplastic behaviour. Moreover, some authors retained the term COC for cysts and CCOT for solid lesions displaying more aggressive, neoplastic behaviour.[4] With the increase in collaborative studies and subsequent publication of cases, it became apparent that these ghost cell lesions could present in a dualistic manner as either cystic or neoplastic variants.

Praetorius *et al* attempted to resolve this controversy by dividing ghost cell lesions of the jaws into a cystic, solid-neoplastic and malignant counterparts, termed COCs, dentinogenic ghost cell tumours and ghost cell odontogenic carcinomas respectively.[6] Currently, most authors seem to agree on this delineation and consequently, the name was reverted to COC in the 2017 WHO classification.[1] This classification initially introduced by Praetorius *et al* has been adapted over the years to further subdivide COCs into four categories:[7]

- Type 1: Simple cystic COC

- Type 2: Odontoma-associated COC
- Type 3: Ameloblastomatous proliferating COC
- Type 4: COC associated with other benign odontogenic tumours

This simplified classification emphasised various other lesions that may be seen in association with COCs. Nonetheless, the academic deliberation continued, and over the years many different classifications systems have been developed.[6,8,9] Some authors argue that type 3 and 4 COCs should be categorised as neoplastic variants due to the associated neoplastic lesions.[9,10] In the type 4 category, COCs have been reported in association with ameloblastic fibromas, adenomatoid odontogenic tumours, odontoameloblastomas and odontogenic myxomas.[7,9] The complexity of odontogenesis explains the possible occurrence of hybrid lesions.[9] Ide *et al* illustrated a case where the cystic lining of a COC showed varying histological features corresponding to other developmental odontogenic cysts, reiterating the divergent capacity of odontogenic epithelium.[11]

The treatment of COCs is based on the complete removal of the lesion via enucleation and curettage, with subsequent long-term follow-up. Two-stage treatment techniques, including marsupialisation and active decompression with distraction sugosteogenesis, have gained recent attention in the literature. These techniques have shown favourable clinical outcomes, but further studies with adequate follow-up periods are needed to validate the long-term success of these methods.[12,13] Type 3 and 4 COCs should be treated based on the biological behaviour of the associated lesion.[10] This supports the classification proposed by Li *et al*, where these subtypes are categorised under the neoplastic variant as they present with similar biological behaviours and have the same treatment approach.[9] COCs have a reported recurrence rate of 5.3% with a 0.9% malignant transformation potential.[7]

Several studies have described the epidemiological presentation and histopathological findings of the different subtypes of ghost cell lesions of the jaws based on the classification by Praetorius *et al*.[7,14,15] However, information is limited in the literature on the detailed radiological features of COCs, obtained from small case series and isolated case reports.[16–20] In this study, the clinical and radiological features of histologically confirmed cases of COCs were analysed according to subtypes based on the Praetorius *et al* classification. Given the biological diversity of COCs, emphasis was placed on cases exhibiting atypical or aggressive radiological presentations. This information may assist the clinician to better understand the radiological spectrum of COCs.

Materials and methods

The study was conducted following approval by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference number: 505/2020). All procedures followed the ethical standards of the Helsinki Declaration of 1975, as revised in 2008.

Histologically confirmed cases of COCs were retrospectively reviewed in a 20-year period (1999-2019). All cases with available radiological examinations were selected from the archives of three tertiary institutions (Pretoria Oral and Dental Hospital, Pretoria, South Africa, Tygerberg Oral Health Care Centre, Cape Town, South Africa and Piracicaba Dental School, São Paulo, Brazil). The following clinical information was reviewed: age at diagnosis, gender, main complaint, clinical duration and anatomical site. Cases were excluded based on the unavailability of radiological examinations and cases without a confirmed histological diagnosis. The radiological features were analysed by two clinicians with experience in the field of maxillofacial and oral radiology and any disagreements were resolved by consensus. The information was analysed, with emphasis on the clinical and radiological features of the different subtypes of COCs.

