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Case Report

Mandibular ghost cell odontogenic carcinoma: a case report and review of literature

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Abstract: Ghost cell odontogenic carcinoma (GCOC) is a rare malignant odontogenic tumor, Only 37 cases of GCOC have been reported in the English-language literature to date. This case presents an additional case, a 47-year-old Chinese man presented with a slow-growing mandibular lesion with history of ameloblastoma. The panoramic radiograph shows an ill-defined mixed radiolucency with radiopacity in the mandible. The histological examination confirms the diagnoses as a GCOC. Immunohistochemical examination was performed to detect Ki-67 and MMP-9 which are considered as predictive factors for cell proliferation and tumor invasion. This case was managed by wide surgical resection of tumor and reconstruction of the defect by free vascularized fibular flap. Six months follow- up period shows no signs of recurrence.

Keywords: Ghost cell odontogenic carcinoma, malignant odontogenic tumor, transformation

Introduction

Ghost cell odontogenic carcinoma (GCOC) is an extremely rare malignant odontogenic epithelial tumor which arises from odontogenic epithelial remnants within jaw or from the transformation or degeneration of benign lesions [1]. (GCOC) is a rare manifestation of such tumors, and may develop either as a de novo tumor or arise from a previously existing calcifying cystic odontogenic tumor, dentinogenic ghost cell tumor or calcifying odontogenic cyst [2].

In this case report, we report a rare case of GCOC in the mandible which has transformed from an ameloblastoma lesion that was observed 7 years ago, then describe its clinical-pathological features, radiological images and treatment performed.

Case report

A 47-year-old Chinese man was referred to the Department of Oral and Maxillofacial oncology Surgery, West China College of Stomatology, Sichuan University. The Patient reported that he has found swelling of the left side mandible 21 years ago with gradual and slow growth, 7 years ago; the left mandibular swelling was treated by curettage with histopathology diagnosed as ameloblastoma. Since 1 year of his visit to our department, a painless lesion was slowly growing of the left mandible, the physical examination has revealed facial asymmetry, bucco-lingual swelling which is tender, soft, and palpable measuring over 8 cm in greatest dimension, the gingival mucosa was normal; there was no obvious numbness of lower lip. The swelling was extending from the left mandible to the right mandibular canine. Enlarged cervical lymph nodes were not found on physical examination, and both lungs were clear on chest X-ray. Panoramic X-ray film revealed an aggressive multilocular mixed radioluncy with radiopaque foci in the mandible which extends from the left of mandibular ramus to the right manbular canine, the Panoramic X-ray shows root resorption (**Figure 1**). Based on the patient's history, the clinical diagnosis was a recurrence of ameloblastoma, the patient under-

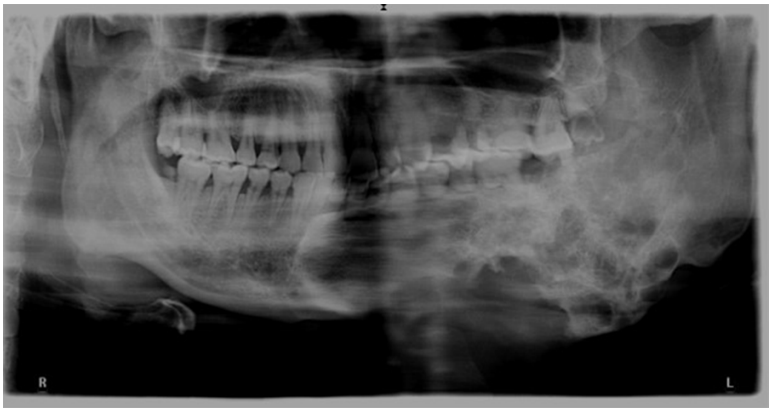

Figure 1. Panoramic radiograph, showing an ill-defined multilocular mixed radiolucency with radiopacity, showing root resorption of teeth within the lesion.

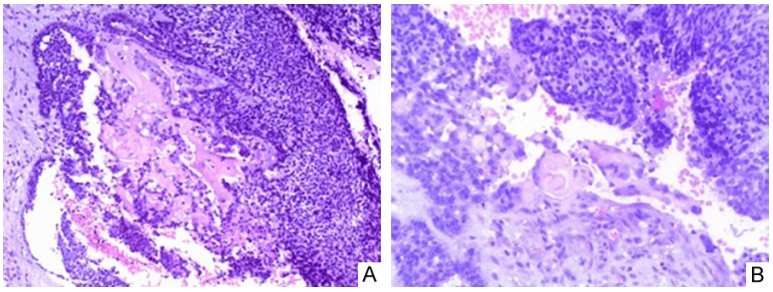

Figure 2. Histopathological findings of surgical specimen. Photomicrograph of ameloblastic like islands and Ghost cells with odontogenic epithelium (A) (H&E magnification ×100). Ghost cells were aggregated in different densities (B) (H&E magnification ×200).

