Ghost cell odontogenic carcinoma arising in the background of a calcifying odontogenic cyst

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Disclosure

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Ethics

This study was approved by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference no.: 622/2020). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later versions. This article does not contain any studies with animal subjects performed by the any of the authors.

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ABSTRACT

Ghost cell odontogenic carcinoma (GCOC) is a rare malignant neoplasm, representing 3% of all ghost cell lesions of the jaws. They can arise *de novo* or from a pre-existing calcifying odontogenic cyst (COC) or dentinogenic ghost cell tumour (DGCT). A systematic review of the literature reported only 12 cases of a GCOC arising from a pre-existing COC. This report highlights an additional case of a GCOC arising from a pre-existing COC after three years in an adolescent male. The patient initially presented with a painless swelling of the right mandibular corpus. Panoramic radiographic examination showed an expansive unilocular radiolucent lesion. After three years the radiographic features appeared more aggressive with increased expansion and cortical perforation. A wide surgical resection was performed, whereby the lesion was diagnosed as a GCOC. Due to the rarity of these neoplasms, limited information is available regarding their biological behaviour. One-year follow-up revealed no clinical signs of recurrence.

KEYWORDS: Odontogenic cysts, Odontogenic tumours, Ghost cell lesions of the jaws, Malignant transformation, Maxillofacial radiology

INTRODUCTION

Ghost cell lesions of the jaws are rare, representing 0.4% of all head and neck lesions [1]. They may occur centrally within bone or in peripheral soft tissues. Much academic deliberation has occurred over the terminology of these ghost cell lesions due to their diverse biological behaviours. These lesions can occur as cystic, solid or malignant tumours termed calcifying odontogenic cyst (COC), dentinogenic ghost cell tumour (DGCT) and ghost cell odontogenic carcinoma (GCOC) respectively. The 2017 World Health Organization (WHO) classification of head and neck tumours, defines COC as a simple cyst lined by ameloblastoma-like epithelium containing localised accumulations of ghost cells [2]. The solid counterpart, termed DGCT, consists of infiltrating ameloblastomatous epithelium with varying degrees of basaloid cells. In addition, these tumours contain ghost cells and material resembling dentinoid [2]. Malignant transformation of the aforementioned lesions may occur, resulting in an entity termed GCOC. This odontogenic carcinoma can also arise *de novo* [3] and is characterised by cytological evidence of malignancy and an infiltrative growth pattern with aberrant ghost cell keratinisation and dentinoid deposition [2].

GCOC represents 3% of all ghost cell lesions of the jaws with only limited cases reported in the literature [3,4]. Ikemura *et al* first described the neoplasm in 1985 as a malignant calcifying odontogenic tumour [5]. GCOCs have a strong male predilection (4:1) and can occur in a wide age range (13-86 years) with a mean age of 40 years [4]. These neoplasms have a high prevalence amongst Asian patients [4], frequently occurring as a swelling in the maxilla. Radiographically, they present as a mixed radiolucent-radiopaque lesion with poorly defined margins. Due to the rarity of

these lesions, limited information is available regarding their behaviour, with some tumours exhibiting indolent growth and others having a fatal outcome [4]. An international collaborative study called for more publications of these neoplasms to improve current understanding of this rare entity [3].

This case report highlights the rare occurrence of a GCOC arising from a pre-existing COC after three years in an adolescent male.

CASE REPORT

A 12-year-old male patient presented with a one-year history of a painless swelling involving the right mandibular corpus. The patient's medical history was non-contributory. On examination the overlying skin and mucosa were intact. A panoramic radiograph showed a well-demarcated unilocular radiolucent lesion in the right mandibular corpus (Fig. 1). The lesion resulted in significant bony expansion and root resorption of the first molar. Additionally, the second molar was impacted and the developing third molar displaced. The clinical suspicion was that of an ameloblastoma. An incision biopsy was performed and submitted for histological assessment.