Results

Clinical Features

Following the inclusion criteria, 27 diagnosed cases of COC were included in the study with the majority being classified as type 1 (20 cases), whereas six cases were classified as type 2. Due to the rarity of type 3 and 4 COCs, only one case was classified as type 3 and no type 4 cases were diagnosed from the three institutions over a 20-year period. Table 1 summarises the pertinent clinical and radiological characteristics. The sample included an almost equal gender distribution with a male predominance noted in type 2 COCs. The mean age of presentation was higher in type 1 COCs (31 years) when compared to type 2 (22 years). Clinical information was unavailable for six patients. Localised swelling was the main clinical presentation in all subtypes with the majority being asymptomatic (18/21 cases). Pain was an infrequent finding (3/21 cases), and only seen in type 1 COCs. Four cases presented with additional signs of tooth mobility. The reported mean duration was 16 months with the shortest duration seen in type 2 COCs (6 months). In the overall sample, COCs had a mandibular predilection (16/27 cases). Type 1 COCs were equally distributed between the maxilla and mandible, whereas type 2 COCs showed a predilection for the mandible. The majority of cases were concentrated in the anterior mandibular region, with two cases involving the ramus. Mandibular COCs had a tendency to cross the midline (9/16 cases), whereas none of the anterior maxillary cases crossed the midline.

Table 1: Clinical and radiographic features of patients with Calcifying Odontogenic Cysts

Features	Results (%)			
	Type 1 (n=20)	Type 2 (n=6)	Type 3 (n=1)	Total (n=27)
Age, years (range)	31 (12-67)	**22** (11-36)	20	29 (11-67)
Gender	10M/10F (1:1)	**4M/2F** (2:1)	1M	15M/12F (1.3:1)
Main complaint				
Asymptomatic swelling*	12/15 (80.0%)	5/5 (100%)	1 (100%)	18/21 (85.7%)
Painful swelling*	**3/15** (20.0%)	-	-	3/21 (14.3%)
Tooth mobility*	2/15 (13.3%)	2/5 (40.0%)	-	4/21 (19.0%)
Clinical duration, months (range)	19 (3-72)	**6** (4-7)	24	16 (3-72)
Site				
Maxilla	10 (50.0%)	1 (16.7%)	-	11 (40.7%)
Mandible	10 (50.0%)	**5** (83.3%)	1 (100%)	16 (59.3%)
Borders				
Well demarcated	16 (80.0%)	6 (100%)	1 (100%)	23 (85.2%)
Focal loss of demarcation	**4** (20.0%)	-	-	4 (14.8%)
Internal structure				
Unilocular	13 (65.0%)	5 (83.3%)	1 (100%)	19 (70.4%)
Unilocular with scalloped margins	**2** (10.0%)	-	-	2 (7.4%)
Multilocular	**5** (25.0%)	1 (16.7%)	-	6 (22.2%)
Density				
Radiolucent	8 (40.0%)	3 (50.0%)	1 (100%)	12 (44.4%)
Mixed	12 (60.0%)	3 (50.0%)	-	15 (55.6%)
Effects on surrounding tissue				

Bony expansion	**13** (65.0%)	3 (50.0%)	1 (100%)	17 (63.0%)
Root resorption§	**14/16** (87.5%)	4 (66.7%)	1 (100%)	19/23 (82.6%)
Tooth displacement§	9/16 (56.3%)	**4** (66.7%)	1 (100%)	14/23 (60.9%)
Tooth impaction§	3/16 (18.8%)	**4** (66.7%)	1 (100%)	8/23 (34.8%)
Cortical destruction/thinning	**4** (20.0%)	1 (16.7%)	1 (100%)	6 (22.2%)
Displacement of anatomical structures†	**7** (35.0%)	1 (16.7%)	-	8 (29.6%)

M: Male; F: Female.

