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CASE REPORT

Odontogenic ghost cell tumour with clear cell components: clear cell odontogenic ghost cell tumour?

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A case of odontogenic ghost cell tumour (OGCT) with clear cell components was encountered in the mandible of a 63-year-old man. The tumour revealed ameloblastomatous-type epithelial components accompanied by clusters of ghost cells and dentinoid juxtaposed to the odontogenic epithelium. In addition, some areas of the tumour tissue showed sheets and islands of clear, glycogen containing epithelial cells, which were separated by a thin fibrous connective tissue stroma. Both ameloblastic and clear cells exhibited positive immunoreactivities for cytokeratin 19 and AE1/3. It is not known whether this tumour represents a clear cell change of a pre-existing OGCT or a separate and distinct neoplasm derived *de novo* from the odontogenic epithelium. This tumour was given the term 'clear cell OGCT' because it captures the clear cell components, which is one of the most prominent distinguishing features of the tumour.
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A 63-year-old Korean man visited to the Department of Oral and Maxillofacial Surgery, Chosun University Dental Hospital, in March 2000, with a painless swelling in the anterior mandibular edentulous alveolar ridge. The patient had undergone four anterior mandibular tooth extraction 20 years prior. He had first noticed the mass 10 years prior. The mass grew slowly until this time. Physical examination revealed an expansion of the buccal and lingual cortical plates in the anterior mandible. Oral examination disclosed a firm to indurated tumour mass in the floor of mouth, measuring 4 cm × 3 cm. There were neither tenderness nor mucosal ulcerations. Regional lymphadenopathy and paresthesia of the lower lip were not apparent. A panoramic and occlusal radiogram showed a relatively well-circumscribed, multilocular radiolucent lesion that was expanding bucco-lingually. The inferior border of the mandible was intact. The pre-operative computed tomogram (CT) revealed a multilocular soft tissue density mass showing marked destruction of the anterior mandible. The tumour mass perforated the bucco-lingual cortical bone extending into the floor of mouth (Fig. 1). Cervical and submandibular lymph nodes were not enlarged. A provisional diagnosis of an ameloblastoma or a giant cell granuloma was tentatively made.

Microscopy of an incisional biopsy specimen taken prior to the definitive surgery showed the tumour tissue to be composed of sheets and small islands of odontogenic epithelium containing numerous ghost cells with focal calcification (Fig. 2A). The tumour was composed of a thin epithelial lining of columnar basal cells showing reverse polarity supporting cells resembling those of the stellate reticulum. In addition, dentinoid materials were also observed, which were in direct contact with the tumour cell nests (Fig. 2B). These were not calcified, were mostly amorphous in appearance, and there were no apparent dentinal tubules. Neither areas of necrosis nor atypical mitosis or pleomorphism were found. Therefore, the pathological diagnosis of an odontogenic ghost cell tumour (OGCT) was made.

After an incisional biopsy, marginal mandibulectomy with an iliac bone graft was performed in March 2000. At surgery, although no apparent tumour invasion into the genioglossus or geniohyoid muscles was detectable, a bucco-lingual expansion of the cortical plates with bone destruction was grossly noted. The lesion appeared somewhat cystic and contained serous fluid inside. There has been no evidence of recurrence or metastasis for 3 years and 2 months after surgery. The patient is currently being followed up. Microscopically, the resected specimen showed similar histological features to the incisional biopsy materials. In addition, the tumour tissue revealed sheets and islands of clear or finely granular epithelial cells, which were separated by a thin fibrous connective tissue stroma (Fig. 3A). Glomeruloid structures rimmed by a thickened hyalinized basement membrane were also observed (Fig. 3B). These clear cells appeared to have a gradual transition to

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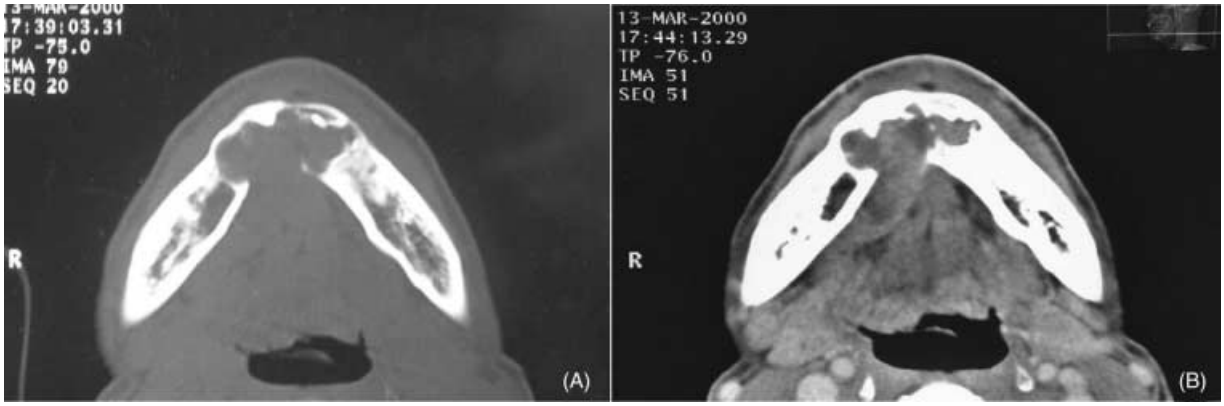

Figure 1 Computed tomography revealed a multilocular soft tissue density mass of the anterior mandible extending into the floor of mouth (A: bone level; and B: soft tissue level).

