

Ghost cell odontogenic carcinoma: A case report

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ABSTRACT

Ghost cell odontogenic carcinoma (GCOC) is a rare malignant neoplasm characterized by the presence of ghost cells. It is considered to originate from either a calcifying odontogenic cyst (COC) or a dentinogenic ghost cell tumor (DGCT). Its clinical and radiographic characteristics are non-specific, including slow growth, locally aggressive behavior, and eventual metastasis. This case report describes a 43-year-old Thai man with plain radiographs and cone-beam computed tomographic images revealing a unilocular radiolucency with non-corticated borders surrounding an impacted left canine associated with radiopaque foci around the cusp tip. Based on the microscopic findings, the lesion was diagnosed as GCOC. Partial maxillectomy of the right maxilla was performed, and radiotherapy was administered. An obturator was made to support masticatory functions. Three years later, the lesion showed complete bone remodeling and no signs of recurrence, and long-term follow-up was done regularly. (*Imaging Sci Dent* 2021; 51: 203-8)

KEY WORDS: Odontogenic Cysts; Odontogenic Tumors; Diagnostic Imaging; Cone-Beam Computed Tomography

A classification of odontogenic ghost cell lesions of the jaws was established, with an emphasis on the origin and nature of these lesions and their microscopic characteristics, including calcifying odontogenic cyst (COC), dentinogenic ghost cell tumor (DGCT), and ghost cell odontogenic carcinoma (GCOC).¹ The term “ghost cells” to describe odontogenic ghost cell lesions of the jaws was introduced in 1946 by Thoma and Goldman.² These 3 types of tumors manifest diverse non-specific clinical and radiographic features, making their diagnosis challenging. In 2005, The World Health Organization (WHO) referred COC as a calcifying cystic odontogenic tumor (CCOT) and CCOT was redefined as COC, a developmental cyst in the new WHO classification in 2017.³ DGCT was classified as a neoplastic variant of COC based on its solid growth pattern. Due to its tendency to show aggressive growth, GCOC was classified as the

malignant counterpart of COC and DGCT.⁴ The most frequently occurring odontogenic ghost cell lesion is the cystic pattern of COC, which accounts for about 1%-2% of all odontogenic tumors.^{1,5} DGCT and GCOC rarely occur, especially GCOC, which is an exceptionally rare malignant odontogenic tumor. Approximately 50 cases of GCOC have been described since it was first reported.⁷ The first case of GCOC was documented in 1985 by Ikemura et al.⁶ This tumor originated from a typical COC in which malignant transformation occurred simultaneously in the maxilla. GCOC is characterized by an intra-osseous location, with an occurrence of approximately 7% in the head and neck region, and accounts for about 0.37% of all odontogenic tumors in the oral cavity.^{4,6} GCOC occurs most commonly in the maxillary bone, which accounts for 67% of cases, at a mean age of 40 years, with a 2 : 1 male predominance, and has a tendency to affect patients of Asian descent disproportionately.^{1,8} The imaging findings of GCOC present a mixed radiolucent and radiopaque pattern more frequently than a radiolucent pattern. Furthermore, 90% show poorly defined borders, unlike

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Fig. 1. A panoramic radiograph demonstrates a large, poorly demarcated, mixed radiopaque-radiolucent lesion, and unclear boundaries of the left nasal cavity and maxillary sinus. An embedded upper left canine tooth with numerous radiopaque components is present within the lesion.

COC and DGCT, which have well-defined borders.⁹ Pathologically, GCOC was reported to arise *de novo* in most cases (55%), followed by through a malignant transformation of COC and DGCT (32.5%) or ameloblastoma and other odontogenic tumors (7.5%).¹⁰ The ability of COC or DGCT to transform into the malignant variant has been linked to levels of Ki-67 and matrix metalloproteinase 9 expression, which is associated with the proliferation, invasion, and prognosis of GCOC.¹⁰ The recommended treatment for GCOC is wide surgical excision with clean margins. No research to date has been able to draw definitive conclusions regarding the effectiveness of adjunctive radiotherapy with or without chemotherapy due to the rarity of this tumor.^{7,11} The recurrence rate is higher in the maxilla (44%) than in the mandible (38.5%); the 5-year survival rate has been reported to be about 73%, and distant metastasis is rare, with only 4 reported cases of pulmonary and cranial metastases.¹² This report presents a rare case of GCOC in the left maxilla of a 43-year-old Thai male patient and describes its clinicopathological features, radiological findings, and the treatment that was performed.