went an incisional biopsy, and the specimen was histopathologically examined, which confirms the diagnosis as a GCOC of the mandible (**Figure 2**). The immunohistochemical analyses for MMP-9 and Ki-67 revealed a positive reaction against MMP-9 and a less of reaction against Ki-67 (**Figure 3**). The patient was treated surgically under general anesthesia; the approach used was lower cheek flap and the lesion was totally excised along with free margin, the resection extended from right mandibular first premolar to the left ramus of the mandible, the condyle was left untouched, the defect was reconstructed by free vascularized fibular flap. The patient returned for a one year follow-up postoperatively where healing was noted to be appropriately progressing (**Figure 4**). There has been no evidence of recurrence and metastasis for about 6 months.

Discussion

GCOC is a rare and malignant neoplasm characterized by high mitotic activity and clusters of ghost epithelial cells. It shows locally aggressive behavior and infiltrative growth [3]. As the term "Ghost cell odontogenic carcinoma" underlines the odontogenic source because of the ameloblast-like cells, "Ghost" is due to the presence of shadows of keratinized epithelial cells with wet keratin [4]. It usually arises as a swelling on the jawbone, commonly occurs on the maxilla, and is most prevalent in men (males/females =4:1). Depending on pervious published cases, the GCOC appears to be more common in Asians than other races especially Asian males in their fourth decade of life [2, 5]. It could cross the midline in the mandible but it unusually occurs in maxilla. The GCOC was first described by Gorlin et al in 1962 as a distinct pathological entity [5]. The first well-documented case of a malignancy arising in the calcifying odontogenic cyst to appear in the English language literature was reported by Ikemura et al in 1985 [6]. In this article, the authors report the 38th case of GCOC described in the English language published literature, in which also, the authors summarize all cases and features of GCOC (**Table 1**). According to the literature, 23 cases reported were Asian individuals, 6 were white and 4 were black. GCOC has more prevalence in males than females (30:8), with higher incidence in the maxilla than in the mandible (24:14), 12 cases appeared radiolucent on radiograph, while 15 cases appeared as mixed radiolucent-radiopaque.

GCOC often arises from a precedent calcifying odontogenic cyst that is left without management for several years [7]. Calcifying odontogenic cysts are divided into two benign forms: a calcifying cyst odontogenic tumor, described as a "benign cystic neoplasm of odontogenic origin, characterized by an ameloblastoma-like epithelium with ghost cells that may calcify", and a dentinogenic ghost cell tumor, a "locally

