Clinico-Pathologic Conference: Case 5

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Clinical Presentation

A 46 year-old Korean man presented with a 2 month-history of a painful swelling on his left maxillary gingiva. Intraoral examination demonstrated a gingival swelling around the left lateral incisor and canine of the maxilla. The swelling was 4 cm in diameter, exhibiting redness and tenderness on palpation. The left central incisor and the lateral incisor were extruded with slight mobility. Panoramic and periapical radiographs revealed a periapical radiolucency extending from tooth #9 to 11, with radio-opaque foci (Figs. 1, 2). CT view showed an expansile lesion thinning the cortex of the anterior maxilla (Fig. 3).

Differential Diagnosis

Based on the clinical and radiological description, the lesion was a painful maxillary swelling of short duration and presented as an ill defined mixed radiolucent lesion with radio-opaque foci. A single radio-opaque focus had a radio-density similar to dental hard tissues, mainly dentine. A wide range of differential diagnoses including, inflammatory lesions such as osteomyelitis, non-odontogenic malignancies such as chondrosarcoma, osteosarcoma and metastatic tumours as well as odontogenic malignancies namely, ameloblastic fibro odonto/dentino sarcoma or

ghost cell odontogenic carcinoma which present as ill defined mixed radiolucent/radio-opaque lesions can be considered. In addition, benign non-odontogenic tumours such as cemento-ossifying fibroma or benign odontogenic tumours containing hard tissues namely calcifying epithelial odontogenic tumour (CEOT), calcifying cystic odontogenic tumour, adenomatoid odontogenic tumour (AOT) and dentinogenic ghost cell tumour (DGCT) can also be considered in the differential diagnosis.

The clinical description indicated a rapidly enlarging painful lesion, however, no mucosal ulceration which is usually seen associated with a rapidly enlarging lesion was observed. In addition, the lesion had displaced the root of the canine, indicating a fairly long standing lesion. Although, malignancy of odontogenic origin containing dental hard tissue is a possible diagnosis, discrepancies in the clinical and radiological description does not allow the exclusion of locally aggressive benign non-odontogenic tumours and odontogenic tumours containing hard tissues such as CEOT and DGCT. Benign non-odontogenic tumours such as cemento-ossifying fibroma were excluded as radiologically it contains a well defined radiolucent rim indicating the capsule which was not evident in the present lesion. In addition, although AOT predominantly occurs in the anterior maxilla, clinical description of the aggressive lesion described in the present case did not fit with the recognized behaviour of AOT, which is non aggressive. Moreover, as malignancy of odontogenic origin containing dental hard tissue is very rare, with only few cases documented in literature, a locally aggressive but benign odontogenic tumour containing dental hard tissue is the most likely diagnosis.

Absence of associated signs such as lymphadenopathy, fever, leukocytosis and predisposing conditions such as trauma, Paget's disease, Diabetes etc., as well as occurrence of the lesion in the maxilla, which has a good blood supply

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Fig. 1 Panoramic radiograph

Fig. 2 Periapical radiograph

exclude the possibility of chronic suppurative osteomyelitis. Discrepancies in the clinical and radiological description which also pointed towards a slow growing long standing lesion, was used to exclude other non-odontogenic malignancies such as chondrosarcoma, osteosarcoma and metastatic carcinoma. In addition, the fact that osteosarcomas and metastatic malignancies commonly occur in the mandible as well as the age of the patient could also be used exclude above mentioned lesions.

Diagnosis and Discussion

The patient was initially treated with a conservative surgery under the provisional diagnosis of calcifying

Fig. 3 Axial CT view

odontogenic cyst. Grossly, submitted specimens were fragmented soft tissue containing an amount of calcified materials. Calcified material crumbled upon application of pressure. The cross-sectional surface of the specimens was solid without cystic spaces.

Microscopically, the lesion demonstrated ameloblastomatous epithelial proliferation in a mature connective tissue stroma. Epithelial islands or sheets showed peripheral palisaded cells and central stellate reticulum-like cells. Numerous ghost cells were present associated with the proliferative epithelial islands and also as aggregates in the stroma (Fig. 4). In the epithelial islands, a part of stellate reticulum-like cells were transforming into ghost cells. In the stroma, foreign body reaction around the ghost cells was also detected. Dystrophic calcification was often seen within the aggregates of ghost cells (Fig. 5). Amorphous, acellular materials termed dentinoid were frequently detected in close contact with the epithelial islands or ghost cells, as well as in the surrounding stroma (Fig. 6). Based on the histopathologic findings, a final diagnosis of dentinogenic ghost cell tumour was made. The patient was under the follow-up instead of a further resection. There was no sign of recurrence at 9 months post surgery.

