Calcifying Epithelial Odontogenic Tumour Showing Malignant Transformation: a Case Report and Review of the Literature

Yi ZHONG[1,2], Li WANG[1,2], Tiejun LI[3], Xin Ming CHEN[1,2]

Calcifying epithelial odontogenic tumour (CEOT) is a rare and benign odontogenic neoplasm that affects the jaws. Here we present a maxillary case of CEOT showing features of malignant transformation, and a review of the literature.

Key words: *calcifying epithelial odontogenic tumour, malignant transformation, review*

Calcifying epithelial odontogenic tumour (CEOT), first described in 1955 by Pindborg, accounts for 1% to 2% of odontogenic tumours[1,2]. Although CEOT was described as a benign, slow-growing, occasionally locally aggressive neoplasm, there have been three cases of malignant CEOT of the mandible, and one case of CEOT of the mandible showing microscopic features of potential malignant behaviour reported in the English literature[3-6]. To the best of our knowledge, malignant CEOT of the maxilla has not yet been reported. The present case report describes a case of CEOT of the maxilla showing malignant transformation.

1 The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Key Laboratory of Oral Biomedicine Ministry of Education, School and Hospital of Stomatology, Wuhan University, Wuhan, P.R. China.
2 Department of Pathology, School and Hospital of Stomatology, Wuhan University, Wuhan, P.R. China.
3 Department of Pathology, Peking University School and Hospital of Stomatology, Beijing, P.R. China.
Dr Yi ZHONG and Dr Li WANG contributed equally to the article.

Corresponding author: Dr Xin Ming CHEN, Department of Pathology, School and Hospital of Stomatology, Wuhan University, Wuhan, 430079, P.R. China. Tel: 86-27-87686229; Fax: 86-27-87873260; E-mail: xmchen301@yahoo.com.cn

Case report

A 49-year-old man was referred to the Department of Oral and Maxillofacial Surgery, School and Hospital of Stomatology, Wuhan University, with an approximate one-year history of a painless swelling at the right anterior region of the maxilla. One month prior to presentation, the mass had become ulcerated and painful. Oral examination showed a diffuse swelling from the maxillary right central incisor to the first molar region measuring 2.5 cm × 2.5 cm. The overlying palato-gingival mucosa was reddish and an ulcer was observed in the palatal overlying mucosa from the maxillary right canine to the maxillary first molar region, measuring 1.5 cm × 1.5 cm. The mobility and dislocation of the maxillary right first and second premolars were noted. Radiographic examination revealed a unilocular radiolucent lesion with a poorly demarcated border, extending from the maxillary right second incisor to the maxillary right first molar region, and focal opacities in the centre of the radiolucent areas (Fig 1). No significantly enlarged lymph nodes in the neck were palpated. General evaluation including a chest X-ray and abdominal sonography showed no evidence of distant metastasis. Laboratory findings, including complete blood count, blood biochemistry and urine analysis, were within normal limits.

Although a biopsy specimen from the superficial area of the lesion revealed a typical microscopic appearance of CEOT, the clinical and radiographic features were suggestive of a locally aggressive lesion. Therefore, the patient received a bilateral partial maxillary resection from the maxillary left canine to the maxillary right first molar.

Grossly, the tumour measured 4 cm × 3 cm × 3 cm and was solid with a greyish-yellow appearance on the sectional plane and destruction of the surrounding bone tissue. The palatal cortical bone was perforated and the covering mucosa was ulcerated. Microscopically, there was a gradual transition from the components of benign CEOT to the components of malignant CEOT, which comprised approximately 40% of the entire tumour. In particular, the periphery was mostly malignant (Fig 2). The central portion of the tumour showed the typical features of CEOT, which was characterised by irregular strands, cords, and nests of polyhedral epithelial cells with clear cytoplasm and ample eosinophilic cytoplasm in a bland fibrous stroma, and eosinophilic, homogeneous hyaline material often with calcification (Figs 3A to 3C). The tumour cells were positive for the Congo red stain (Fig 3D). However, they did not show nuclear atypia or pleomorphism, and few mitotic figures were observed. The malignant components were composed of islands of polyhedral tumour cells with nuclear pleomorphism and increased mitotic activity (Fig 4A). Microscopic foci of central microcystic degeneration and necrosis were noted in the squamous islands, the peripheral layer of which showed discohesive areas of epithelioid morphology alternating with areas imparting a pseudoglandular appearance (Fig 4B). In addition, infiltration into adjacent bone and blood vessels could be observed (Figs 4C and 4D).