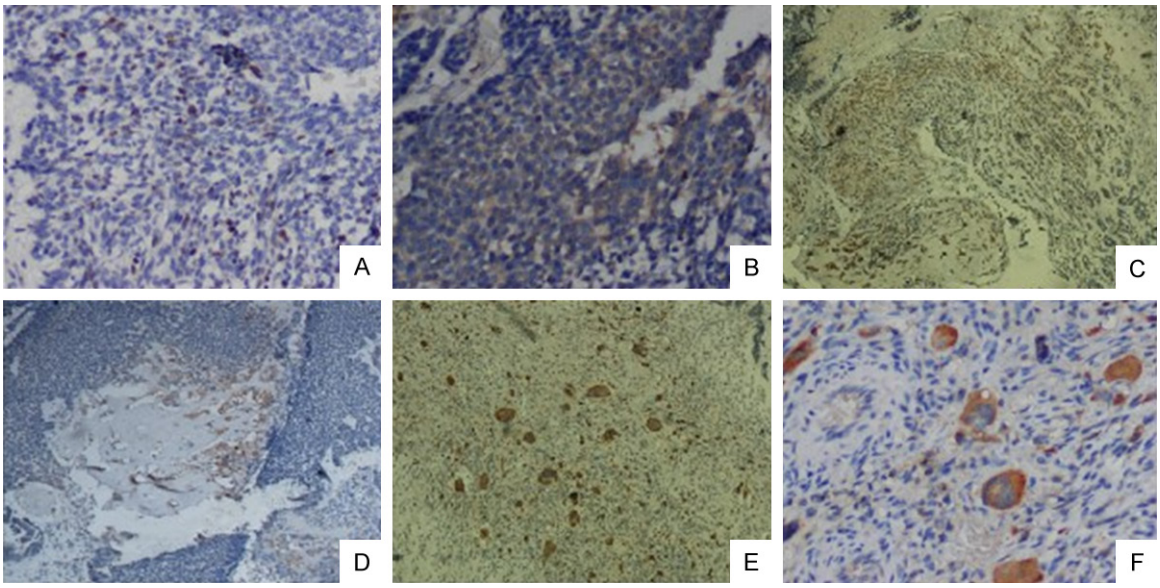

Figure 3. Immunohistochemistry. A. Expression of Ki-67 antigen in GCOC. Ki-67 antigen was expressed in the nuclei of epithelial cells, but not in ghost cells. The epithelial cells of GCOC show moderate positive reaction for Ki-67 (immunohistochemistry specimen, original magnification ×200). GCOC is showing MMP-9 protein expression both in stromal cells and tumor cells. B. The cytoplasm of tumor cells shows strong MMP-9 protein expression (immunohistochemistry Specimen, original magnification ×200). C and D. Stromal cells at the bone-neoplasm interface of GCOC show strong MMP-9 protein expression (immunohistochemistry Specimen, original magnification ×100). E. Stromal cells of GCOC show strong MMP-9 protein expression (immunohistochemistry Specimen, original magnification ×100). F. Stromal cells of GCOC show strong MMP-9 protein expression (immunohistochemistry specimen, original magnification ×200).

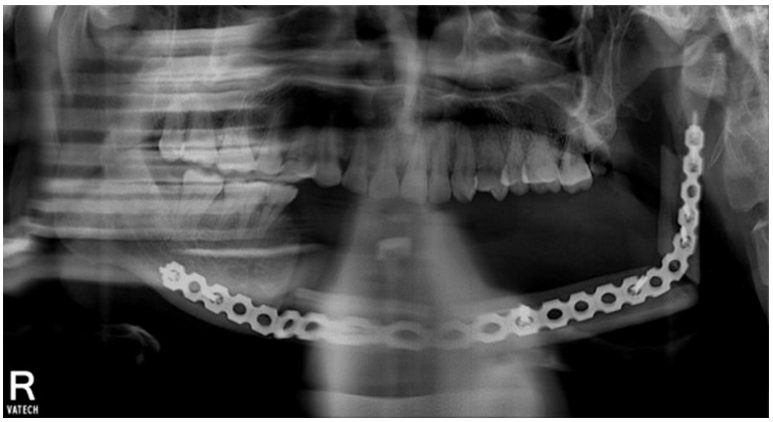

Figure 4. Panoramic radiograph, showing a six-month follow-up postoperatively with no evidence of recurrence.

invasive neoplasm characterized by ameloblastoma-like islands of epithelial cells in a mature connective tissue stroma" [3]. Although the origin of the GCOC is likewise not fully known, there are three suggested pathogenic mechanisms explaining the histogenesis of an odontogenic carcinoma. The first describes a GCOC arising secondary to a benign calcifying cyst odontogenic tumor or a dentinogenic ghost cell tumor. The second mechanism suggests that GCOCs arise from another odontogenic tumor such as ameloblastoma, a recurrent malignant neoplasm with the previously mentioned features. The third describes a GCOC arising de novo, this was characteristic of 12 (40%) of the reported cases, in which GCOC is not associated with preceding dentinogenic ghost cell tumor or calcifying cystic odontogenic tumor. The de novo type could potentially represent a secondary onset from an undiagnosed primary lesion. Diagnostic criteria have been established for calcifying cyst odontogenic tumor, dentinogenic ghost cell tumor, and GCOCs. However, these tumors represent a heterogeneous group due to broad clinical and radiological diversity and variable biological behaviors [3]. Our case presents a male patient in the fourth decade and depends on patient medical history, the GCOC arising