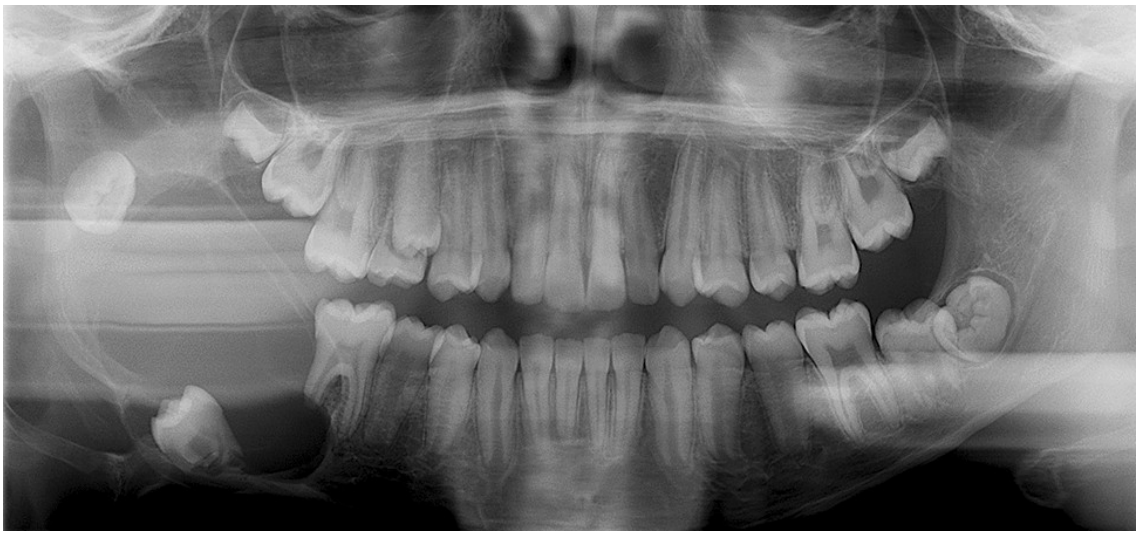

Fig. 1 Panoramic radiograph at first presentation. Unilocular radiolucent lesion in the right mandibular corpus with associated root resorption of the right first molar and displacement of the second and third molar teeth. No overt internal calcifications were noted

Histopathological evaluation showed a benign odontogenic cystic lesion lined by an ameloblastomatous-type epithelium with numerous superficial ghost cells, which in areas underwent dystrophic calcification (Fig. 2). The wall of the cyst consisted of dense fibrous connective tissue with a mild mixed chronic inflammatory cell infiltrate and scattered inactive odontogenic epithelial islands. No solid areas with increased cellularity and cytological atypical were identified at this stage.