The Ki-67 labelling indices for the malignant area were 15% and for the benign area 3%. The majority of the tumour cells showed strong positivity for staining CK19 and pan-cytokeratins. A diagnosis of 'calcifying epithelial odontogenic tumour showing malignant transformation' was made on the basis of the above findings. The patient has been followed up for 2 years and no sign of recurrence was noted.

Discussion

CEOT is a rare benign odontogenic tumour with no gender predilection. The age of patients ranges from 8 years to 92 years at the time of diagnosis with a mean of 36.9 years. Two-thirds of CEOTs arise in the mandible, and one-third in the maxilla[7]. When located in the maxilla, patients may sometimes complain of nasal stuffiness, epistaxis and headache[2,5]. Ng and Siar[8] reported a predilection for the maxilla in Asians, contrary to the higher mandibular prevalence in Westerners. Approximately 80% of CEOTs are located in the premolar and molar regions[2]. The CEOT typically presents as an intraosseous, expansile, painless mass that exhibits slow growth[9]. Peripheral cases account for 5% of CEOTs[10]. Radiographically, according to the study by Kaplan et al[11], 58% of CEOTs are unilocular, 27% multilocular and 15% nonloculated. Histologically, a typical CEOT shows sheets of variably sized, polyhedral epithelial cells with well-defined borders and distinct intercellular bridges. Rounded, eosinophilic, amyloid deposits within sheets of tumour cells are commonly noted. The amyloid substance in CEOT occasionally undergoes mineralisation, producing sheets of concentric calcifications known as Liesegang rings that are considered by some to be pathognomonic for this tumour. The neoplastic cells in CEOT may also show marked pleomorphism and varying nuclear-to-cytoplasmic ratios in the form of giant or small nuclei. None of these features, however, is thought to represent malignancy. Furthermore, abnormal mitotic figures are rare in CEOT, and if present, should raise suspicion of malignant transformation[1,4].

Malignant odontogenic tumours are exceedingly rare[9]. Malignancy was confirmed based on the following criteria: histological findings of infiltrative growth, atypical cytological features, and focal necroses or clear evidence of distant metastatic spread[12]. Previously, only three cases of malignant CEOT and one case of CEOT showing microscopic features of potential malignant behaviour have been reported in the English literature[3-6]. A summary of these four cases is presented in Table 1. All of the four cases are mandibular tumours, appear to affect the elderly and show no gender predilection. Among them, two cases arose from benign CEOT after repeated local recurrences[4,6] and one case showed pulmonary metastasis. The malignant CEOT reported by Basu et al[3] had a history of 62 years. All the patients underwent resection of the mandible with the surgical margins free of the tumour cells. Apart from the case reported by Basu, the remaining three cases showed no recurrence.

The present case had many documented attributes of benign CEOT. The complaint included a painless fixed swelling at the right anterior region of the maxilla, which was comparable with a CEOT. There were supportive radiological findings and the typical histological appearance of a CEOT. The tumour in this case appeared mainly as a unilocular radiolucency, with amorphous internal opacification and a poorly demarcated sclerotic rim. Part of the tumour showed typical

