

Journal section: *Oral Medicine and Pathology*
 Publication Types: *Case Report*

doi:10.4317/jced.51809
<http://dx.doi.org/10.4317/jced.51809>

Ghost cell odontogenic carcinoma: A rare case report and review of literature

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Martos-Fernández M, Alberola-Ferranti M, Hueto-Madrid JA, Bescós-Atín C. Ghost cell odontogenic carcinoma: A rare case report and review of literature. J Clin Exp Dent. 2014;6(5):e602-6.
<http://www.medicinaoral.com/odo/volumenes/v6i5/jcedv6i5p602.pdf>

Received: 23/06/2014
 Accepted: 12/08/2014

Article Number: 51809 <http://www.medicinaoral.com/odo/indice.htm>
 © Medicina Oral S. L. C.I.F. B 96689336 - eISSN: 1989-5488
 eMail: jced@jced.es
Indexed in:
 Pubmed
 Pubmed Central® (PMC)
 Scopus
 DOI® System

Abstract

Objectives: Ghost cell odontogenic carcinoma is a rare condition characterized by ameloblastic-like islands of epithelial cells with aberrant keratinization in the form of Ghost cell with varying amounts of dysplastic dentina.

Material and Methods: We report a case of a 70 year-old woman with a rapid onset of painful swelling right maxillary tumor. Magnetic resonance showed a huge tumor dependent on the right half of the right hard palate with invasion of the pterygoid process and focally to the second branch of the trigeminal. Radiological stage was T4N0. The patient underwent a right subtotal maxillectomy with clear margins. Adjuvant radiotherapy was given. The patient was free of residual or recurrent disease 12 months after surgery.

Results: The tumor was 3,9cm in diameter. It was spongy and whitish gray. Microscopically the tumor was arranged in nets and trabeculae, occasionally forming palisade. Tumoral cells had clear cytoplasm with vesicular nuclei. There was atypia and mitosi with vascular and perineural invasion. The excised tumor was diagnosed as a GCOC.

Conclusions: Ghost cell carcinoma is a rare odontogenic carcinoma. Its course is unpredictable, ranging from locally invasive tumors of slow growth to highly aggressive and infiltrative ones. Wide surgical excision with clean margins is the treatment of choice although its combination with postoperative radiation therapy, with or without chemotherapy, remains controversial.

Key words: *Ameloblastic carcinoma, calcifying odontogenic cyst, Ghost cell carcinoma, keratinizing epithelial odontogenic cyst, maxillary tumor, odontogenic carcinoma.*

Introduction

Ghost cell odontogenic carcinoma [GCOC] is a rare malignant odontogenic epithelial tumor with features of calcifying odontogenic cysts that can arise as a de novo tumor or from a previously existing calcifying cystic odontogenic tumor [CCOT] or dentinogenic ghost cell tumor [DGCT] after multiple recurrences (1). Its occurrence constituting about 0,37% to 2.1% of all odontogenic tumors (2). The GCOC was first described by Gorlin *et al.* in 1962 as a distinct pathological entity (3). Since then there have been approximately 30 cases reported in the literature to date. In 2005 The World Health Organization [WHO] classified them under the category of odontogenic tumours (4). The most characteristic histological feature is the presence of ghost cells, epithelial cells that have lost their nuclei leaving only a faint outline of the original nuclei. The presence of ghost cells is not a specific feature, they could be seen in others tumors such as pilomatricoma, craniopharyngioma, odontoma and ameloblastic fibro-odontoma (2).

This article reports a new case of GCOC in the right maxilla in a 70 year-old woman and describe its clinico-pathological features, radiological images and treatment performed.

Material and Methods

A 70 years old woman was referred by her dentist to our Oral and Maxillofacial Surgery Department at Vall d'Hebron Hospital in August 2013. She reported pain and rapid expansion of a mass located on the alveolar buccal surface of the right maxilla during the previous three weeks. She denied any clinical symptoms or lesions prior to this episode. No neurological deficit was referred to. The patient explained that initially was treated with Amoxiciline-Clavulanic acid 875mg/8h during one week due to the suspicious of periapical abscess but no improvement was shown.