Case Report

A 43-year-old Thai man, who had experienced sensitivity over the left ala of his nose for 2 months, visited the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University, Thailand. The patient reported extraction of an upper left deciduous canine tooth at a private clinic 2 months previously. After extraction, the swelling progressed without reduction for about 1 month. He visited the private clinic again and periapical radiography was performed, which showed an embedded upper left permanent canine, including small radiopaque foci inferiorly.

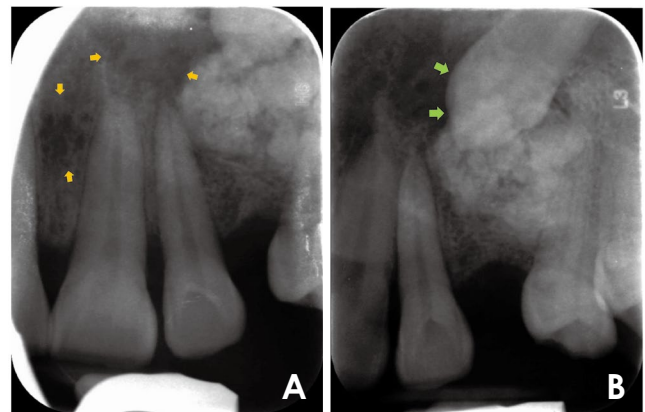


Fig. 2. A. A periapical radiograph demonstrates abnormal trabecular architecture in the apical region and mesial aspect of the upper left incisors (arrows). B. Tooth-like structures surrounded with thin radiolucent rims are present between the apical area of the upper left lateral incisor and first premolar. The dental follicle of the embedded tooth is missing (arrows).

An extraoral examination revealed mild swelling of the left cheek with disappearance of the nasolabial fold. An intraoral examination revealed unremarkable changes in the overlying gingiva and mild swelling of the buccal vestibular area from the left maxillary central incisor to the left maxillary first premolar. The lesion appeared as a soft consistency on palpation at the palatal aspect of the left maxillary canine, which clinically absent. The electrical pulp testing was performed and showed non-vital teeth at the left maxillary central incisor and lateral incisor. Panoramic radiography revealed a unilocular radiolucent lesion surrounding the embedded tooth associated with a small number of non-homogeneous radiopaque components, indistinct boundaries, and diverse roots of the left maxillary lateral incisor and left maxillary first premolar teeth (Fig. 1). The periapical radiographs