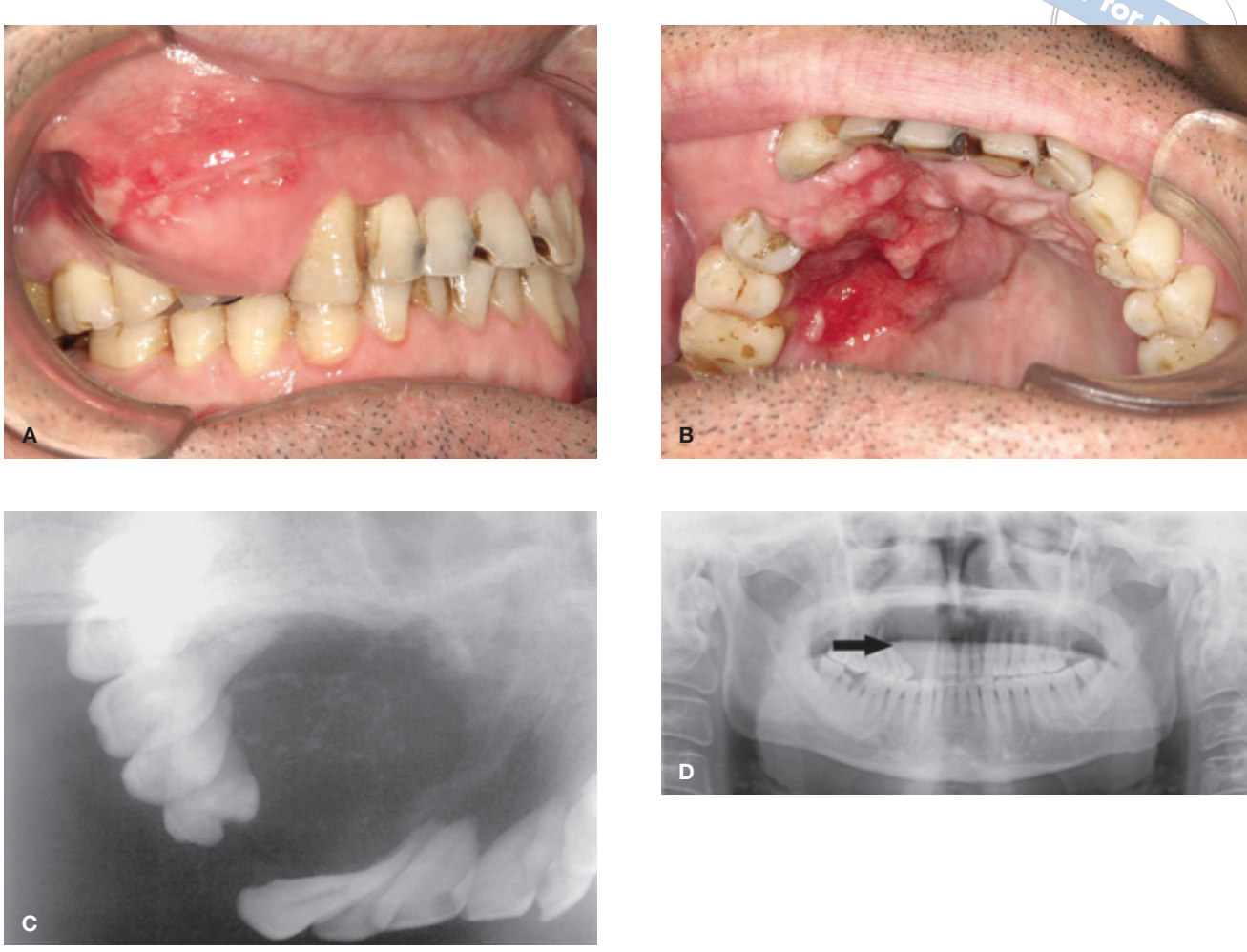

Fig 1 (A, B) Oral examination showed a diffuse swelling from the maxillary right central incisor to the first molar region measuring 2.5 cm × 2.5 cm. The overlying palato-gingival mucosa was reddish, and ulcer formation was observed in the palatal overlying mucosa from the maxillary right canine to the maxillary first molar region, measuring 1.5 cm × 1.5 cm. The mobility and dislocation of the maxillary right first and second premolars were noted. (C, D) Radiographic examination revealed a unilocular radiolucent lesion with a poorly demarcated border extending from the right second incisor to the right first molar region, and focal opacities in the centre of the radiolucent areas.