The patient was in good health. Extraoral examination did not show any pathological signs. The overlying skin was smooth and normal. No ulceration was observed. Enlarged cervical lymph nodes were not found on physical examination. Intraoral examination showed an expansive non-fluctuant mass of 5cm in the right maxilla with palatine protrusion involving the second premolar and first molar which presented mobility (Fig. 1).

- Complementary Tests:

A complete blood test was performed but no alterations were found. Chest x-ray showed no evidence of distant metastasis. Intraoral incisional biopsy was done under local anesthetic and the tissue was submitted to the Department of Oral Pathology. The first histopathological examination showed an infiltration by morphologically suggesting carcinoma ameloblastic lesion.

The radiographic study also included an ortopantomograph and magnetic resonance imaging [MRI]. Panora-

mic radiograph demonstrated a large, poorly demarcated mixed radiopaque-radiolucent lesion with destruction of the buccal and palatine cortical plates associated with 15 and 16 root resorption without crossing the midline. MRI showed a huge expansive tumor committed to the right half of the palate and alveolar ridge side, but without reaching the midline. This lesion located at the level of molar area of the alveolar ridge was infiltrating the pterygoid process and invading the right nostril and the maxillary sinus. There was a tooth [first molar] included in the lump and also partially including the second premolar. It reached a maximum diameter of 40 x 32 x 34 mm. There seemed to be focally produced infiltration of the second trigeminal branch. No other changes in the elements of the oral cavity or significantly enlarged lymph nodes were observed. Radiological stage was informed as T4N0 (Fig. 1).



Fig. 1. Clinical and MRI examination. a) Intraoral photograph showed an expansive non-fluctuant mass, ovoid in shape, on the right maxilla with palatine protrusion including 2nd premolar and 1st molar. Overlying mucosa was intact. b) MRI T1 before operation. Axial plane shows the tumor's extension through the right side of the palate involving 2nd premolar and 1st molar without reaching the midline. The mass showed variable densities and bony erosion of the maxilla.

- Treatment:

Based on these clinical findings surgical resection was decided under the diagnosis of ameloblastic carcinoma. The tumor was resected under general anesthesia with nasotracheal intubation by Weber-Ferguson approach without infraorbital incision extension (Fig. 2). An extended maxillectomy was performed from the maxillary tuberosity to the superior lateral incisor and the tumor was excised with clear margins. The defect left by the tumor was reconstructed with a temporal rotation flap over an osteosynthesis plate collocated in right maxillary region (Fig. 2). Bone cement was placed in the temporal fossa due to enhance the aesthetic results. Adjuvant radiotherapy treatment after surgery was performed during November 2013 [total cumulative dose: 52 Gy], and the patient was followed up for 12 months with no evidence of recurrence or distant metastasis.

Entire specimen was sent for histopathological evaluation. The sample measured 5.8 x 5.4 x 4cm in total and included palate and maxillary sinus floor (Fig. 3). The final

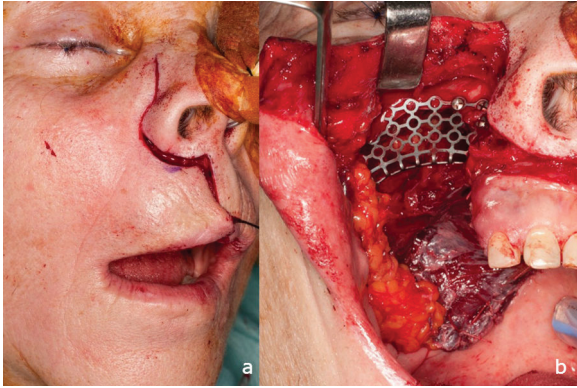


Fig. 2. Tumor resection. a) Weber-Ferguson approach without infraorbital extension was performed. b) Right subtotal maxillectomy was conducted to achieve total tumor resection with clean margins. The defect was reconstructed with a Temporal rotation flap above an osteosynthesis plate in the right maxillary region to achieve greater malar projection.