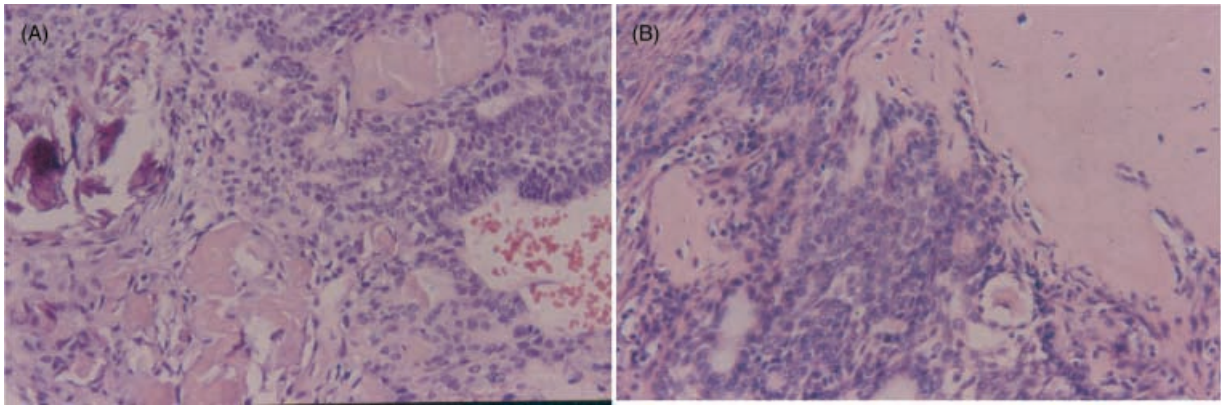

Figure 2 (A) Tumour composed of sheets and islands of odontogenic epithelium, including numerous clusters of ghost cells with focal calcification (×200). (B) Amorphous dentinoid deposition juxtaposed to the ameloblastic epithelium (×100).

ameloblastic cells in some areas. Mitotic figures or cellular and nuclear atypism of the tumour cells were rarely observed. The clear cells showed mild periodic acid-Schiff staining, but mucin stain was negative. Both ameloblastic and clear cells showed positive immunoreactivities for cytokeratin AE1/3 and cytokeratin 19 (Fig. 3C). S-100 protein was not detected in the tumour cells.

Comments

Diagnostic confusion prevails with regard to uniform and proper designation of an OGCT. The OGCT, also referred to as a dentinogenic ghost cell tumour, is known as a solid variant of the calcifying odontogenic cyst (COC), although there is confusing and controversy regarding the integration or segregation of these two lesions (1, 2). There are many histological features in common with an ameloblastoma, but an OGCT has characteristic ghost cells and dentinoid (1, 2). This may arise from a pre-existing COC or *de novo*. The tumour is a locally aggressive and a malignant tumour with similar features has also been described (2, 3). The case in this report is believed to fulfil the criteria of OGCT based upon the histological findings of ameloblastomatous-type epithelial components together with clusters of ghost cells and dentinoid intimate association with the odontogenic epithelium. Although this case was grossly cystic, no epithelial lining typical to COC could be found in the microscopic specimens examined. The most interesting aspect of this lesion was the presence of prominent clear cell components. To our knowledge, this distinctive tumour with clear cell components does not appear to have been reported previously.

Odontogenic neoplasms with significant clear cell components are quite uncommon. Several investigators (4–7) have regarded a clear cell neoplasm of an odontogenic origin to be potentially malignant, and is best termed a 'clear cell odontogenic carcinoma' (CCOC). However, in the current WHO classification (1992) (8), clear cell odontogenic tumour (CCOT) is defined as a benign but locally invasive neoplasm. In the present case, clinical data, including a radiographic examination, did not indicate any malignant features. This case was diagnosed 20 years after a tooth extraction at the same site. However, it is not clear whether this tumour was present before the extraction. While the presented tumour had clear cell components, it showed

