Peripheral Clear Cell Variant of Calcifying Epithelial Odontogenic Tumor: Case Report and Review of the Literature

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Abstract Calcifying epithelial odontogenic tumor (CEOT) is classified as an uncommon, benign, odontogenic neoplasm that is exclusively epithelial in origin. Of all reported cases, peripheral tumors account for 5–6 %, among which clear cell variants are still rare. A rare case of peripheral clear cell variant of CEOT occurring in the mandibular gingiva of a 47-year-old female is presented.

Keywords CEOT · Peripheral · Clear cell

Introduction

Calcifying epithelial odontogenic tumor (CEOT) is an uncommon lesion that accounts for less than 1 % of all odontogenic tumours. By far the most common CEOT location is intraosseous, but it also may be extraosseous. The extraosseous or peripheral variant was first observed by Pindborg in 1966, represents approximately 6 % of the total cases of CEOT [1]. Under microscopic examination, the classical pattern of CEOT is a combination of cords, nests, or sheets of polyhedral epithelial cells, amyloid-like deposits, and concentric calcified structures (Liesegang rings). Clear cell variant of CEOT (CCEOT) was first described by Abrams and Howell [2]. It is characterized by

polyhedral epithelial cells alternating with huge epithelial cells with a clear, foamy cytoplasm; distinct cell borders; moderate variation in size; some vacuolated nuclei; and no extreme hyperchromatism or bizarre nuclei [1].

In this case report, we describe an interesting case of a peripheral CCEOT in the mandibular gingiva. This case adds to the very few cases of peripheral CCEOT reported in the literature.

Case Report

A 47-year-old female was referred for evaluation of an asymptomatic gingival swelling of 8 months duration. Clinical examination revealed a well defined, non-tender, non-ulcerated, smooth surfaced, roughly oval, firm, nodular growth on the lingual gingiva, extending from the permanent mandibular left lateral incisor to the first premolar, measuring about 1 cm × 1 cm in size, and having the same colour as that of the adjacent normal mucosa (Fig. 1). Oral hygiene was fair. No mobility of teeth was observed in the area of concern. Intra-oral periapical radiograph revealed no alveolar bone loss (Fig. 2). There was no report of local trauma and the patient presented no para-functional habits. The patient's medical, family and social history was non-contributory.

Considering the benign nature of the lesion based on the clinical and radiologic findings, an excisional biopsy was performed under local anaesthesia. On reflecting the mucogingival flap, a well circumscribed tumor mass, easily separable from the surrounding tissues was found. The mass was yellowish in colour, soft in consistency, roughly oval in shape and measured approximately 0.8 cm × 0.5 cm in size. Haematoxylin and eosin stained sections showed connective tissue stroma containing polyhedral, epithelial cells

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Fig. 1 Intraoral photograph showing growth present on the mandibular lingual gingiva

Fig. 2 Intraoral periapical radiograph showing no evidence of bone resorption

with dense eosinophilic cytoplasm, hyperchromatic nuclei and prominent intercellular bridges admixed with cells exhibiting a clear vacuolated cytoplasm. Foci of calcification were also seen (Fig. 3). Areas of eosinophilic, homogenous material representing amyloid deposition (Fig. 4) was confirmed by the ‘apple-green birefringence’ of the Congo red stain under polarized light microscopy (Fig. 5). Immunohistochemically, the tumour cells were immunopositive for pancytokeratin (clone: AE1/AE3, Dako, Carpinteria, CA, dilution 1:500) (Fig. 6), ck14 (clone: NCL-L-LL002, Novocastra Laboratories, Newcastle, England, dilution 1:200) (Fig. 7) and negative for S-100 protein (Dako, dilution 1:10,000). Vimentin (clone: Vim 3B4, Dako, dilution 1:400) stained cell periphery or part of the cytoplasm, with a consistent but non-homogenous positivity (Fig. 8). Based on clinical, radiological, histopathological, and immunohistochemical findings, the case was diagnosed as a peripheral clear cell variant of calcifying epithelial odontogenic tumor (CCEOT). Six month post operative follow-up found no recurrence (Fig. 9).

Fig. 3 Photomicrograph showing polyhedral epithelial cells admixed with clear cells and amyloid like material (Haematoxylin and Eosin stain, $\times 100$)

Fig. 4 Photomicrograph showing amyloid like material stained bright red with Congo Red ($\times 100$)

Discussion

The peripheral CCEOT is said to arise from epithelial rests of dental lamina or basal cells of the gingival surface epithelium [3]. It has been shown both histochemically and in electron microscopy, that the clear cells in CCEOT contain glycogen [4]. In CCEOT, clear cell areas may be a minor focal component or may constitute the majority of the tumor tissue [3]. In the present case, clear cell areas constituted the major portion of the tumor mass. The diagnosis of CCEOT is usually based on the finding of some areas of typical polyhedral epithelial cells within the tumor [3]. In peripheral CCEOT, calcification is minimal or may be totally absent [2]. Calcified material in small quantity was observed in the present case, but it was not in

Fig. 5 Photomicrograph showing apple-green birefringence of amyloid deposits in connective tissue as observed under polarized light (Congo red stain, $\times 100$)

Fig. 7 Photomicrograph showing tumor cell displaying immunopositivity for CK14 ($\times 100$)

Fig. 6 Photomicrograph showing tumor cells displaying immunopositivity for cytokeratin cocktail (AE1/AE3) ($\times 100$)

Fig. 8 Photomicrograph showing cytoplasmic positivity for vimentin in some tumoral cells ($\times 400$)

the form of Liesegang rings. CK14 is the main intermediate filament of odontogenic epithelium, and is observed in the dental lamina, in the reduced enamel epithelium and in almost all cell of the enamel organ [5]. In the present case, CK14 was detected in all cells. Vimentin positivity may suggest odontogenic epithelium in the early stage of dental germ development [5]. Kasper et al. [6] showed vimentin restricted to a brief ontogenetic phase in odontogenesis, the so called bell stage. Our findings were consistent with the findings of Crivelini et al. [5].