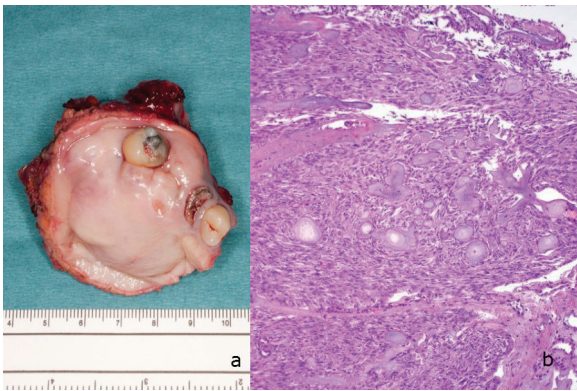


Fig.3. Pathological study. a) The total measurements of the sample sent for histopathological evaluation were 5.8 x 5.4 x 4cm and included palate and maxillary sinus floor. b) Photomicrograph of ameloblastic like islands and Ghost cells with odontogenic epithelium (H&Ex100).

outcome of the pathological study informed of a tumor lesion that consisted of a proliferation of cells with clear cytoplasm and vesicular nuclei, of ameloblastic appearance, which are arranged in large and irregular nests, with some peripheral lurch. Other smaller nests, hyperchromatic cells and atypia and mitosis were observed. Anucleated eosinophilic aggregates [Ghost cells] were trapped in the epithelium with concentric laminated structures and calcification (Fig. 3). The neoplastic cellularity of bone infiltrates palate and maxillary sinus floor. Neither the squamous surface of the palate nor the alveolar gingival epithelium was affected. Presence of perineural and vascular permeability was observed. In our case the diagnosis of GCOC was possible only after the resected specimen was carefully examined histologically.

Discussion

GCOC is a rare malignant odontogenic tumor that although it can appear as “de novo” the most probable

mechanism of development is a malignant transformation after multiple recurrences of a preexisting CCOT or other odontogenic tumor (5-7). Occasionally, some cases of Ameloblastoma associated with GCOC have been reported (8). According to the 2005 World Health Organization guidelines (4), GCOC is usually diagnosed on the basis of atypical histological features, groups of ghost cells, necrosis, prominent mitoses, infiltrative growth pattern, aggressive behavior, and high expression of Ki-67 and p53 (5). Several investigations show a high ki-67 and p53 expression in GCOC and a low one in CCOT (9-14). Nevertheless, further research is required to determine if these biomarkers of cell proliferation activity can be used to determine more probabilities of malignant transformation or high recurrence rate. The main differential diagnosis is ameloblastic carcinoma and the identification of Ghost Cell is the clue to diagnosis of Ghost cell odontogenic carcinoma.

Numerous names have been used to describe GCOC due to its diverse histopathologic characteristics. This tumor has been described as malignant CCOT, odontogenic ghost cell carcinoma, carcinoma arising in a CCOT, aggressive epithelial ghost cell odontogenic tumor, dentinogenic ghost cell ameloblastoma and malignant calcifying ghost cell odontogenic tumor. The odontogenic origin is widely accepted. The cells responsible for the CCOT are dental lamina remains within either the soft tissue or bone. Therefore, CCOT are cysts of primordial origin and are not associated with the crown of an impacted tooth (15). It most often occurs as an intraosseous lesion whereas peripheral extraosseous localization in the soft tissue is rare.

A review of the approximately 30 cases reported in the literature to date show that the average age is 40 years [13-72 years] with a male predominance, particularly in Asians (16,17). GCOC are more common in maxilla. It could cross the midline in the mandible but it is unusual in maxilla. The most common clinical presentation is a painful swelling with local paraesthesia associated with root resorption and/or tooth displacements. It may cause expansion of the mandible or maxilla. Its radiographic appearance is usually a mixed radiolucent and radiopaque pattern with different degrees of bone destruction and poorly defined [90%] rather than well-defined borders [11%] (18). Generally, its course is unpredictable, at times indolent and at others potentially fatal. Distant metastasis is extremely rare although to date 2 cases with pulmonary metastasis have been reported (16,19). The clinical features of previously reported GCOC and the present case are summarized in table 1.