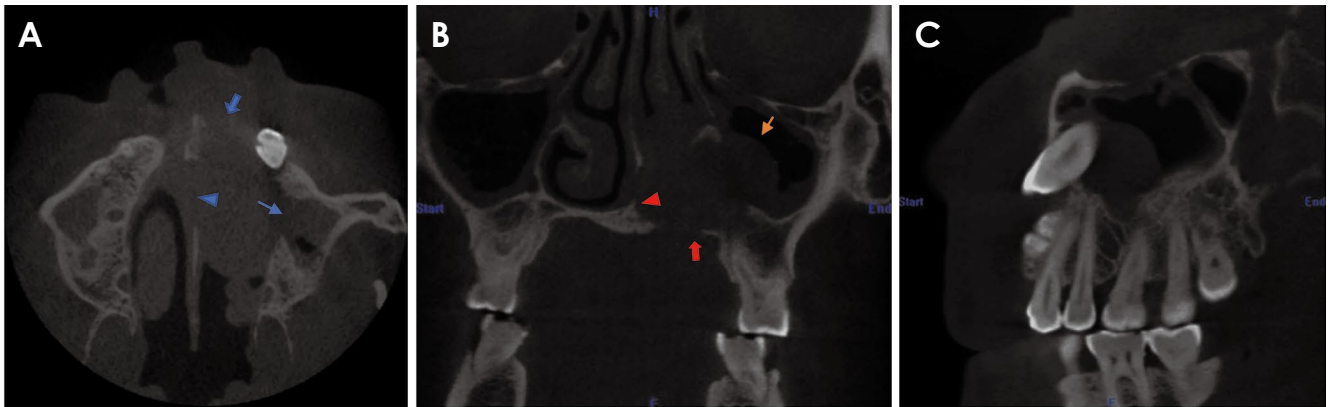


Fig. 3. A. An axial cone-beam computed tomographic image demonstrates the involvement of many structures, such as the incisive foramen, nasal septum, nasal cavities, the lateral wall of the left nasal cavity, and the medial wall of the left maxillary sinus. The image depicts perforation of the labial plate/medial wall of the maxillary sinus and the lateral wall of the nasal cavity (arrows). B. A coronal cone-beam computed tomographic image demonstrates involvement of the left inferior turbinate and nasal septum, causing nasal septum deviation to the right side. The image also depicts perforation of the palate, lateral nasal wall, and medial wall of the maxillary sinus (arrows). C. A sagittal cone-beam computed tomographic image demonstrating partial involvement of the lesion in the anterior part of left maxillary sinus associated with mucositis.

showed a normal apical root shape, without root resorption but with irregular widening of the periodontal ligament space surrounding the root of the lateral incisor. The findings were otherwise within normal limits. Diffuse radiolucent trabeculations were present at the area between the root of the central incisors and the apical region of the upper left central and lateral incisor. The follicle of the embedded tooth had disappeared. The small group of radiopaque components was surrounded with very thin radiolucent rims and presented an abnormal configuration of tooth-like structures (Fig. 2). The differential diagnosis included a benign odontogenic cyst or tumor with a concomitant infection, COC with odontoma, cystic odontoma with embedded tooth, or odontogenic carcinoma. Axial cone-beam computed tomographic (CBCT) images showed involvement of the incisive foramen and the left and right nasal cavities, from the anterior apertures to at least the anterior one-third of the right nasal cavity and anterior two-thirds of the left nasal cavity. Involvement of the anterior half of the nasal septum with mild right deviation was observed. The left lateral nasal wall, or medial wall of the left maxillary sinus, was involved. The lower part of the left nasolacrimal canal showed partial loss of cortication. Perforation of the labial plate was detected across the midline to the mesial aspect of the left maxillary second premolar (Fig. 3A). The coronal image presented involvement of an inverted Y region comprising the left lateral nasal wall and medial wall of the maxillary sinus. The anterior part of the left inferior and middle turbinates was involved, with obstruction of the left ostium.