Significant differences between the subtypes were indicated in **bold**.

* Four patients presented with more than one complaint; clinical information was missing for 5 cases classified as type 1 and one case classified as type 2

§ Four cases presented in edentulous areas, all limited to type 1. Therefore, only 23/27 cases were seen in association with teeth

† Maxillary sinus, nasal cavity or inferior alveolar nerve

Radiological Features

Well-demarcated borders were seen in all cases. However, four cases showed focal areas with loss of demarcation, all limited to type 1 COCs. Unilocular COCs were more common (21/27 cases) than multilocular variants (Fig. 1). Scalloped margins in unilocular variants were only seen in type 1 COCs. There were six cases that had a multilocular appearance, five classified as type 1 COCs and one case classified as type 2. More than half of all cases (15/27 cases) exhibited internal calcifications. Associated odontomas (type 2 COCs) were seen in six cases (Fig. 2), with three cases having additional internal calcifications. Bony expansion was seen in 17/27 cases and appeared to be less common in type 2 COCs. Of the 23 cases where teeth were involved, 19 cases showed root resorption, with tooth displacement and impactions seen in 14 and eight cases respectively. Root resorption appeared more common in type 1 COCs, with tooth displacement and impaction more commonly seen in type 2 cases. Loss of cortical integrity, although infrequently seen, was more common in type 1 COCs compared to type 2 (Fig. 3). This feature typically only involved larger lesions. Overall, the majority of the maxillary COCs (7/11 cases) resulted in the displacement of the maxillary sinus and/or nasal cavity walls, with one case obliterating the sinus cavity (Fig. 4). Only one case was classified as type 3, which exhibited aggressive behaviour, being highly expansive with cortical destruction (Fig. 5).