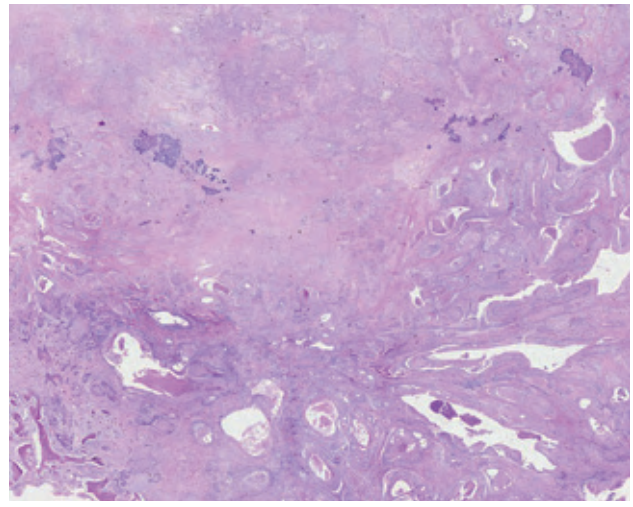

Fig 2 Microscopically, there was a gradual transition from the components of benign CEOT to the components of malignant CEOT, which comprised approximately 40% of the entire tumour. In particular, the periphery was mostly malignant (original magnification ×10).