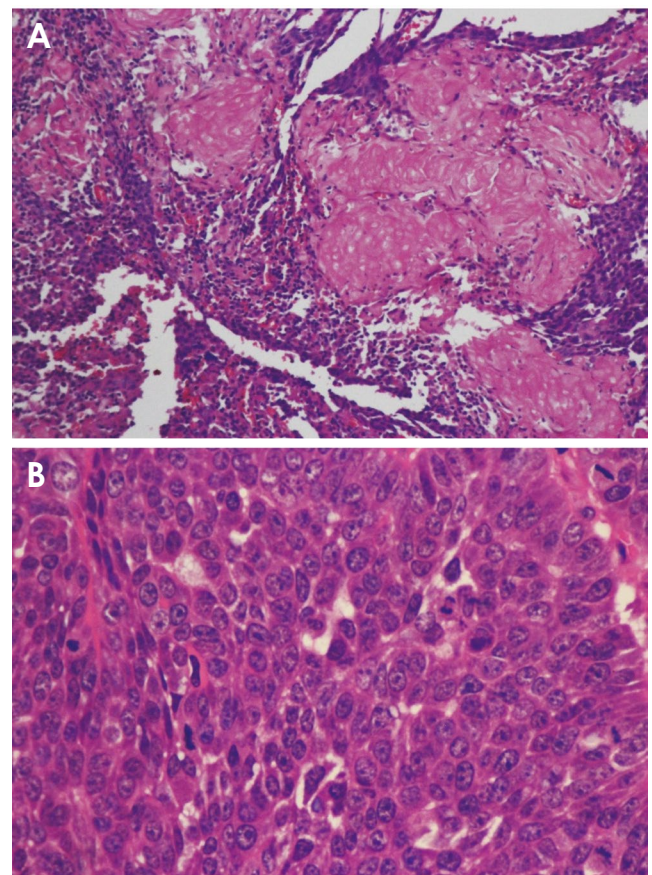


Fig. 4. A. The microscopic features in a low-power view demonstrate the cellularity of pleomorphic epithelial cells with hyperchromatic nucleuses and abundant ghost cells (H&E stain, $\times 40$). B. The microscopic features in a high-power view show prominent mitotic activity in pleomorphic epithelial cells (H&E stain, $\times 400$).

Some tooth-like structures were located between the root of upper left lateral incisor and the second premolar, with the embedded canine located superior-posteriorly. Perforation of the palatal region at the apical root level of the left lateral incisor to first molar area was observed (Fig. 3B). A sagittal image showed normal posterior and superior walls of the maxillary sinus. The lesion extended into the anterior half of the left maxillary sinus with generalized sinus mucosal thickening (Fig. 3C). An incisional biopsy was performed under local anesthesia from the labial surface of the left central incisor to the first premolar area. The entire specimen was sent for histopathological evaluation. The microscopic examination demonstrated abundant ghost cells, dentinoid materials, and pleomorphic epithelial cells with prominent mitotic figures as a result of GCOC (Fig. 4). The final diagnosis was determined to be GCOC. Partial maxillectomy was then performed under general anesthesia and histopathology was done once again to confirm the final diagnosis of GCOC. The lesion recurred 2 months later, and total excision was performed in conjunction with chemotherapy and radiotherapy. Six months after completion of the excision, radiotherapy, and prosthesis reconstruction, the patient showed no signs of recurrence. After 2 years of follow-up, the patient remained in a good condition without any signs of recurrence. Long-term periodic examinations of this patient were performed.

Discussion

The patient described herein did not have any symptoms associated with a long-standing impacted tooth composed of a group of tooth-like structures resembling compound odontoma. The disease may have originated from an odontogenic tumor (e.g., odontoma) or an impacted tooth that progressed into a malignant GCOC. An impacted tooth associated with odontoma is suggestive of long-standing benign COC, which showed slow growth and painless symptoms before transformation to GCOC. Alternatively, a tumor may develop from compound odontoma into a cystic odontoma before transformation. The clinical presentation of painful rapid growth after extraction is usually considered to correspond to an infection or a malignant lesion. Almost all case reports of GCOC arising from multiple recurrences of COC or DGCT describe painful rapid growth characteristics during GCOC transformation, although this process may be painless in the first phase.^{4,7,12} This patient presented with painful rapid growth similar to what was reported in a 21-year-old African man diagnosed with *de novo* GCOC.¹¹ However, transformations from benign ameloblastoma and

calcifying epithelial odontogenic tumor into GCOC usually involve a painless swelling.^{4,13} In the case described herein, the tumor was found in the maxillary bone, corresponding to most previous case reports.^{4,6,7,9,11,12} The age and sex of this patient were consistent with most previous cases, as GCOC has been reported to show a male predominance and a tendency to occur around 40 years of age.^{4,6,7,13}

