CASE REPORT

# Odontogenic ghost cell carcinoma with pulmonary metastasis

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## ABSTRACT

Odontogenic ghost cell carcinoma (OGCC) is an exceptionally rare malignant odontogenic epithelial tumor. It is characterized by ameloblastic-like islands of epithelial cells with aberrant keratinization in the form of ghost cells with varying amounts of dysplastic dentin. Malignant histological characteristics include infiltration, cellular pleomorphism, numerous mitosis and necrosis. Its biological behavior varies from slow-growing locally invasive lesions to rapidly growing highly aggressive tumors. OGCC metastasizing to distant sites is extremely rare. Only three cases of metastasis have been reported in literature. We are reporting the case of a 54-year-old male patient who presented with tender swelling in the malar region. Histopathological examination revealed OGCC and he received postoperative radiotherapy. Two years later, he presented with a lung mass. Biopsy from the lung lesion showed the same morphology as that of maxillary tumor with scattered ghost cells. This case points to the aggressive behavior of OGCC and its metastatic potential. It also highlights the need for long-term follow-up of these patients.

***Key words:*** Maxillary pathology, odontogenic ghost cell carcinoma, odontogenic tumors, pulmonary metastasis

## INTRODUCTION

Odontogenic ghost cell carcinoma (OGCC) is a rare odontogenic tumor characterized by the presence of ghost cells. It can appear as a de novo tumor or may arise in a preexisting calcifying odontogenic cyst (COC). Until now, only 31 cases of OGCCs have been reported in literature. Because of the limited number of published cases, the clinical behavior of the tumor is not well-understood. Local recurrences have been reported, but distant metastasis is extremely rare. Only three cases of metastasis have been reported in medical literature.

## CASE REPORT

A 54-year-old male presented with pain in the left malar prominence and epistaxis.

On examination, there was tenderness in the malar region. Intraorally left gingivobuccal sulcus showed a smooth swelling measuring 3 cm × 3 cm. Imaging showed irregular soft tissue density mass in the left maxillary antrum measuring 4.6 cm × 4.5 cm × 3.8 cm with destruction of the wall.

Biopsy revealed poorly differentiated carcinoma. Total maxillectomy was done.

The maxillectomy specimen showed a solid gray-white growth, filling the antrum. Microscopy showed a neoplasm composed of islands of odontogenic epithelium resembling that of ameloblastoma [Figure 1] and epithelial cells transforming into ghost cells [Figures 2-4]. There were areas of calcification and necrosis. Focal cellular areas composed of pleomorphic cells with increased nuclear cytoplasmic ratio and hyperchromatic nuclei were noted. Mitotic rate was high in these cellular areas [Figure 5]. MIB1 labeling index was around 50–60%, suggesting high proliferative activity.

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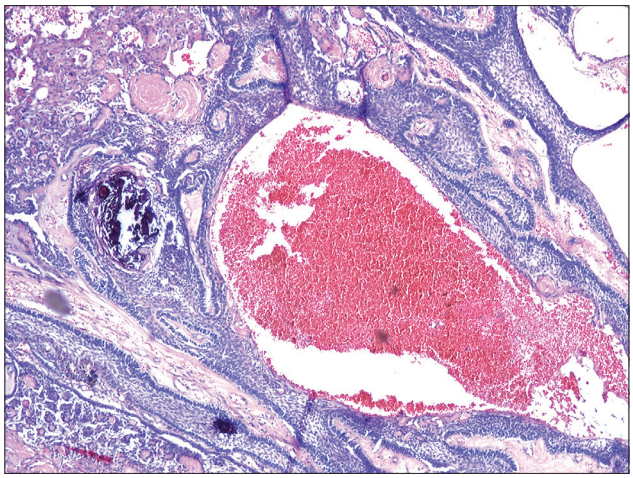

**Figure 1:** Photomicrograph showing ameloblastoma-like epithelial proliferation and hemorrhagic areas (H&E stain, ×100)