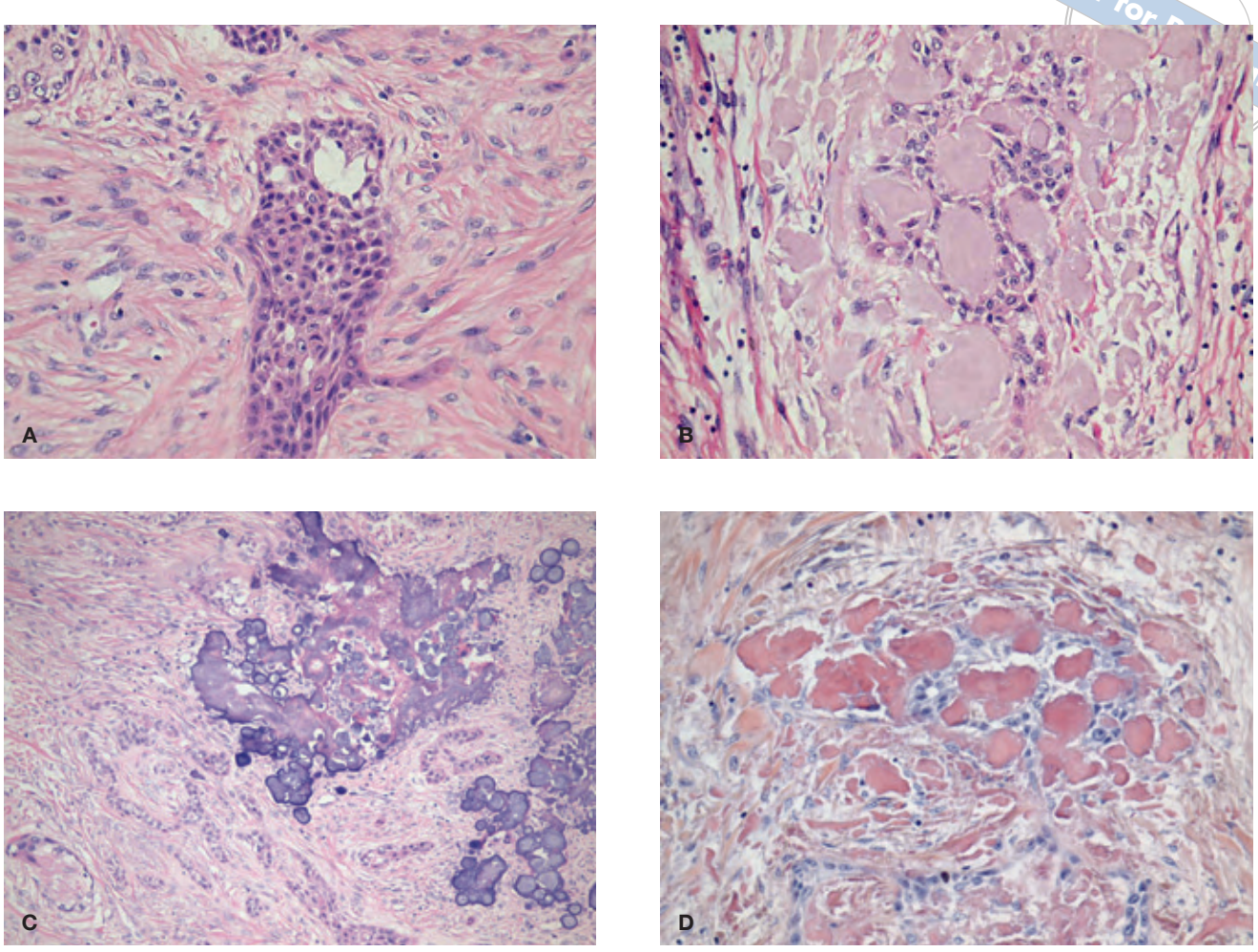

Fig 3 (A–C) The central portion of the tumour showed the typical features of CEOT, which was characterised by irregular strands, cords, and nests of polyhedral epithelial cells with clear cytoplasm and ample eosinophilic cytoplasm in a bland fibrous stroma, and eosinophilic, homogeneous hyaline material that was often calcified (original magnification ×400 [A and B], ×200 [C]). (D) The tumour cells were positive for the Congo red stain (original magnification ×400).

histological features of a CEOT and part also showed evidence of malignant transformation.

The previously reported three cases of malignant CEOT had clinical evidence of metastasis[3,4,6], while the present case presented no clinical findings of metastasis. However, the present case showed similar histopathological features to those of the previous malignant cases, thus showing polyhedral epithelial tumour cells displaying not only pleomorphism but also increased abnormal mitosis. Moreover, the tumour was characterised by unequivocal evidence of focal necroses. The neoplasm also displayed an infiltrating growth pattern with sheets of tumour cells invading bone marrow spaces. In the absence of overt clinical confirmation of malignancy such as metastasis, histological evidence of malignancy is essential for establishing diagnosis. The immunocytochemical labelling of Ki-67 also indicated an over three-fold increase of the labelling indices in the suspected malignant area of the tumour compared with the benign areas.