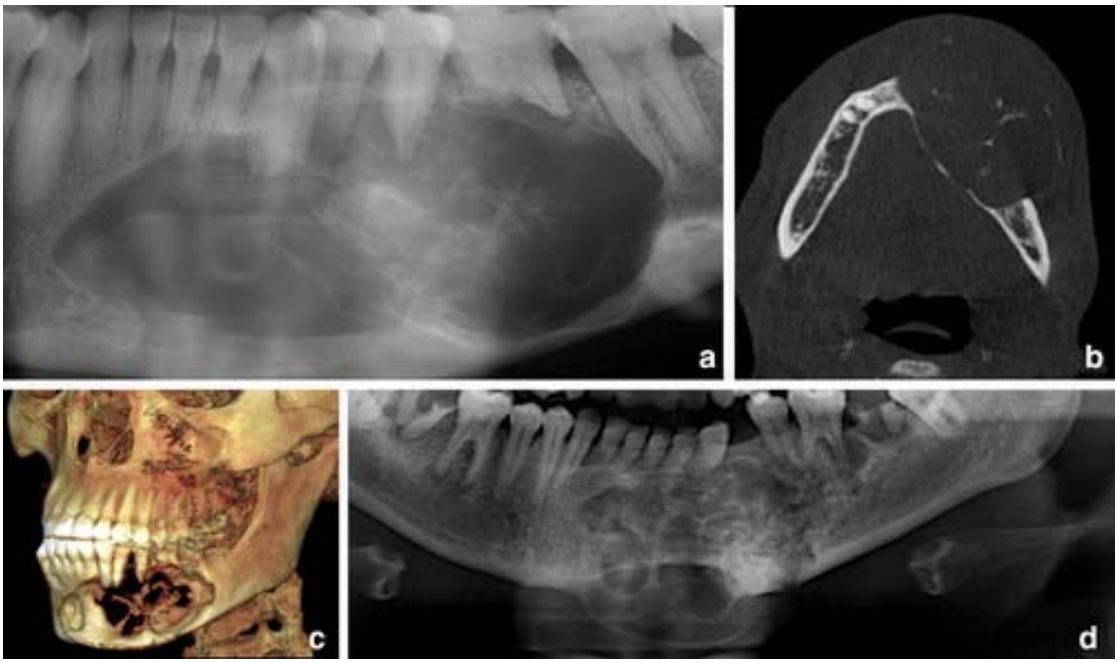

Figure 1 COCs with a multilocular radiographic appearance. (A) Panoramic radiograph, (B) axial and (C) three-dimensional CBCT images showing an expansive multilocular lesion resulting in root resorption as well as cortical thinning and destruction. (D) Panoramic radiograph exhibiting a well-demarcated multilocular lesion with bony expansion and cortical thinning.