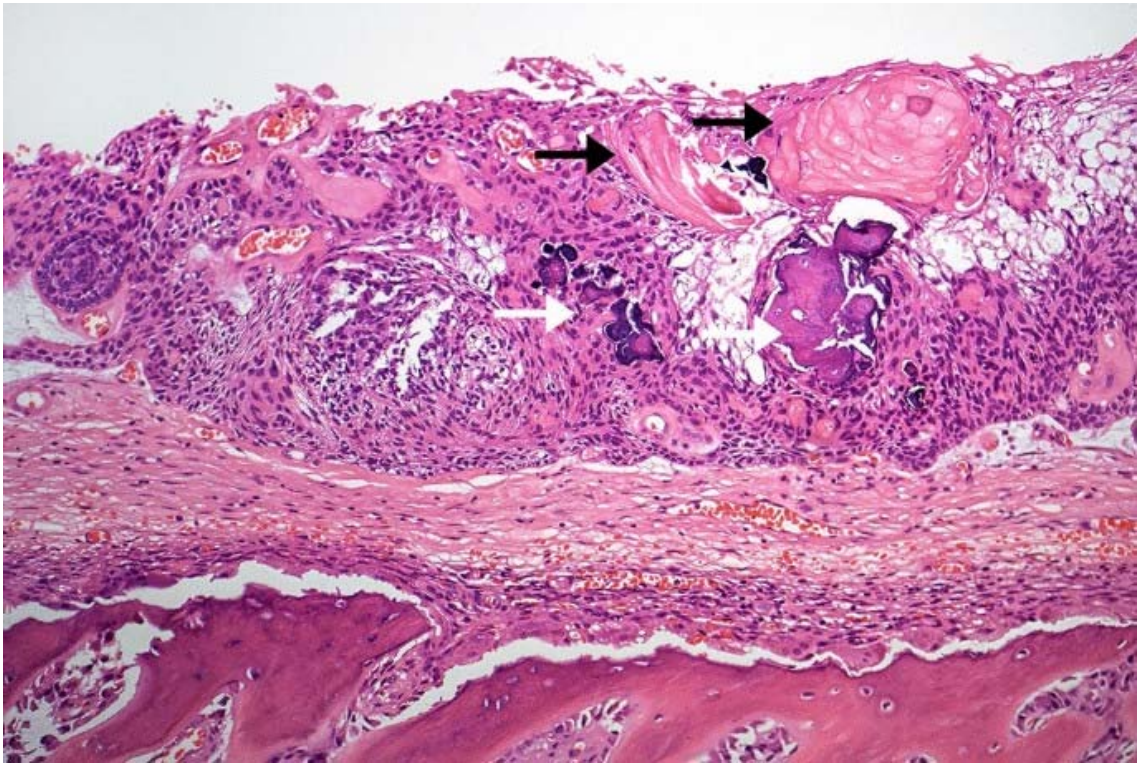

Fig. 2 Biopsy at first presentation. Hematoxylin and eosin (H&E)-stained section showing a cystic lesion lined by an ameloblastomatous-type epithelium with numerous superficial ghost cells (black arrow) undergoing dystrophic calcification (white arrow) (original magnification x 100

Following the histopathological diagnosis, a cone-beam computerised tomography (CBCT) scan was performed for surgical planning. CBCT imaging revealed a well-demarcated lesion with cystic and solid soft tissue-filled areas measuring 4.8 cm in greatest dimension (Fig. 3A-D). The lesion appeared unilocular with scalloped borders. Coronal (Fig. 3A) and axial (Fig. 3C) slices revealed significant bucco-lingual expansion and cortical thinning. Small calcifications, which were unseen on the panoramic radiograph, were identified. At this stage, the patient was unfortunately lost to follow-up, despite numerous telephonic attempts.

Three years later the patient returned with radiographic evidence of significant progression of the lesion. The margins appeared more irregular, with increased expansion. The lesion extended anteriorly, resulting in additional root resorption of the right second premolar. At this time, varying amounts of internal calcifications could be visualised on the panoramic radiograph (Fig. 4). CBCT imaging revealed a soft tissue lesion with internal calcifications (Fig. 5A-F). Increased bony expansion was notable, with the lesion now measuring 9.1 cm in greatest dimension. In addition, areas of cortical disruption were visible (Fig. 5C&F). A wide surgical resection was performed (Fig. 6A&B) and submitted for histological assessment.

