Malignant transformation of calcifying cystic odontogenic tumour – a review of literature

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Calcifying cystic odontogenic tumour (CCOT) has been classified as an odontogenic tumour. Ghost cell odontogenic carcinoma (GCOC) is the malignant counterpart of CCOT. This paper aims to review the literature regarding malignant transformation of CCOT.

A literature search was done via the National Library of Medicine PubMed interface, searching for articles relating to malignant transformation of CCOT. From these articles, references were obtained, and from their references lists, pertinent secondary references were also identified and acquired.

After reviewing the literature, we found 26 cases of GCOC which developed from CCOT. Malignant transformation of CCOT was seen more commonly in the maxilla. Histologically, changes such as increased nuclear/cytoplasmic ratio, atypical mitotic figures have been reported after malignant transformation. Immunohistochemical analysis has shown an increased expression of ki-67 and p53 in tumour cells.

Malignant transformation of CCOT, although rare, mostly takes place in recurrent and long standing cases.

Key words: calcifying cystic odontogenic tumour, malignancy, ghost cell odontogenic tumour, review, Gorlin cyst, odontogenic cyst.

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Introduction

A calcifying cystic odontogenic tumour (CCOT) is a heterogeneous group of lesions. It is a relatively rare odontogenic lesion which exists either as a cystic or a solid variant and is characterised by varied clinical, radiographical and biological features [1]. CCOT presents both central (intraosseous) and peripheral (extraosseous) locations. The central CCOT appears as a unilocular or multilocular destructive radiolucent lesion containing irregular calcifications [2]. Various terminologies used for CCOT include calcifying odontogenic cyst, Gorlin cyst, calcifying ghost cell odontogenic tumour and epithelial odontogenic ghost cell tumour, keratinizing calcifying odontogenic tumour [3].

In 2005, the World Health Organization Classification of Head and Neck Tumors reclassified CCOT as an odontogenic tumor and gave it the name of "calcifying cystic odontogenic tumor" [4]. CCOT has been classified as SNOMED code 930/0 [5].

Calcifying cystic odontogenic tumour is a developmental cyst of odontogenic origin and constitutes about 0.37% to 2% of all odontogenic tumours [2]. CCOT are cysts of primordial origin and not associated with crown of any impacted tooth. Cells believed to be responsible for the CCOT are rests of Serres [6]. CCOT may occur as a central lesion or as a peripheral lesion (although rare) [7].

Material and methods

A comprehensive review of the available literature relating to malignant transformation of CCOT was undertaken using Medline, PubMed, Google Scholar and SCOPUS in all languages. We used the following keywords for searching: calcifying cystic odontogenic tumour, malignancy and ghost cell odontogencic carcinoma from 2003–2013. We also used the "Related Articles" feature of PubMed to identify further references of interest within the primary search. These articles were obtained, and from their references lists, pertinent secondary references were also identified and acquired. The process was repeated until no further new articles could be identified. The abstracted literature was also reviewed. The type of manuscripts included was case reports and case series.

Results

Ghost cell odontogenic carcinoma (GCOC) is a rare tumour which is a malignant counterpart of CCOT [8]. Ghost cell odontogenic carcinoma may arise as a denovo tumour or from previously existing CCOT [9]. Ghost cell

odontogenic carcinoma is seen to arise from CCOT after multiple recurrences [10]. One third cases of ghost cell odontogenic carcinoma are reported to be derived from a preexisting CCOT and malignant transformation may take several years [11]. However some of the ghost cell carcinoma may develop without history of CCOT [12–14].

Recurrent CCOT and GCOC are more common in the maxilla [8, 15]. Painful swelling with local paraesthesia is the most common symptom of ghost cell odontogenic carcinoma [12]. Some authors reported of infiltrative growth, root resorption and tooth displacements in cases of GCOC [16, 17]. Radiographic examinations showed a mixed radiolucent-radiopaque lesion with a moderately defined border. CT scan demonstrated bone expansion and bone destruction with irregularly shaped calcified inside the lesion. Magnetic resonance images showed a mass with high signal intensity [8].

Histopathological examination revealed acystic or solid appearance. Li *et al.* reported an ameloblastoma-like epithelia with prominent features being presence of lots of ghost cells, dysplastic uncalcified dentin or osteodentin. Increased nuclear/cytoplasmic ratio with 1–2 nucleoloi and atypical mitotic figures were also reported [18]. According to Motsugi *et al.*, tumour cells densely proliferates the epithelial component and the nucleus of tumour cells were enlarged and variable in size [11].

Immunohistochemical analysis of GCOC by Motossugi *et al.* revealed that 70% of tumour cells were reactive for p53 and ki-67 index was 4% to28% [11]. Expression of ki-67, MMP-9 and TIMP-1 was stronger in GCOC when compared to CCOT [19]. MMP-9 in stroma is associated with invasive ability of CCOT and GCOC and ki-67 is associated with increased cellular proliferation. According to Gomes *et al.*, there is a variable expression of syndecan-1 in stellate reticulum, stromal cells and basal cells of CCOT and GCOC and might be associated with the biology of these tumors [20].

A total of 8 cases have been reported in the literature from 2003-2013 where ghost cell odontogenic carcinoma has probably developed from CCOT. These cases are enlisted in Table 1 [8, 13, 14, 16–18, 21, 22].

Some cases of metastasis have been reported after GCOC. Of the 29 patients diagnosed, 5 died of local recurrence and metastasis to brain and lung has been reported [13]. The most commonly employed treatment was surgery with wide excision. In some cases radiotherapy and chemotherapy has been performed but their effectiveness was not evaluated [8].

Conclusions

After reviewing the literature we conclude that recurrent and long standing case of CCOT can undergo malignant transformation. GCOC, the malignant form of CCOT can metastasize and can even lead to deaths. So it is mandatory to follow up the patients with CCOT for possible eventual development of malignant counterparts.

Authors declare no conflict of interest.

Table 1. Malignant transformation of CCOT

Author (year)	Number of cases
Li and Yu (2003) [21]	1
Cheng *et al.* (2004) [16]	1
Goldenberg *et al.* (2004) [22]	1
Nazeretian *et al.* (2007) [13]	1
Sun *et al.* (2007) [14]	1
Li and Gao (2009) [18]	1
Arashiyama *et al.* (2012) [8]	1
Mokhtari *et al.* (2013) [17]	1

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