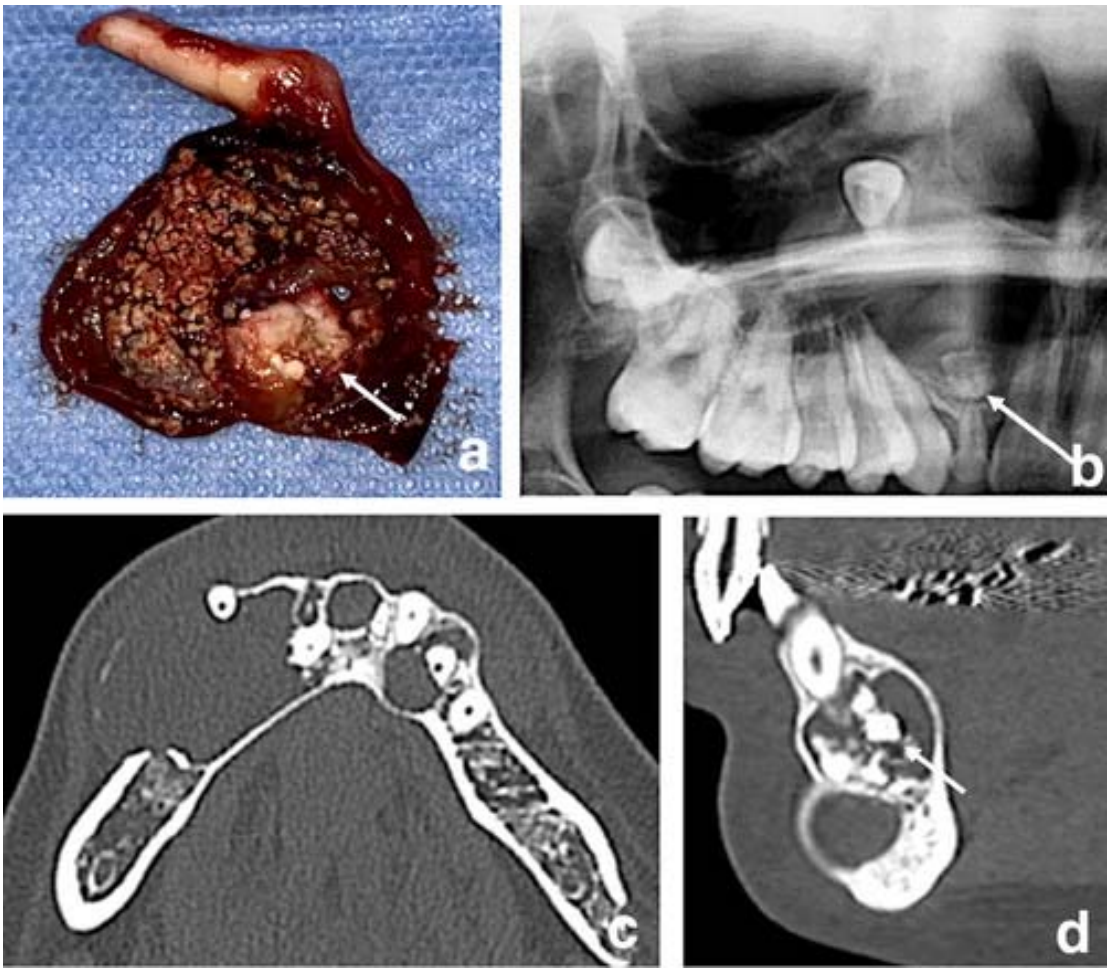

Figure 2 COCs associated with odontomas (arrows) (type 2). (A, B) The numerous calcifications seen in the enucleation specimen were not clearly visible on conventional imaging. (C) Axial and (D) sagittal CT images showing a multilocular mixed lesion with cortical expansion and focal areas of cortical destruction. Internal calcifications and an associated odontoma (arrow) were also noted.

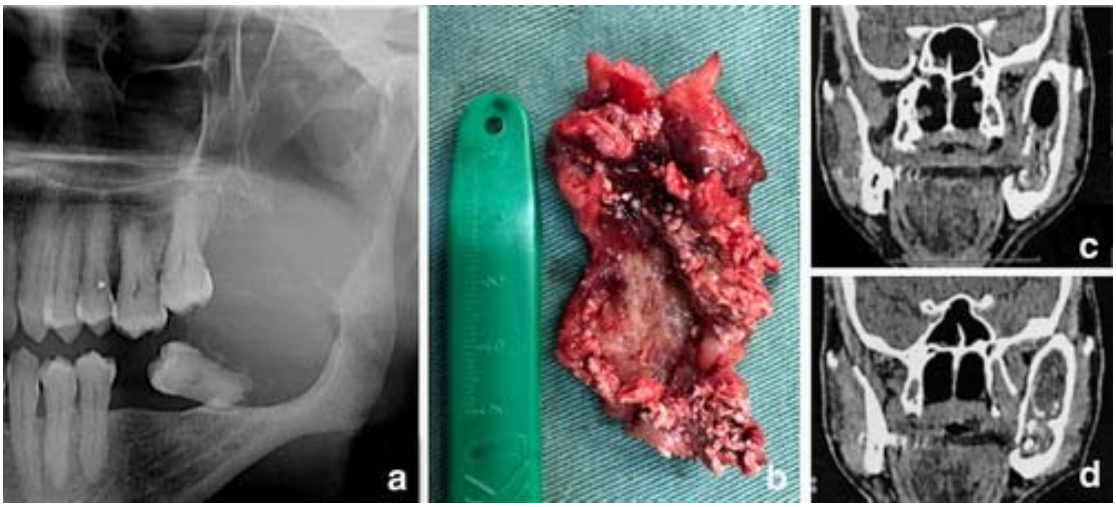

Figure 3 COC with atypical presentation involving the left ramus. (A) Panoramic radiograph showing a well-demarcated mixed lesion causing root resorption and loss of demarcation at its anterior aspect. (B) Enucleation specimen showing numerous luminal calcifications. (C, D) Coronal CT images illustrating scalloped margins with internal calcifications and lingual cortical disruption.