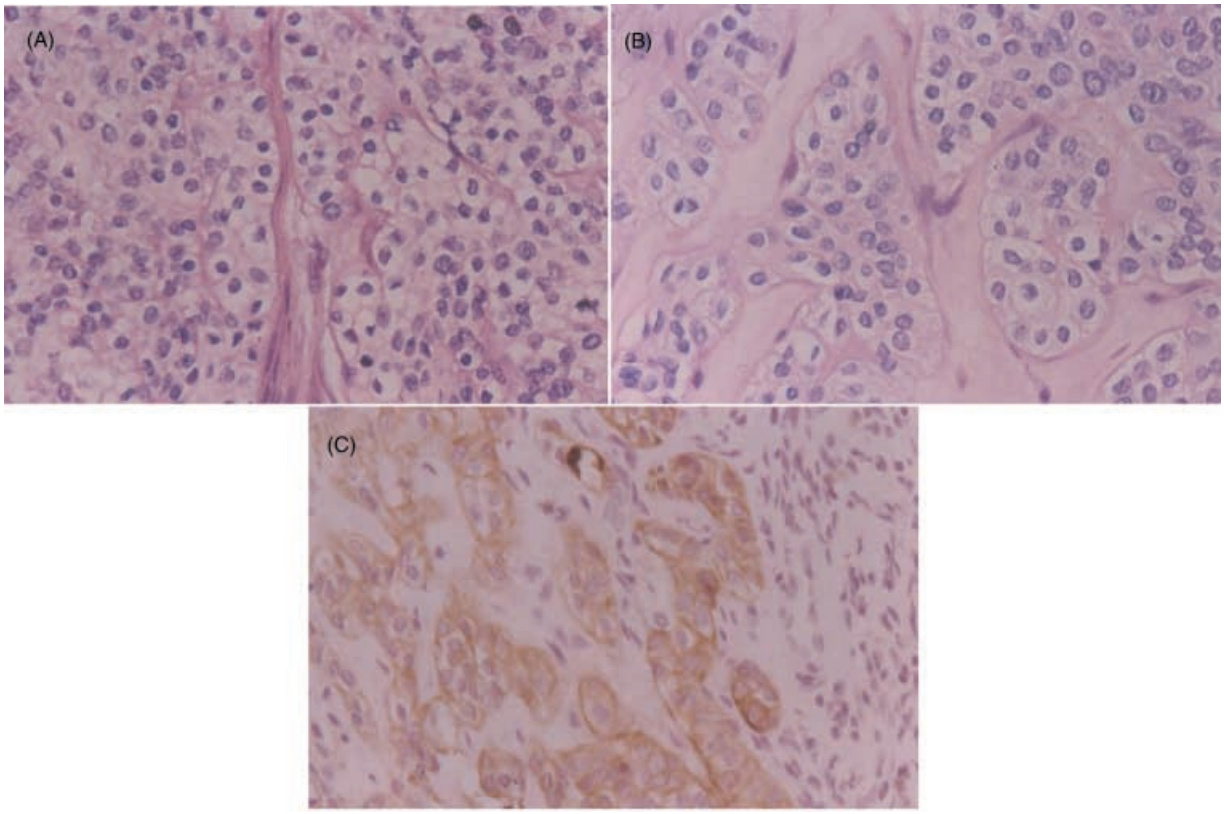

Figure 3 (A) Tumour consisted of sheets and islands of clear cells separated by a thin fibrous stroma (×100). (B) Glomeruloid structures rimmed by a thickened hyalinized basement membrane (×200). (C) Clear cells showed a positive immunoreactivity for cytokeratin 19 (×200).

neither cellular anaplasia nor recurrence. Nonetheless, clear cells were one of the main epithelial components of this tumour. As the emerging evidence suggests that all of odontogenic neoplasms showing notable components of clear cells likely represent a low-grade malignancy (7), the tumour was considered to have at least a low-grade malignant potential. Local recurrence or metastasis has not been found, but a close follow-up is necessary.

One would have to speculate about its pathogenesis. In the presence of a transion from the clear to ameloblastic cells, we could exclude the possibility that the lesion represents a subtype of a so-called hybrid odontogenic tumour of OGCT and CCOC. Recently, Kumamoto et al. (4) and Miyauchi et al. (9) reported CCOT with dentinoid induction. Moreover, a case of CCOC with ghost cells and inductive dentin formation was described (10). Those studies suggested that some CCOT possess epithelial–mesenchymal inductive capacity (4, 9, 10). In addition, CCOT noted histopathological evidence supporting ameloblastic differentiation and the presence of epithelial strands and cords suggestive of dental lamina (4). Whilst considering the histological variety of the dental lamina remnants, Wysocki et al. (11) mentioned that the clear cells might be immature odontogenic epithelial cells. In this case, both ameloblastic and clear cells showed positive immunoreactivities for cytokeratin 19 and AE1/3, indicating an odontogenic epithelial origin (4, 5, 9). Considering the outcomes of these previous reports (4, 5, 9, 10), both ameloblastic and clear cells might reflect an epithelial–mesenchymal interaction during tumourigenesis of the odontogenic epithelium. The ghost cells might result from the abnormal terminal differentiation towards the keratinocytes or the process of apoptosis of the odontogenic cells (3). However, inductive effects do not result in the formation of ghost cells. Therefore, it is believed that a CCOC with ghost cells and inductive dentine formation, which was described by Ariyoshi et al. (10), appears to be a clear cell variant of OGCT. Despite the histomorphological features that in part mimic CCOT or CCOC, it is not known whether this tumour represents a clear cell differentiation of a pre-existing OGCT or a separate and distinct neoplasm derived *de novo* from the odontogenic epithelium. Further case studies will be needed to clarify their true nature. Overall, the term 'clear cell OGCT' is preferred, because it captures the clear cell components, which is one of the most prominent distinguishing features of the tumour.

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