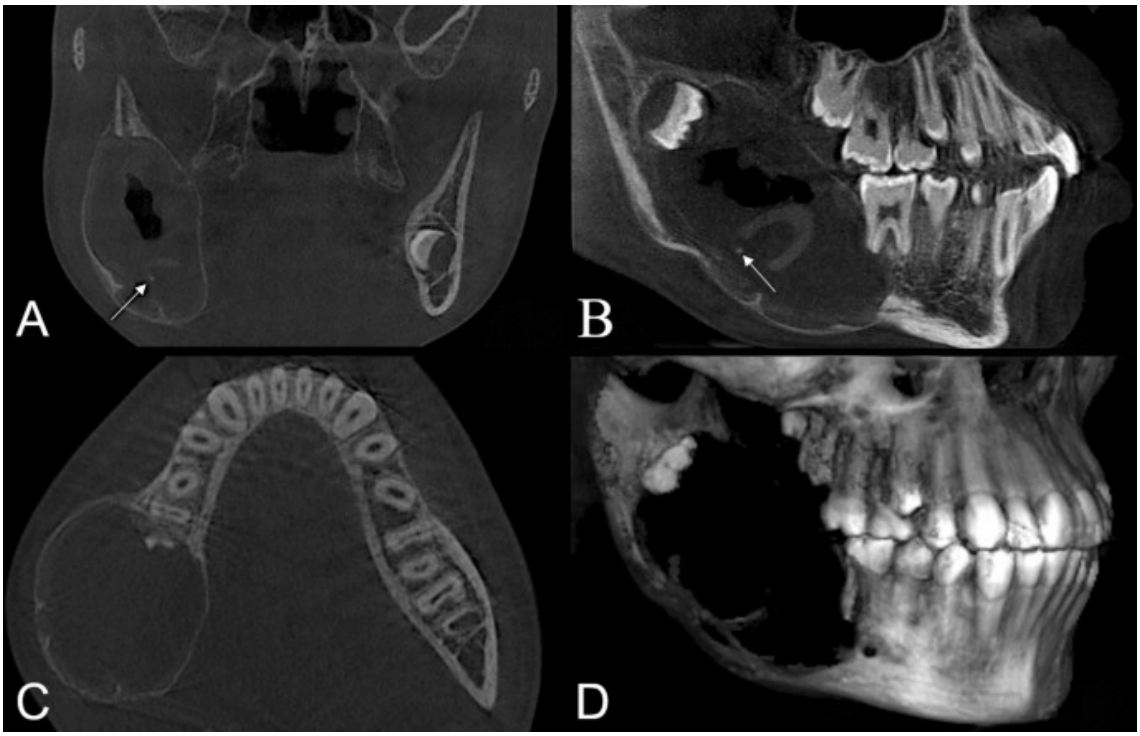

Fig. 3 Coronal (A), sagittal (B), axial (C) and three-dimensional reconstructed (D) CBCT images showing a well-demarcated lesion with cystic and solid areas. Small internal calcifications were noted (arrow)

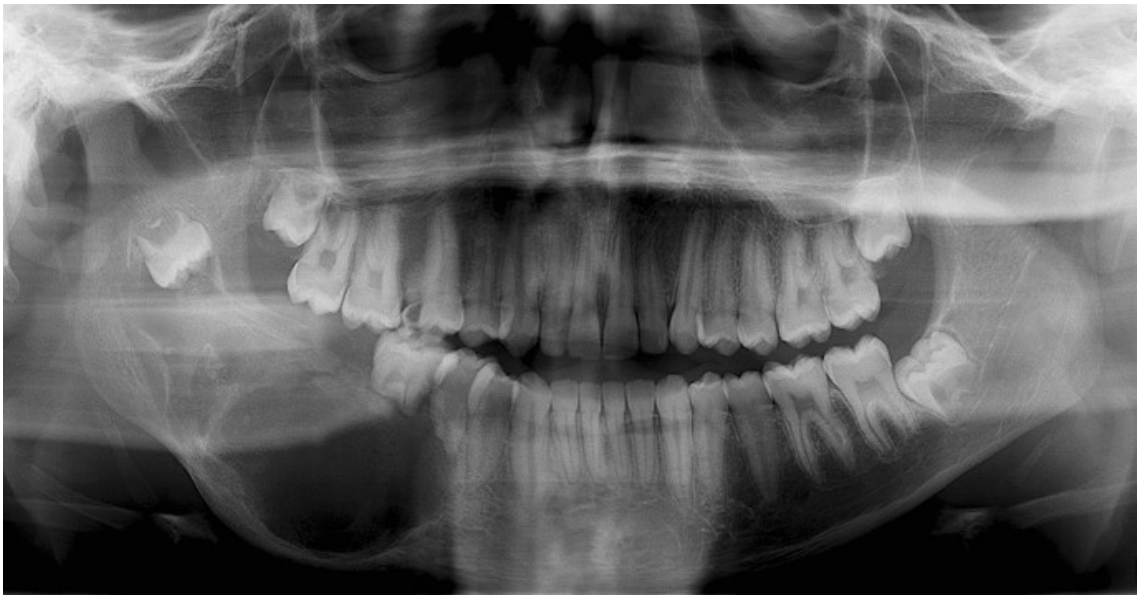

Fig. 4 Panoramic radiograph after 3 years. Anterior extension of the lesion with additional root resorption of the second premolar and scattered internal calcifications