Dentinogenic ghost cell tumour (DGCT) was formerly considered as a solid variant of calcifying odontogenic cyst (COC). In 1981, the name of DGCT was proposed first by Praetorius et al. [1] who tried to resolve the question on the cystic or neoplastic nature of the COC. Also, several other names, such as calcifying ghost cell odontogenic tumour [2], dentinoameloblastoma [3], and epithelial odontogenic ghost cell tumour [4], had been suggested. In addition to

Fig. 4 Numerous ghost cells either associated with ameloblastomatous epithelial proliferation or in the stroma

Fig. 5 Ghost cells undergoing calcification

Fig. 6 Dentinoid

terminology, there has been some controversy regarding the classification of this group of lesions. According to a recent WHO classification of odontogenic tumour, COC was re-named by Praetorius and Ledesma-Montes as calcifying cystic odontogenic tumour (CCOT) and ghost cell odontogenic tumours were classified into three entities [5]. The first, the CCOT, is characterized by a well-defined, cystic, painless, slowly growing neoplasm that rarely recurs. The second, the DGCT, is a locally invasive neoplasm which shows more aggressive behavior and recurrence. The third entity is a malignant counterpart of CCOT and DGCT, named as ghost cell odontogenic carcinoma (GCOC). In 2008, international collaborative study on ghost cell odontogenic tumours was published [6]. Under the WHO guideline, the authors analyzed 122 cases of CCOT, DGCT, and GCOC from 14 institutions in Mexico, South Africa, Denmark, the USA, Brazil, Guatemala and Peru. This study attempted to clarify the clinic-pathologic features of the three entities and propose a useful classification under the WHO classification guidelines. And then, they suggested slightly modified classification from the original one by Praetorius et al. which was very simple and needed only minimal modifications to incorporate all the reviewed cases and those previously reported (Table 1). CCOT was classified into 4 subtypes; 3 original subtypes (type 1–3) and additional the fourth (type 4). DGCT was subdivided into two types: central (type 1) and peripheral (type 2). Classification of the ghost cell odontogenic tumours was completed with adding the malignant counterpart GCOC, which was classified into 3 subtypes.

Since the first description of DGCT by Fejerskov and Krogh although they used the term “calcifying ghost cell odontogenic tumor” [2], approximately 32 cases of DGCT have been reported in English literature. In the recent review of DGCT [7], patients ranged in age from 12 to 75 years, with the mean age of 40.27 years. The mean age of DGCT is higher than that of CCOT [6]. There was no clear predilection for sex in the recent review [7], whereas a slight predilection for men was documented in the WHO book published in 2005 [5]. Although DGCT may occur in any tooth-bearing area of the jaws, their review demonstrated a slight predilection for the mandible [7]. Radiographs show a well-defined, mostly unilocular radiolucent to mixed radiolucent/radiopaque appearance depending on the amount of calcification [5]. However, multilocular appearance has been also reported at least 5 cases [7]. Displacement and mobility of adjacent teeth may be observed and root resorption of involved teeth is a common finding [5]. Histologically, the presence of ghost cells within the proliferative ameloblastomatous epithelium is the essential characteristic for the diagnosis. It contains variable quantities of dentinoid in the surrounding stroma, as well as in close contact with the epithelial islands or

Table 1 Classification of the ghost cell odontogenic tumours by Ledesma-Montes et al. [6]

Calcifying cystic odontogenic tumour (CCOT)	
CCOT type 1	Simple cystic CCOT
CCOT type 2	Odontoma-associated CCOT
CCOT type 3	Ameloblastomatous proliferating CCOT
CCOT type 4	CCOT associated with benign odontogenic tumours other than odontoma
Dentinogenic ghost cell tumour (DGCT)	
DGCT type 1	Central, solid, aggressive variant
DGCT type 2	Peripheral, less aggressive variant
Ghost cell odontogenic carcinoma (GCOC)	
1. GCOC arising ‘ <i>de novo</i> ’	Not associated with a previous DGCT or CCOT, but with area suggesting DGCT
2. GCOC ex-CCOT	GCOC arising from a previous CCOT
3. GCOC ex-DGCT	GCOC arising from a previous DGCT

ghost cells. Also, dysplastic calcification may be found within the aggregates of ghost cells. The prognosis of the DGCT seems to be depending on the treatment provided. The recurrence rate of DGCT after resection was reported up to 50% of reviewed cases with follow-up data [7]. As DGCT has a high recurrence rate after limited local resection, a wide local resection with an adequate safety margin appears to be the treatment of choice [7, 8]. The malignant transformation of the DGCT after several recurrences has been documented [9]. Therefore, patients with recurrent DGCT should be under the long-term follow-up. Further study of many more cases of DGCT is necessary to clearly define its nature, clinical behavior and prognosis.

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