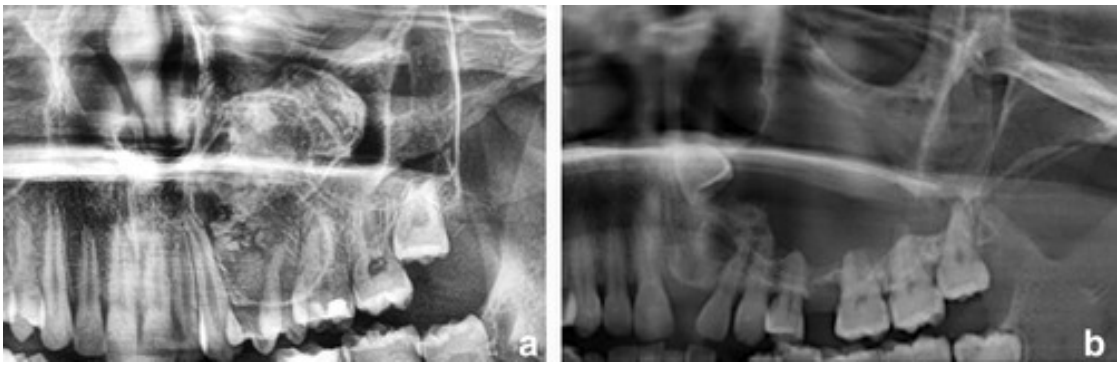

Figure 4 Maxillary COCs causing displacement of anatomical structures. (A) Panoramic radiograph showing a well-demarcated mixed lesion resulting in displacement of the walls of the left maxillary sinus. (B) Panoramic radiograph showing a COC associated with an impacted left maxillary central incisor that resulted in root resorption and encroachment of the left maxillary sinus.