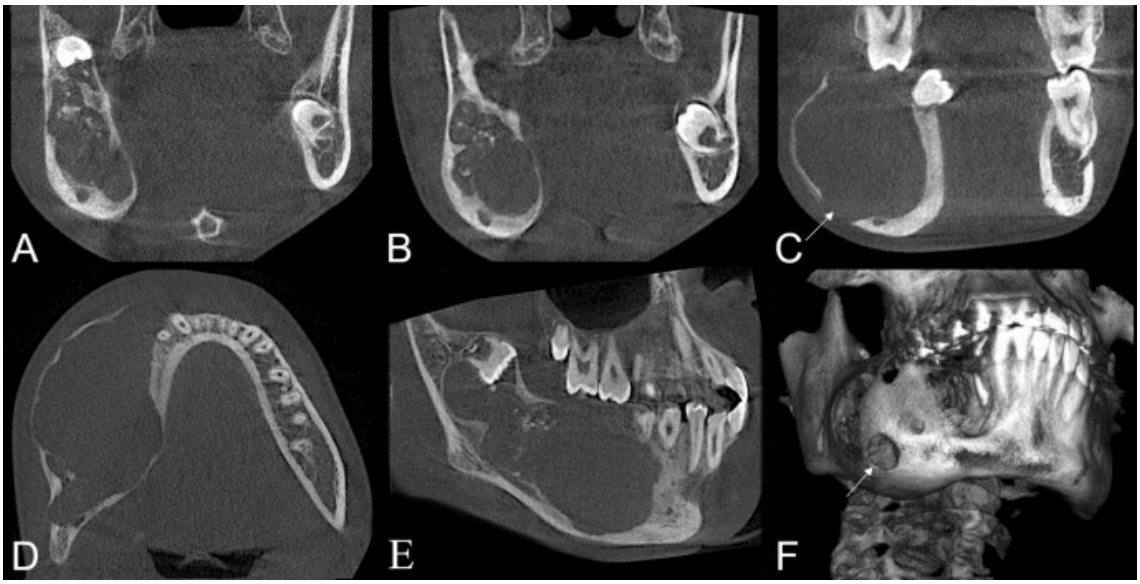

Fig. 5 Coronal (A, B and C), axial (D), sagittal (E) and three-dimensional reconstructed (F) CBCT images after 3 years showing a soft tissue lesion with internal calcifications. The tumour showed increased expansion with cortical disruption (arrow)

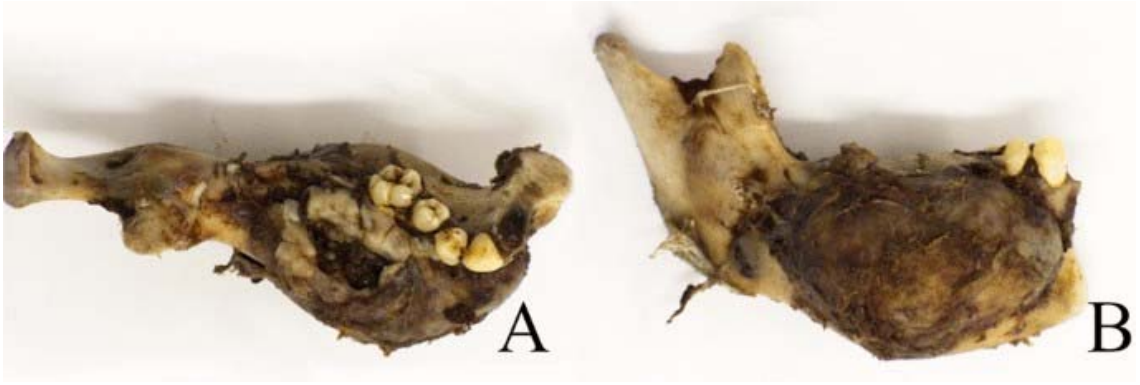

Fig. 6 Superior (A) and lateral view (B) of the resection specimen

Histological evaluation of sections taken from the main tumour showed a malignant odontogenic carcinoma. This tumour consisted of sheets and cords separated by thin bands of fibrous connective tissue (Fig. 7A). Small tumour islands infiltrated the surrounding fibrous connective tissue. The tumour cells showed a moderate amount of eosinophilic cytoplasm with hyperchromatic nuclei and discernible nucleoli. Prominent nuclear pleomorphism and abundant mitotic figures were identified (Fig 7B). Focal islands of ghost cells (Fig. 7C) and dentinoid material were seen throughout the tumour. There was no definitive evidence of perineural or lymphovascular invasion. A Ki-67 immunohistochemical stain showed a high proliferation index of approximately 40% (Fig. 7D). The tumour appeared to be completely excised at all surgical margins.