The recommended treatment for GCOC is wide surgical excision. Postoperative adjuvant irradiation, with or without chemotherapy, is controversial and any standard treatment has been evaluated. The overall five-year survival rate has been reported to be approximately 73% although long-term follow-up is highly recommended after therapy due to its unpredictable course (1).

Table 1. Clinical features of reported cases of odontogenic ghost cell carcinoma.

Case	Author	Age/Gender	Race	Location	Follow-up
1	Gorlin <i>et al.</i> (3)	45/M	White	Mandibular	Local recurrence (death)
2	Ikemura <i>et al.</i> (20)	48/M	Asian	Maxillary	Intracranial extension(death)
3	Ellis and Shmookler (15)	55/F	Black	Mandibular	Local recurrence
4	Ellis and Shmookler (15)	17/M	N/A	Maxillary	Local recurrence
5	Ellis and Shmookler (15)	46/M	White	Maxillary	Local recurrence
6	Grodjesk <i>et al.</i> (19)	46/M	White	Maxillary	Distant metastasis (death)
7	Scott and Wood (21)	33/M	Black	Maxillary	Local recurrence
8	McCoy <i>et al.</i> (22)	13/F	Black	Maxillary	No recurrence
9	Dubiel-Bigaj <i>et al.</i> (23)	42/M	N/A	Maxillary	N/A
10	Siar and Ng (24)	39/M	Asian	Maxillary	Local recurrence
11	Alcalde <i>et al.</i> (25)	72/F	Asian	Maxillary	No recurrence
12	Folpe <i>et al.</i> (13)	20/M	N/A	Maxillary	Local recurrence
13	Lu <i>et al.</i> (17)	24/M	Asian	Maxillary	Local recurrence
14	Lu <i>et al.</i> (17)	31/F	Asian	Maxillary	No recurrence
15	Lu <i>et al.</i> (17)	19/M	Asian	Maxillary	Local recurrence (death)
16	Lu <i>et al.</i> (17)	39/M	Asian	Mandibular	Local recurrence
17	Kamijo <i>et al.</i> (26)	38/M	Asian	Maxillary	No recurrence
18	Kim <i>et al.</i> (18)	33/M	N/A	Mandibular	No recurrence
19	Li and Yu (27)	43/M	Asian	Maxillary	No recurrence
20	Cheng <i>et al.</i> (16)	36/M	Asian	Mandibular	Local recurrence
21	Cheng <i>et al.</i> (16)	35/M	Asian	Maxillary	Distant metastasis (death)
22	Cheng <i>et al.</i> (16)	33/M	Asian	Maxillary	Local recurrence
23	Cheng <i>et al.</i> (16)	44/M	Asian	Mandibular	Local recurrence
24	Goldenberg <i>et al.</i> (2)	36/M	Asian	Maxillary	Local recurrence
25	Sun <i>et al.</i> (28)	30/M	Asian	Maxillary	No recurrence
26	Roh <i>et al.</i> (10)	55/M	N/A	Mandibular	No recurrence
27	Slama <i>et al.</i> (29)	89/M	N/A	Manidbular	Local recurrence (death)
28	Li BH <i>et al.</i> (9)	47/M	Asian	Mandibular	Local recurrence
29	Zhu ZY <i>et al.</i> (11)	51/M	Asian	Maxillary	No recurrence
30	Arashiyama <i>et al.</i> (6)	68/M	Asian	Mandibular	No recurrence
31	Present Case	70/F	White	Maxillary	No recurrence

Abbreviation: NA, not available.

Conclusions

Ghost cell carcinoma is an uncommon odontogenic carcinoma. All reported cases demonstrated malignant histological features such as cellular pleomorphism, mitosis and necrosis with anucleated eosinophilic aggregates [ghost cells] in association with odontogenic epithelium. The biological behavior of GCOC is unpredictable, some cases are characterized by relatively indolent growth and others by aggressive behavior. A multidisciplinary team including a pathologist with expertise in evaluating odontogenic neoplasms is essential to determine proper treatment and optimal outcome although wide excision with clean margins is highly recommended. However, more studies are needed to determine whether adjuvant treatment is necessary. Long-term surveillance is mandatory in all cases.

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Conflict of Interest

The authors declare that they have no conflict of interest.