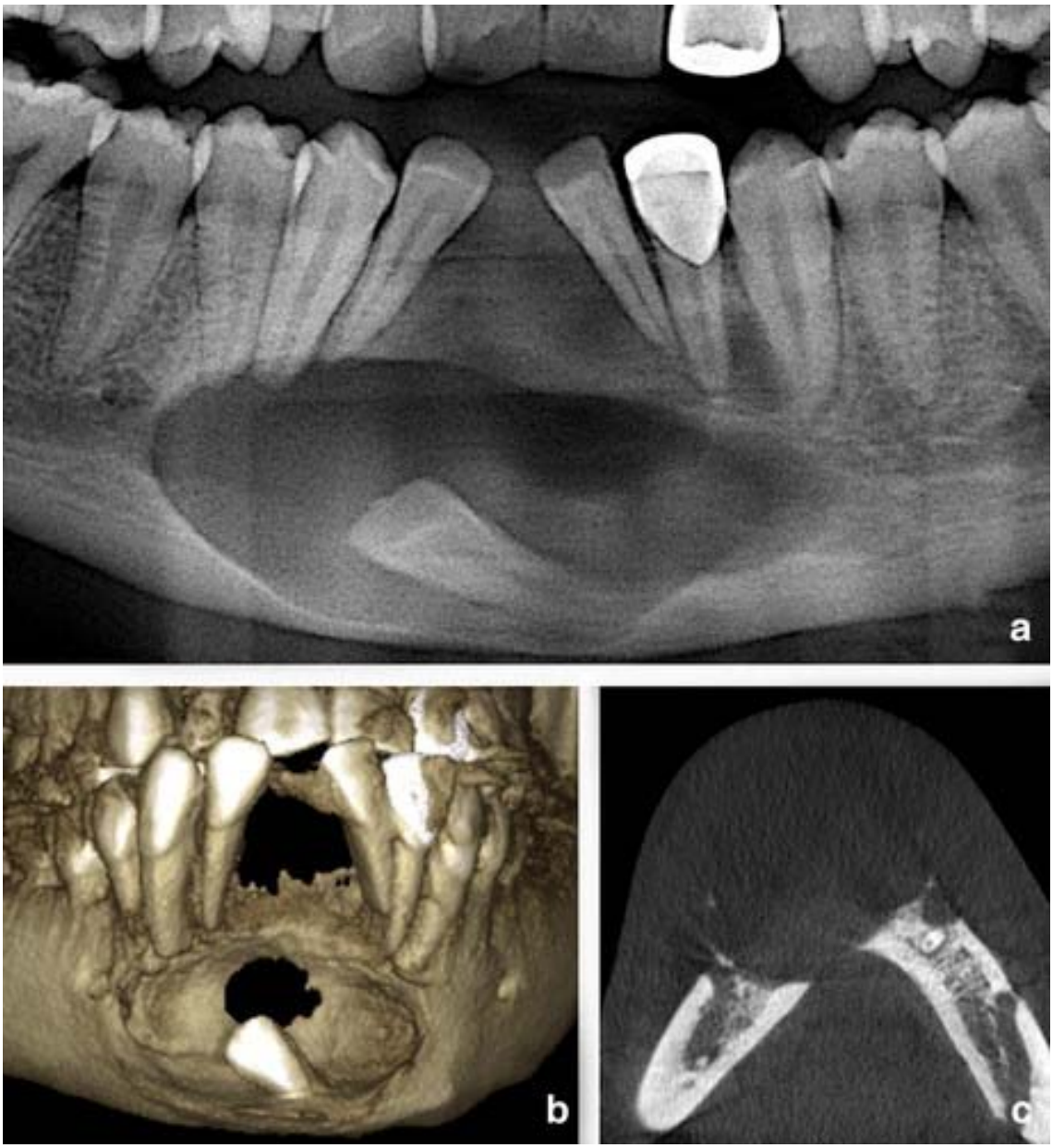

Figure 5 Ameloblastomatous proliferating COC (type 3). (A) Panoramic radiograph, (B) three-dimensional and (C) axial CBCT images showing a highly expansive lesion with destruction of the buccal and lingual cortices.

Discussion

COCs account for less than 2% of all central odontogenic lesions,[21,22] and represent 90% of ghost cell lesions of the jaws.[7,14] Simple cystic COCs (type 1) represent the most common subtype (70%), followed by type 2 (24%). [7,10,14] Types 3 and 4 are exceedingly rare, representing only 6% of all COCs in an almost equal frequency.[7] The rarity of these subtypes makes accurate deductions on their presentation difficult. In the current sample the frequency of each subtype mirrored that of previous reports.

COCs typically present during the second and third decades of life (mean age of 30 years) with an almost equal gender distribution (1.2:1 male to female ratio).[7,9,10,23,24] Type 2 variants seem to occur in younger patients when compared to type 1 COCs, with a peak incidence in the second decade.[7,8,10,15] A wide variation in age of presentation amongst type 3 and 4 COCs was reported in the literature.[7,14] The demographic presentation in the current sample corresponded to previously reported reviews.

COCs usually present clinically with swelling, with a mean duration of four years, ranging from 6 months to 28 years.[7,10] Most COCs are asymptomatic, however large destructive lesions and those with secondary infection may present with pain.[19] COCs typically reach an average size of 3.7 cm.[7,10,20] Understandably type 3 and 4 COCs usually reach the largest mean size, followed by type 1, with type 2 COCs exhibiting the smallest overall size.[7] COCs resulting in spontaneous exfoliation or tooth mobility have also been reported in previous studies.[8] In the current study most cases presented as an asymptomatic swelling, with associated pain seen most commonly in type 1 cases. This could be explained by the fact that symptoms are often seen in association with larger, destructive lesions.[22] In the current sample, the reported clinical duration was the lowest in type 2 COCs. This variant is usually discovered earlier as radiographs are often performed to investigate unerupted teeth.

COCs typically show a slight predilection for the maxilla (59%) over the mandible (41%).[7,9,10] The anterior region of the maxilla, followed by the molar region of the mandible, are the most commonly affected subsites.[7,10] Differences in anatomical sites have however been reported in different race groups, with some reporting a mandibular predominance.[8,10,14,16,23,24] In the current study COCs had a wide distribution in the jaws, with the anterior mandible being most frequently affected. The incidence of mandibular cases having a tendency to cross the midline also corresponded with other reports.[10] Reportedly, most type 2 COCs present in the maxilla, with more than half arising in the anterior region.[7,14] Interestingly, in the current sample, this subtype showed a strong mandibular predominance.