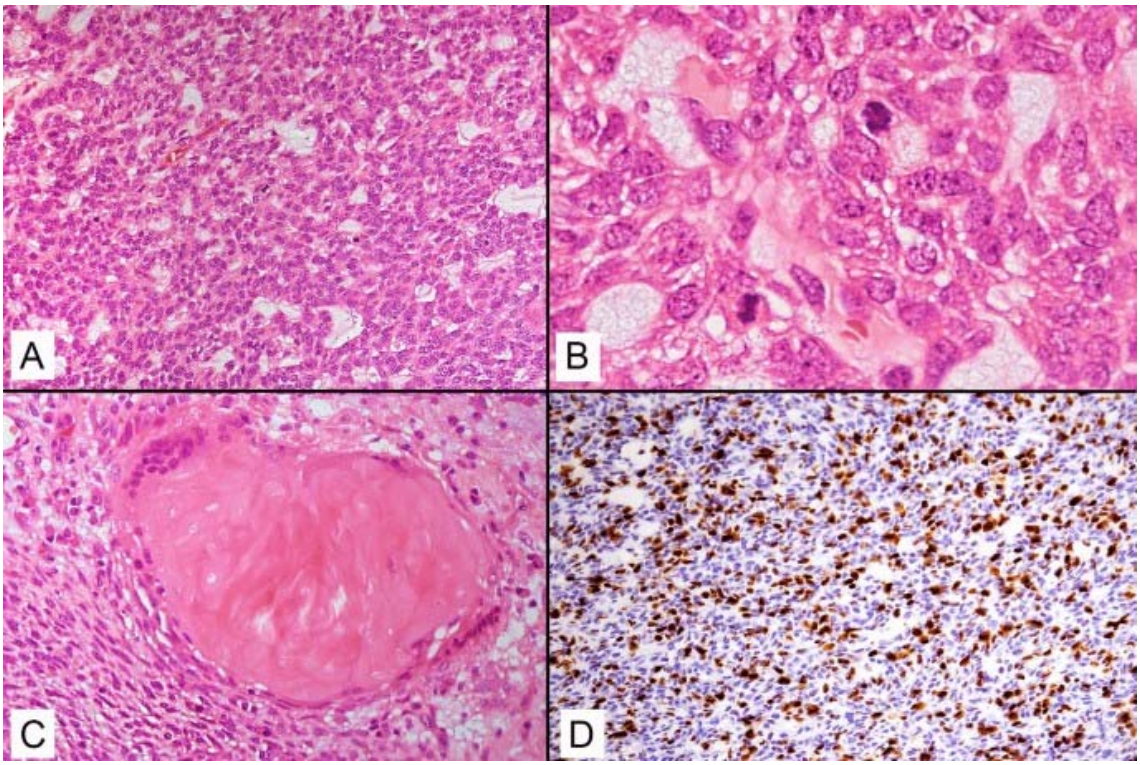

Fig. 7 Histology of main tumour from resection specimen. H&E-stained section (A) showing a malignant odontogenic tumour consisting of sheets of neoplastic cells with prominent nuclear pleomorphism (original magnification x 200), abundant mitotic figures (B) (original magnification x 300), focal islands of ghost cells (C) (original magnification x 200), and a high proliferation index of 40% via Ki-67 immunohistochemical staining (D) (original magnification x 200)

Post-operative healing was uneventful and one-year follow-up revealed no clinical signs of recurrence.

DISCUSSION

Calcifying odontogenic cysts account for less than 2% of all central odontogenic entities, [6] but represent 90% of ghost cell lesions of the jaws [1,3]. COCs usually present during the second and third decades of life with an almost equal gender distribution (1.2:1 male to female ratio) [3,7,8]. Some authors have however reported a significant male predominance [9,10]. These cysts have a slight predilection for the maxilla (59%) over the mandible (41%) [3,7,8]. The maxillary anterior and mandibular posterior regions are the most commonly affected sites [3,7]. The main clinical finding is swelling in the affected region of varying durations, ranging from 6 months to 28 years [3,7].