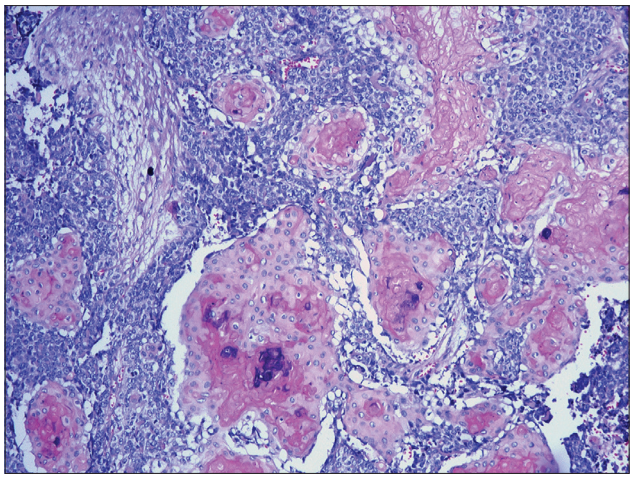

**Figure 2:** Photomicrograph showing islands of epithelial cells admixed with ghost cells (H&E stain, ×100)

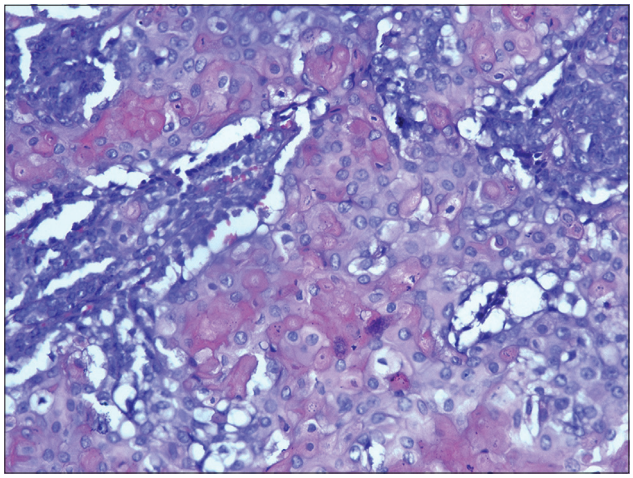

**Figure 3:** Photomicrograph highlighting the features of ghost cells with loss of nuclei and preserved cell outlines (H&E stain, ×200)

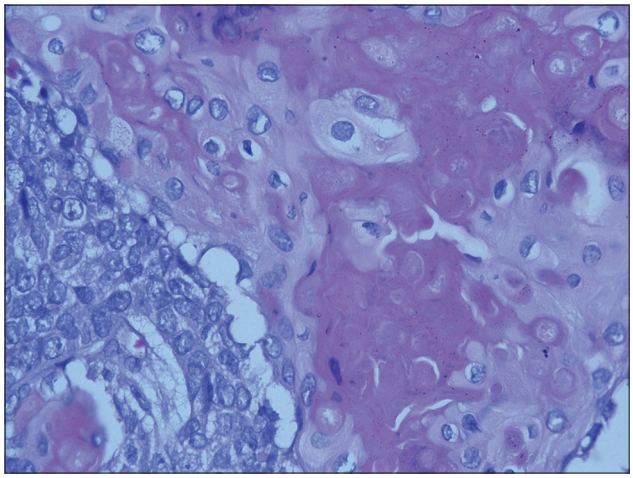

**Figure 4:** Higher power of the ghost cells (H&E stain, ×400)

Based on these findings, diagnosis of ghost cell odontogenic carcinoma was made.

The patient was given postoperative radiotherapy. Two years later, the patient presented with dyspnea. Imaging showed a mass lesion in the lower lobe of the lung. Biopsy of the lung mass showed the similar morphology as the maxillary tumor with ghost cells [Figure 6]. Tumor cells were positive for cytokeratin and p63 and were negative for TTF1 and CK7 [Figure 7].