In the maxillofacial region, conventional radiographs are usually performed in the initial work-up. The disadvantage of conventional radiographs is the superimposition of images with several anatomical structures, which often causes difficulties in interpreting the extension of a lesion, its borders, and the involvement of surrounding structures. The conventional radiographs in this case demonstrated a mixed radiolucent-radiopaque lesion similar to almost all previous cases reported.^{4,6,7,11-13} The presence of an ill-defined border with altered trabecular architecture is carefully considered as indicative of an unusual lesion resulting from infection or malignancy.¹⁴ Atypical borders from conventional radiographs necessitate advanced imaging to provide additional information on lesion extension. CBCT is an advanced imaging modality that provides high-quality 3-dimensional image information on the osseous involvement, extension, and destruction of lesions without superimposition. In lesions with poorly defined borders or wide extension, it is necessary to identify the borders of extension to develop an appropriate treatment and management plan.^{9,15,16} Magnetic resonance imaging (MRI) has been recommended as a way to distinguish soft-tissue borders in tumors that spread to adjacent structures, with substantial benefits for denoting the soft-tissue margin and staging of the tumor mass.^{12,15,16} In this case, CBCT was used to evaluate osseous involvement without MRI to distinguish the soft-tissue borders. The recurrence 2 months after surgery may have been due to the presence of some remnant tumor in the soft-tissue borders that could not be seen on CBCT. Positron emission tomography (PET) combined with computed tomography is useful for evaluating organ metastasis, and oral cancers usually metastasize to the cervical lymph nodes and lung.¹⁵ In this case, a PET scan was taken upon recurrence, and showed no metastasis to the lung or other structures.

The 2017 WHO classification of head and neck tumors divided odontogenic carcinomas into 5 distinct entities, including ameloblastic carcinoma, primary intraosseous carcinoma, sclerosing odontogenic carcinoma, clear cell odontogenic carcinoma, and ghost cell odontogenic carcinoma.¹⁷ Among these tumors, ameloblastic carcinoma is the main histopathological differential diagnosis of ghost cell odontogenic carcinoma. Both types of tumors microscopically

show an infiltrative proliferation of malignant odontogenic epithelial cells. The principal distinction is that ameloblastic carcinoma usually shows features of ameloblastic differentiation, such as peripheral nuclear palisading with reversed polarity and basal vacuolization, whereas GCOC frequently displays a varying amount of characteristic ghost cell keratinization within the epithelial component and juxtaepithelial dentinoid formation. GCOC is considered to be the malignant counterpart of DGCT. Both lesions demonstrate some parallel microscopic features; however, benign DGCT uniformly exhibits bland cytologic features with sparse mitoses. In the present case, the odontogenic epithelial component showed marked cellular and nuclear pleomorphism, hyperchromasia, brisk mitotic activity, necrosis, and angioinvasion, all of which are apparent features of malignancy. These anaplastic changes together with the presence of widely dispersed ghost cells and dentinoid material throughout the tumor supported the definitive diagnosis of GCOC. Furthermore, a thorough microscopic examination identified no evidence of DGCT or COC as a potential precursor lesion. These findings suggest that the case described herein may have arisen *de novo*, similar to most previously reported cases of GCOC.^{1,18}

The treatment of GCOC recommended in most previous studies is wide surgical resection with clear margins.^{4,7,8,11,13} Wide surgical excision with clean margins is the treatment of choice although its combination with postoperative radiation therapy, with or without chemotherapy, remains controversial.¹² Two previous cases of GCOC treatment by adjuvant radiotherapy and chemotherapy were described. The first case was a 70-year-old elderly woman who had a tumor infiltrating the second trigeminal branch; due to the difficulty that this location posed for surgery, adjuvant radiotherapy was administered.¹² The other case was a 48-year-old man in whom the tumor spread into the ethmoid and frontal sinus, and adjuvant radiotherapy and chemotherapy were administered.⁶ This case received wide surgical resection as the initial treatment. The tumor recurred 2 months after surgery and the microscopic examination revealed the involvement of tumor cells in the roof of the left maxillary sinus by means of the floor and orbit. Adjuvant radiotherapy and chemotherapy were performed because the tumor involved vital structures. The natural history of GCOC is unpredictable, as it may range from slow progression to rapid destructive growth, with highly local aggressive characteristics, recurrence, and occasional distant metastases; therefore, substantial long-term follow-up is strongly recommended.

Conflicts of Interest: None

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