Radiologically, COCs usually present as well-defined, unilocular radiolucent lesions with varying degrees and frequencies of internal calcifications.[7,9,10,16] All cases in the current sample had well-demarcated borders, with only isolated type 1 COCs exhibiting focal loss of demarcation. It is postulated that this loss of demarcation is related to secondary infection, as this was the only category presenting with associated pain. In all categories, unilocular lesions were more common than multilocular variants. This corresponds to findings from previous reviews.[7] Multilocular lesions, although rare, have been reported in the literature.[9,10,14,16,17] Multilocularity is often seen in larger lesions and therefore explains the rarity seen among smaller type 2 COCs. Internal calcifications are common, with some studies reporting a mixed appearance in 61% of COCs.[23] CBCT imaging has higher sensitivity in detecting calcifications compared to routine panoramic radiography.[16,20]

Histological evaluation revealed that all cases in the current sample showed calcifications, some of which were not visible during radiographic examination. Varying degrees of internal calcifications were noted in the majority of cases, with a single case whereby the calcifications were only apparent on CBCT imaging. In the current sample, internal calcifications were frequently seen in both type 1 and 2 COCs. Type 3 COCs typically present as purely radiolucent lesions[7], corresponding to the current case.

With regards to the effects on surrounding structures, cortical bone expansion has been considered a common feature in COCs.[7,10,20] In the current sample, bone expansion was more commonly reported in type 1 compared to type 2 COCs. This finding may however be underestimated due to the retrospective nature of the study and limited availability of three-dimensional imaging for all cases. Three-dimensional imaging may be useful in the surgical planning of cases exhibiting aggressive clinical behaviour. COCs are commonly seen in association with impacted teeth, particularly canines, and often cause root resorption[7,10,16,22] In the current sample, root resorption was the most common radiological finding, with tooth displacement being more frequent than impaction. In contrast to previous studies, which reported a higher incidence of impactions in type 1 COCs[7], the current study found impactions to be more frequent in type 2 COCs. The higher frequency of tooth impactions seen in type 2 COCs could be related to their earlier age of onset, where the cyst starts developing in the mixed dentition phase. Furthermore, in the current sample the majority of the impacted teeth were situated in the canine region. COCs exhibiting cortical perforation have also been reported in the literature.[10,16,20] Loss of cortical integrity was noted in a few of the current cases, with type 2 COCs rarely exhibiting this feature. Maxillary involvement is known to cause maxillary sinus displacement or obliteration.[10,20] This was a significant finding in the current sample as the majority of maxillary cases resulted in encroachment of these structures.

Type 2 COCs tend to have lower proliferative activity compared to COCs without odontomas.[19] This corresponds to the current sample where type 2 COCs tended to be asymptomatic, remained well-defined, and showed a decreased incidence of bony expansion and loss of cortical integrity. Interestingly, tooth displacement was more common in this subtype compared to root resorption. In the current sample from three tertiary institutions only a single case of type 3 COC was diagnosed over a 20-year period, highlighting the rarity of such hybrid lesions. This case presented with a significantly more aggressive biological behaviour compared to the other cases in this sample.

A limitation of the current study is its retrospective nature, as clinical information was unavailable in six cases. Advanced imaging was not available for all cases; therefore bony expansion and internal calcifications may have been underreported. Estimations on the size of all lesions could not be made,

as the magnification factor from the radiographs was unknown and not uniform. Additionally, due to the rarity of cases in type 3 and 4 COCs, accurate conclusions on these subtypes could not be made.

Conclusion

Given the fact that COCs may present with a spectrum of indolent to aggressive presentations, the academic debate regarding the cystic versus neoplastic nature of the entity is justifiable. The cases in the current sample presented with diverse clinical behaviours and radiological presentations. The typical radiographic appearance of unilocular cystic lesions with internal calcifications is well documented amongst COCs. The cases in the current sample included COCs with atypical and aggressive radiological appearances. Type 2 COCs typically have a less aggressive clinical behaviour when compared to the other subtypes. These findings emphasise the importance of subdividing COCs to assist the clinician with the recognition of the various presentations, and further guidance with the management of these patients.

Declarations:

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Conflict of Interest: The authors declare that they have no conflict of interest.

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