## DISCUSSION

OGCC is an extremely rare malignancy. Only 31 cases have been reported to date.[1,2] More than half of the reported cases are from Asia. Males are more commonly affected with male: female ratio of 2:1.[3] The peak incidence occurred in the fourth decade with age ranging from 13 to 72 years.[3,4] OGCC generally appears as a painful, hard swelling in the maxilla or mandible.

OGCC is believed to be one end of the spectrum of a heterogeneous entity known as COC also known as Gorlin cyst, first identified by Gorlin in 1962.[5] In the initial years, COC was considered a nonneoplastic cyst. However, later, some of these lesions showed a solid component also. In 1981, Praetorius *et al*. classified COCs into cystic and neoplastic (solid) types.[6] They further classified the cystic type into three subtypes such as simple unicystic, odontoma-producing type and ameloblastomatous proliferating type. The neoplastic (solid) type was called dentinogenic ghost cell tumor because of its tendency to produce dentinoid material. Hong *et al*. proposed the term epithelial odontogenic ghost cell tumor (EOGCT) to these neoplastic solid types and these authors classified the neoplastic form of COC into ameloblastoma ex COC, peripheral EOGCT (which occurred in gingival or alveolar mucosa) and central EOGCT (which occurred intraosseously).[7] Ledesma-Montes *et al*. divided the calcifying cystic odantogenic tumors into four subtypes which included simple cystic, odontoma associated, ameloblastomatous proliferating and CCOT associated with benign odontogenic tumors other than odontomas.[8] They