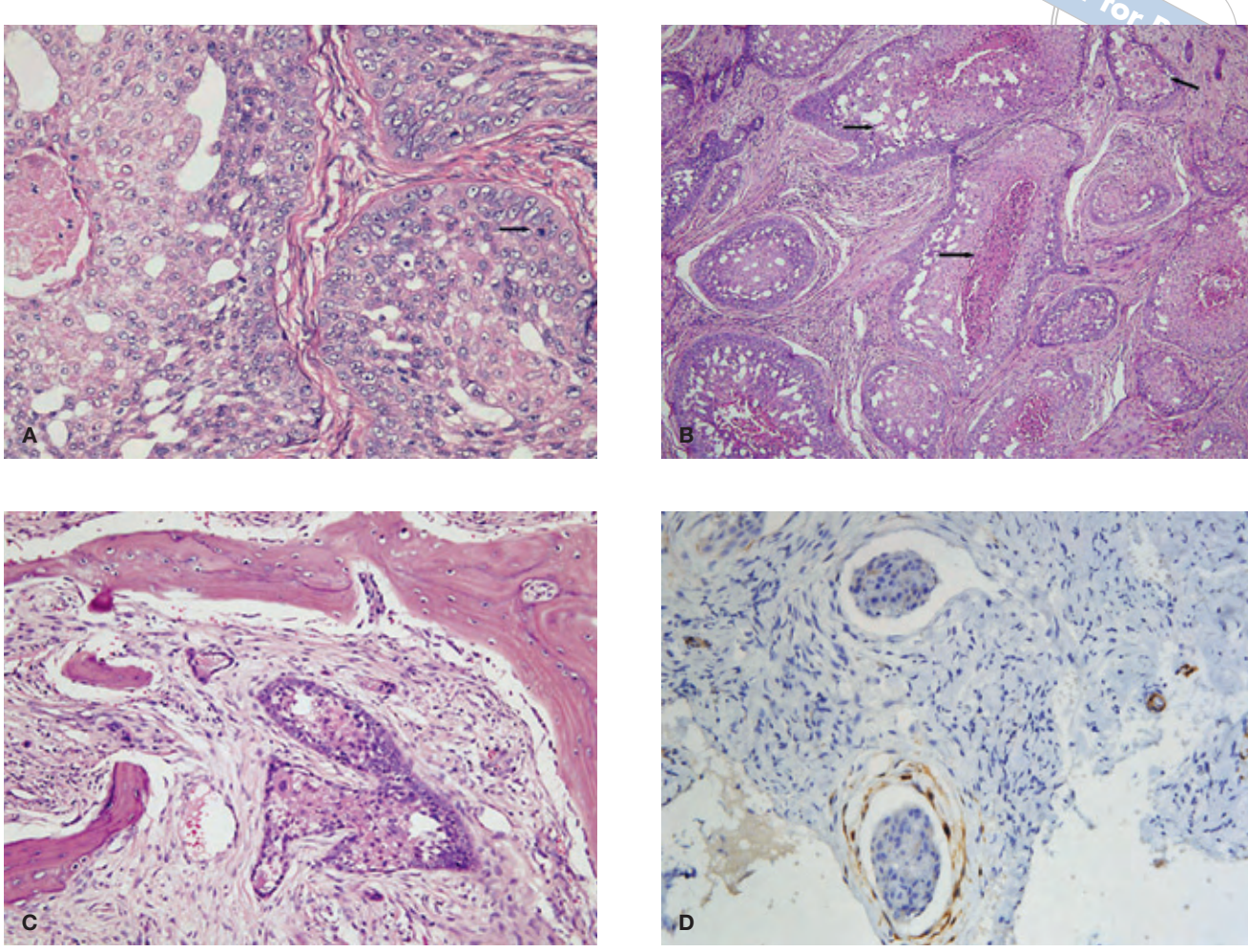

Fig 4 (A) The malignant component was composed of islands of polyhedral tumour cells with nuclear pleomorphism and increased mitotic activity (original magnification ×400). (B) Microscopic foci of central microcystic degeneration and necrosis were noted in the squamous islands (upper right and lower arrows), the peripheral layer of which showed discohesive areas of epithelioid morphology alternating with areas imparting a pseudoglandular appearance (upper left arrow) (original magnification ×100). (C, D) Infiltration into adjacent bone and blood vessels could be observed (original magnification ×200).

CEOT is considered to be an expansile but locally invasive tumour with a high rate of recurrence. Local recurrence is mostly attributable to inadequate treatment[13]. The clinical course is usually that of slow growth and uncommon recurrence, but radiographic evidence of poorly circumscribed borders should suggest the need for removal of bone to ensure tumour-free margins[9]. Maxillary CEOTs should, however, be treated more aggressively, as they tend to grow more rapidly and do not usually remain well confined[2]. The present case, exhibiting clear evidence of malignant transformation, was treated more aggressively, with bilateral partial maxillary resection involving the affected teeth and the margin of the healthy bones. Although the patient showed no sign of recurrence after a 2-year follow-up period, long term follow-up is necessary as the biological behaviour of this rare form of odontogenic tumour showing malignant transformation is yet to be determined.

Table 1 Reported cases of malignant CEOT or CEOT showing microscopic features of potential malignant behaviour

Reference	Age (y)	Sex	Location	Duration (y)	Invasion into the neighbouring tissues	Clinical evidence of metastases	Radio-graphic findings	Treat-ment	Length of follow-up (y)	Recur-rence
Basu et al[3]	75	M	Mandible	62	Yes	Yes	A multilocular cystic lesion	Mandibular resection	2	2 years later
Veness et al[4]	64	F	Mandible	-	Yes	Yes	A well-defined multilocular radiolucency featuring particulate calcification	Segmental mandibulectomy and supraomohyoid neck dissection	1	No
Cheng et al[5]	83	F	Mandible	A few months	Yes	No	A well-defined multilocular radiolucency	Mandibular resection	10/12	No
Kawano et al[6]	54	M	Mandible	-	Yes	Pulmonary metastases	A well-defined lesion with a mixture of radiolucent and radiopaque areas	Segmental mandibulectomy	2	No

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