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

NO of case	Author	Age/ Gender	Race	Location	Radiographic features	Follow-up
1	Gorlin et al [5]	45/M	White	Mandible	N/A	Local recurrence (death)
2	Ikemura et al [6]	48/F	Asian	Maxilla	Radiolucent and radiopaque	Local recurrence (death)
3	Ellis and Shmookler [9]	55/F	Black	Mandible	N/A	Local recurrence
4	Ellis and Shmookler [9]	17/M	N/A	Maxilla	N/A	Local recurrence
5	Ellis and Shmookler [9]	46/M	White	Maxilla	N/A	Local recurrence
6	Grodjesk et al [10]	46/M	White	Maxilla	N/A	Distant metastasis (death)
7	Scott and Wood [11]	33/M	Black	Maxilla	N/A	Local recurrence
8	McCoy et al [12]	13/F	Black	Maxilla	N/A	No recurrence
9	Dubiel-Bigaj et al [13]	42/M	N/A	Maxilla	N/A	N/A
10	Siar and Ng [14]	39/M	Asian	Maxilla	N/A	Local recurrence
11	Alcalde et al [15]	72/F	Asian	Maxilla	Radiolucent and radiopaque	No recurrence
12	Folpe et al [16]	20/M	N/A	Maxilla	N/A	Local recurrence
13	Lu et al [17]	24/M	Asian	Maxilla	Radiolucent and radiopaque	Local recurrence
14	Lu et al [17]	31/F	Asian	Maxilla	Radiolucent	No recurrence
15	Lu et al [17]	19/M	Asian	Mandible	Radiolucent and radiopaque	Local recurrence (death)
16	Lu et al [17]	39/M	Asian	Mandible	Radiolucent	Local recurrence
17	Kamijo et al [18]	38/M	Asian	Maxilla	Radiolucent and radiopaque	No recurrence
18	Kim et al [19]	33/M	N/A	Mandible	Radiolucent and radiopaque	No recurrence
19	Li and Yu [20]	43/M	Asian	Maxilla	Radiolucent and radiopaque	N/A
20	Cheng et al [21]	36/M	Asian	Mandible	Radiolucent	Local recurrence
21	Cheng et al [21]	35/M	Asian	Maxilla	Radiolucent	Distant metastasis (death)
22	Cheng et al [21]	33/M	Asian	Maxilla	Radiolucent	Local recurrence
23	Cheng et al [21]	44/M	Asian	Mandible	Radiolucent	Local recurrence
24	Goldenberg et al [22]	36/M	Asian	Maxilla	Radiolucent and radiopaque	Local recurrence
25	Sun et al [23]	30/M	Asian	Maxilla	Radiolucent and radiopaque	No recurrence
26	Zhu et al [24]	51/M	Asian	Maxilla	Radiolucent	No recurrence
27	Roh et al [25]	55/M	Asian	Mandible	Radiolucent and radiopaque	No recurrence
28	Li et al [26]	47/F	Asian	Mandible	Radiolucent	Local recurrence
29	Nazaretian et al [27]	40/M	Black	Maxilla	Radiolucent and radiopaque	N/A
30	Arashiyama et al [28]	68/M	Asian	Mandible	Radiolucent	No recurrence
31	Martos et al [29]	70/F	White	Maxilla	Radiopaque-radiolucent	No recurrence
32	Li et al [30]	53/M	Asian	Maxilla	Radiolucent	No recurrence
33	Motosugi et al [31]	17/F	Asian	Maxilla	N/A	Local recurrence
34	Castle et al [32]	57/M	White	Maxilla	Radiolucent	N/A
35	Kasahara et al [33]	59/M	Asian	Mandible	Radiolucent and radiopaque	No recurrence
36	Wader et al [34]	61/M	N/A	Mandible	Radiolucent and radiopaque	N/A
37	Del et al [3]	86/M	White	Mandible	Radiolucent	No recurrence
38	Present Case	47/M	Asian	Mandible	Radiolucent and radiopaque	No recurrence

Abbreviations: N/A, not available. M, male. F, female.

from ameloblastoma which also crossed the midline. High expression of Ki-67 and MMP-9 signifies a predictive factor for cell proliferation and tumor invasion, in our case, Ki-67 Nuclear reactivity was exhibited in all areas of both GCOC and ameloblastoma. Ki-67 positive nuclei were scattered in the epithelium islands, Ki-67 antigen was not detected in ghost cells. MMP-9 protein was detected both in the cytoplasm of tumor cells and stromal cells in GCOC and ameloblastoma. GCOC has shown strong MMP-9 protein reactivity in the cyto-

plasm of tumor cells and in the cytoplasm of stromal cells. Stroma in the bone-tumor interface was also strongly positive for MMP-9 protein.

GCOC is treated with wide surgical excision, because GCOC exhibits mortality and recurrence [8]. The postoperative adjuvant irradiation, with or without chemotherapy, is controversial and any standard treatment has been evaluated. The Long-term follow-up is essential to recognize local recurrences or distant metastases [1]. In our case, we performed and recommend the treatment by wide surgical excision with clear microscopic margins without adjuvant irradiation or chemotherapy because there is no evidence to support the efficacy of adjuvant chemo- or radiotherapies.

Conclusion

Early detection of GCOC is crucial, especially because of the possibility of transformation from a benign to malignancy, whether it is a cyst or neoplasm. The treatment of choice is wide surgical excision with clear pathological margins. The long-term period for follow-up is very important to prevent recurrence and to identify possible rare metastases.

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Disclosure of conflict of interest

None.

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