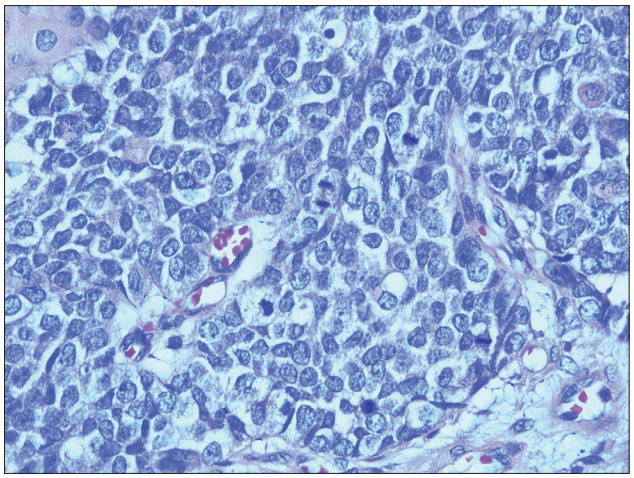

**Figure 5:** Area of high cellularity with increased number of mitotic figures (H&E stain, ×200)

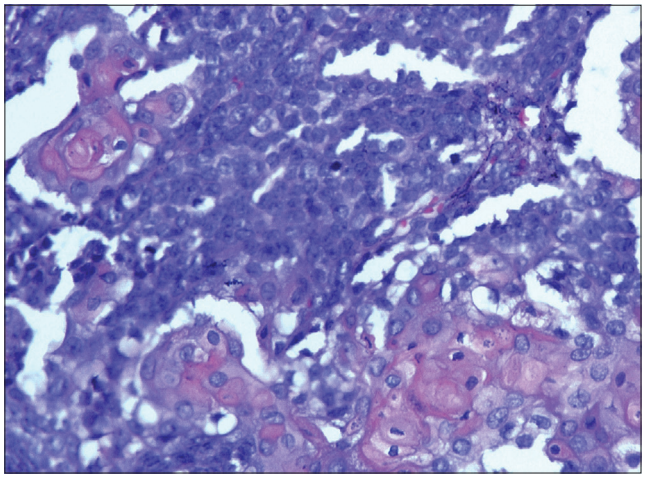

**Figure 6:** Lung biopsy showing ghost cells (H&E stain, ×200)

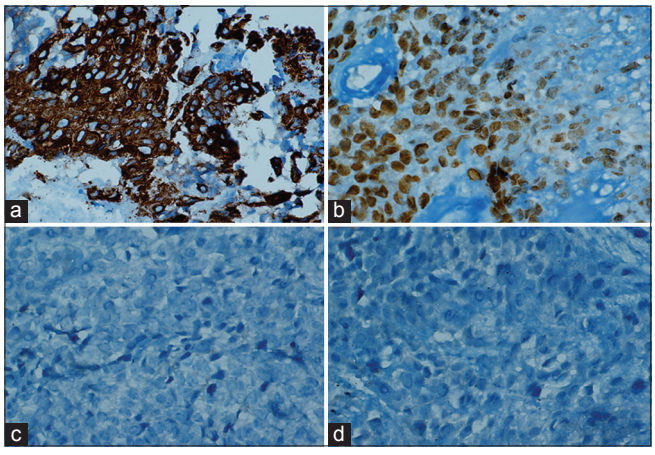


**Figure 7:** Immunohistochemistry on lung tumor showing (a) cytokeratin–positivity (IHC stain, ×100), (b) p63-positivity (IHC stain, ×200) (c) CK7-negativity(IHC stain ×200) and (d) TTF1-negativity (IHC stain, ×200)

separated the dentinogenic ghost cell tumor into central aggressive DGCT and a peripheral nonaggressive counterpart.

The WHO considered all COC as neoplastic and termed the cystic form as calcifying cystic odontogenic tumor and the neoplastic solid form as dentinogenic ghost cell tumor whereas ghost cell odontogenic carcinoma is a malignant odontogenic epithelial tumor with features of one or both of these lesions.[3] In 1985, Ikemura *et al*. described the first well-documented case of malignancy arising in a COC.[9] In their case report, there were areas of COC and foci of malignant transformation.

The histological features of OGCC are an ameloblastoma-like epithelial proliferation, ghost cells that may be calcified, admixed with areas of atypical features such as increased cellularity, pleomorphism, mitosis, necrosis and infiltrative growth pattern.[1,3] The accurate diagnosis of OGCC requires extensive sampling of the specimen as the features of malignancy can be focal and the other areas may show benign histology.

The ghost cells are a characteristic feature of OGCC. They are large polygonal epithelial cells with eosinophilic cytoplasm that have lost their nuclei but maintain a faint outline of cellular and nuclear membrane.[7] The intracytoplasmic keratin preserves the cell outline and the corresponding previous site of the nucleus.[10,11] These cells are resistant to degradation. According to Gorlin, the ghost cells represent different stages of normal or abnormal keratinization.[5] Levy proposed that the formation of ghost cells is due to squamous metaplasia of odontogenic epithelium caused by ischemia.[7] In general, the cell outlines of ghost cells are well-defined but, in some cases, it may be blurred. In such cases, groups of ghost cells will appear fused. Ghost cells may undergo dystrophic type of calcification. Roh *et al*. that suggested some of the cytokines produced by ghost cells play roles in the bone resorption.[12] They detected tartrate resistant acid phosphatase and vitronectin receptor in the ghost cells.[12] Another feature of OGCC is the formation of dentinoid or osteoid material.

The biological behavior of OGCC is unpredictable. These tumors may be indolent or locally aggressive. It can behave as slowly growing locally aggressive neoplasm or rapidly growing highly invasive tumor.[4] The overall 5-year survival rate is estimated to be 73%.[4,9] In the first case of OGCC described by Ikemura *et al*., the patient died due to brain invasion. Locally aggressive and frequently recurring tumors have been reported, but distant metastasis is definitely uncommon. Review of literature shows only three previous cases of metastatic OGCC. In the case described by Grodjesk *et al*., the patient died due to lung metastasis.[11] In the second case, the patient developed metastasis in the skin, lung and brain.[13] The third case was reported by Cheng *et al*. where the patient developed metastasis in the cranium.[1] In our case, 2 years after the initial diagnosis, the patient developed metastasis in the lung. Because of the unpredictable biological behavior of the tumor, a long-term follow-up is recommended.

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## Conflicts of interest

There are no conflicts of interest.

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