Although the gingiva is not a common location for salivary gland neoplasms, microscopically clear cell variants of salivary gland tumors should be included in the differential diagnosis of peripheral CCEOT [7]. In the present case, the presence of amyloid, calcifications, and

Fig. 9 Six-month post operative intraoral photograph

Table 1 Documented cases of Peripheral CCEOT in the literature

Sr. No.	Authors	Age (yrs)	Gender	N	Site	Jaw	Location	Size (cm)	Treatment	Follow-up	Year
1	Abrams and Howell [2]	16	F	1	Gingiva	Mn	Central- lateral incisor	0.5	Excision	FOD, 3 years	1967
2	Wertheimer et al. [9]	20	M	1	Gingiva	Mx	Lateral incisor-premolar	1.5	Excision	NR	1977
3	Ai-Ru et al. [10]	32	F	1	Gingiva	Mn	Premolar-molar	NR	Partial Resection	FOD, 10 years	1982
4	Houston and Fowler et al. [7]	64	M	1	Gingiva	Mx	Premolar	1.5	Excision	FOD, 4 years	1997
5	Houston and Fowler et al. [7]	27	M	1	Gingiva	Mn	Premolar	1.4	Excision	FOD, 4 years	1997
6	Orsini et al. [3]	32	M	1	Gingiva	Mx	Lateral incisor-canine	NR	Excision	FOD, 4 years	2000
7	Mesquita et al. [1]	48	F	1	Gingiva	Mx	canine	2	Excision	FOD, 30 months	2003
8	Anavi et al. [11]	27	M	1	Gingiva	Mn	Canine-premolar	1	Excision	FOD, 1 year	2003
9	Shetty et al. [13]	22	F	1	Gingiva	Mn	Lateral incisor-canine	2	excision	NR	2006
10	Habibi et al. [12]	70	F	1	Gingiva	Mx	Lateral incisor-canine	0.5	excision	NR	2009
11	de Oliveira et al. [14]	43	F	2	Gingiva	Mx	Premolar	2	Excision	FOD, 1 year	2009
						Mn	Incisor	2			
12	Shetty et al.*	47	F	1	Gingiva	Mn	Lateral incisor-first premolar	1	excision	FOD, 6 months	2014

cm centimetres, F female, FOD free of disease, M male, Mx maxilla, Mn mandible, N number of lesions per patient, NR not reported, yrs years

* Present Report

absence of S-100 protein expression; ruled out the diagnosis of clear cell salivary gland tumors.

Hicks et al. suggested that the presence of clear cells in CEOT may confer a more aggressive behaviour to the lesion [8]. In the twelve cases of peripheral CCEOT reported in the literature [1–3, 7, 9–14], including the present case, the presence of clear cell component was not associated with aggressiveness. However, too few cases of peripheral CCEOT have been described to date to reach a clear conclusion regarding the impact of the clear-cell population on the tumors biologic activity. The mean age of the patients with peripheral CCEOT is 37.33 years (range 16–70 years) at the time of diagnosis, and the male to female ratio is 5:7. All cases of peripheral CCEOT were located on the gingiva, with a preference for the anterior to bicuspid areas (11 out of 12 reported cases) (Table 1).

Microscopic findings of CCEOT may be confused with clear cell carcinomas and metastatic renal cell carcinomas which are composed of a monomorphic population of clear cells and whenever a hyalinising lesion is found, its stroma may be confused with the amyloid like material found in CEOT lesions. The microscopic fields characteristic of CEOT, exhibiting islands of polyhedral epithelial cells with pleomorphic nuclei in a hyalinised stroma with extracellular amyloid and concentric calcifications, can be used to distinguish between these lesions [14]. In addition, an

extraosseous clear cell odontogenic carcinoma has not yet been reported. In our case, differential diagnosis from renal metastasis was based on the absence of mitotic figures or atypical cells.

Abrahão et al. [15] reported a unique case of bilateral peripheral CEOT presumptively diagnosed as bilateral pyogenic granuloma that was surgically excised without bone curettage and recurred bilaterally one year later. Although peripheral CEOT is a nonaggressive tumor and recurrence is rare, a favourable prognosis depends on complete excision of the tumor. Furthermore, malignant transformation has not been reported. Recurrence is low and the prognosis is excellent.

This article shows that even though being an extremely rare neoplasm the peripheral CCEOT should be included in the differential diagnosis of localized gingival enlargement mimicking oral hyperplastic/reactive lesions. Every surgically excised gingival mass must be histopathologically examined to rule out the possibility of a neoplasia.

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