Radiographically, COCs present as well-defined unilocular radiolucent lesions with varying degrees and frequencies of internal calcifications [3,7–9]. CBCT imaging has higher sensitivity in detecting

calcifications compared to panoramic radiography [11], as evidenced in the current case. This may be due to the calcifications being situated outside of the focal trough. On average COCs reach a size of 3.7 cm with bone expansion being a common feature [3,7]. They are often seen in association with impacted teeth and usually show accompanying root resorption [3,7,9]. Both of these features were noted in the initial presentation of the current case. Rare multilocular variants [7,9], bilateral COCs [3] and lesions exhibiting cortical perforation have also been reported [7,9,11]. The mainstay surgical treatment of enucleation usually yields no recurrences [8]. In contrast, some authors have reported a recurrence rate of 5.3%, however limited information on the treatment approach was provided. Although rare, the malignant transformation rate of COCs is approximately 0.9% [3].

Ghost cell odontogenic carcinomas are rare, representing less than 3% of all ghost cell lesions of the jaws [3]. They tend to occur later in life than both COCs and DGCTs and show a strong male predilection [3,12–14]. The current case represents the rare occurrence of a GCOC affecting a young individual, however cases have been reported in individuals as young as 13 years of age [4]. Some studies indicate an equal maxilla-to-mandible distribution, whilst others report a maxillary predominance [2–4,12,13]. Cases described in the mandible typically occurred in the molar region [12]. The main clinical features include swelling, pain and rapid growth [3,13,15]. Symptoms suggestive of malignancy, including paraesthesia and ulceration, are reported in varying frequencies [2,4,13].

GCOCs typically show radiographic signs of an aggressive lesion including poorly-defined margins, bony erosion, cortical destruction, root resorption and soft tissue extension [13–16]. Generally the tumour is larger than both COCs and DGCTs, with an average dimension of 6.8 cm [3]. The current case reached a size of 9.1 cm in greatest diameter. Well-defined margins have also been described in a significant number of cases [14]. Maxillary lesions often result in destruction and obliteration of the maxillary sinus [13]. Radiolucent and mixed radiolucent-radiopaque lesions have been reported in equal frequencies [12]. Other authors have noted that pure radiolucent lesions are uncommon [13]. Moreover, a systematic review reported a mixed radiolucent-radiopaque radiographic appearance in approximately 80% of cases [4,13]. These tumours can present with both solid and cystic areas on computerised tomographic (CT) imaging [15]. This can be explained by some lesions having a more solid component caused by intraluminal epithelial proliferation, containing keratinised ghost cells [7]. Furthermore, CT/CBCT imaging better indicates internal calcifications, with magnetic resonance imaging (MRI) studies indicating soft tissue extension/infiltration [9,11,15,17].

GCOC can arise from a benign counterpart (either COC or DGCT) or arise *de novo* [3]. Most cases seem to occur *de novo* [4,12], with approximately 30% of cases reportedly arising from a COC [3,8,14,18–21]. A systematic review of the literature found 12 cases of GCOC arising from a pre-

existing COC[14]. Rarely, GCOC may arise from a pre-existing DGCT. This was reported in a case where a GCOC developed from a DGCT after seventeen years and three recurrences [22]. The biological behaviour of these neoplasms is difficult to predict due to limited case reports. The majority of cases reported a poor clinical outcome with local recurrences, with isolated cases having intracranial extension or distant metastasis [4,13,14]. Radical resection with adequate margins and long term follow-up is the recommended treatment [22]. The adjunct of advanced imaging, especially three-dimensional reconstructions, may assist in surgical planning to avoid secondary surgical procedures [16]. Recurrence has been seen in a significant number of cases, however, the treatment approach was not described [13,14].

In conclusion, the current case documents a GCOC arising from a pre-existing COC after three years in a young adolescent male. This case is unique in that it occurred in a relatively young individual with a rapid biological course to malignancy. The case was treated successfully with wide surgical excision and the patient subjected to regular follow-up visits.

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