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CASE REPORT

Clear cell Cystic Variant of Calcifying Epithelial Odontogenic Tumor

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Abstract Calcifying epithelial odontogenic tumor (CEOT) is a solid, locally aggressive, benign odontogenic neoplasm characterized by sheets and nests of polyhedral epithelial cells exhibiting eosinophilic and less often clear cytoplasm, occasional nuclear pleomorphism without mitotic activity, calcifications, and deposits of amyloid. A cystic variant has been reported only twice. Herein, we present an additional example of cystic CEOT occurring in a 31-year-old male and featuring clear cell epithelial lining with deposits of amyloid and osteodentin.

Keywords Calcifying epithelial odontogenic tumor · Pindborg tumor · Clear cell · Cystic · Amyloid · Osteodentin

Introduction

Initially described by Pindborg in 1955, calcifying epithelial odontogenic tumor (CEOT) is a rare benign odontogenic neoplasm, usually painless and slow growing, but occasionally locally aggressive. Rare peripheral and malignant cases of CEOT have been reported [1–10]. CEOT probably originates from either the reduced enamel epithelium [11, 12], stratum intermedium or the cells of the dental lamina [13]. Radiographically, it presents as a unilocular or multilocular radiolucency with occasional opacities that gradually increase in size. Histologically, it features polyhedral epithelial cells with eosinophilic cytoplasm arranged in sheets and islands and invested in a fibrous connective tissue stroma. Nuclear atypia, however without mitotic activity, is appreciated. Other characteristics include the presence of extracellular eosinophilic material that stains positive for amyloid, as well as dystrophic calcifications [14–17]. Clear cell and cystic variants have also been described [4–6, 18–27]. Herein, we present an additional example of the cystic variant, characterized by a clear cell lining.

Case Report

A 31-year-old male presented with a rapidly growing, asymptomatic left posterior mandibular mass of 2 months duration. Extraoral examination revealed facial asymmetry with diffuse unilateral swelling in the middle and lower third of the face. Intraorally, the overlying mucosa was ulcerated. An ortho pantomogram featured a mixed radiopaque/lucent lesion extending from the distal root of the lower left first molar to the ascending ramus, eroding the cortex, and resorbing the roots of the second and third molars (Fig. 1a). A subsequent CT further characterized the lesion as a mixed lucent/opaque expansile lesion measuring approximately 3.0 × 3.0 × 2.0 cm, that focally eroded the buccal and lingual cortical plates (Fig. 1b). The lesion was excised. Macroscopically, the specimen was

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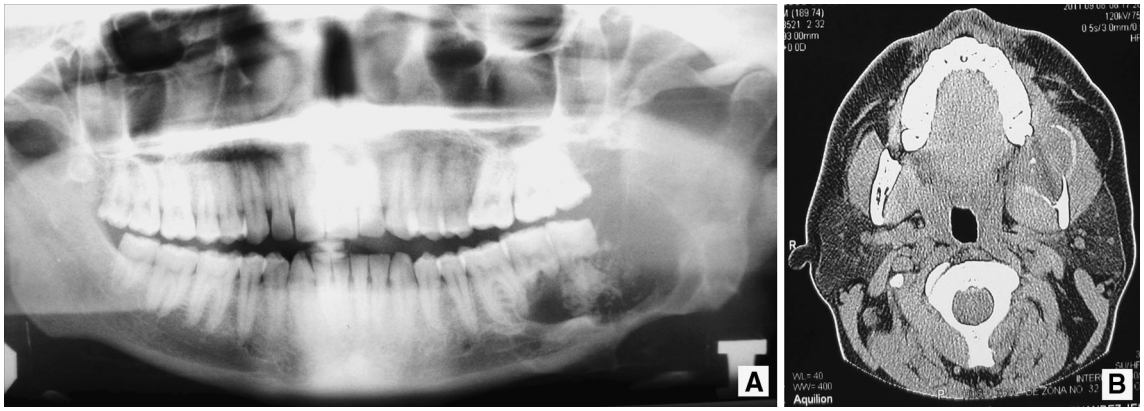

Fig. 1 **a** Orthopantomogram. Unilocular mixed radiopaque/lucent, expansile and locally aggressive lesion, located in the left posterior mandible and ascending ramus; **b** CT. Osteolytic lesion is seen with expansion of surrounding tissue and a central area isodense to bone

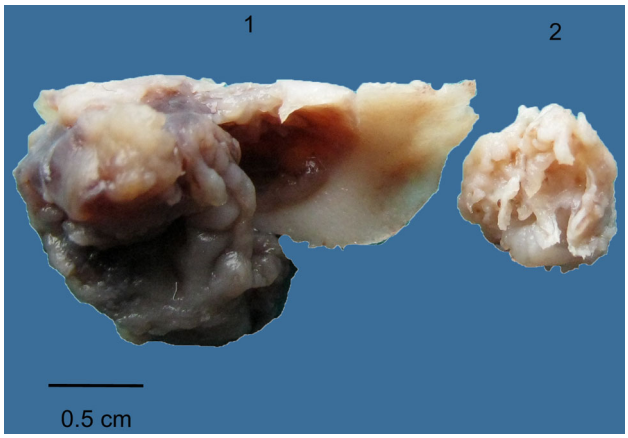

Fig. 2 Gross features. Portion **1** features cystic cavity with projections into the lumen. Portion **2** features calcified spherical and irregular mass

composed of two, irregular in shape, brown and white, fragments, measuring 3.0 × 1.4 × 1.4 cm in aggregate (Fig. 2). One of them was cystic and the other was composed of calcified material. The latter apparently derived from the lumen of the cyst.

Microscopically, the cystic portion of the lesion featured odontogenic epithelial lining characterized by cells with optically clear cytoplasm and centrally located round nucleus (Fig. 3a, b). Necrosis was observed in the superficial aspect of the lining. PAS histochemical stain revealed positive, diastase resistant intracellular granules and extracellular material (Fig. 3c). Eosinophilic hyalinized material, positive for Congo red and exhibiting apple-green birefringence after polarization was also appreciated (Fig. 3d). The calcified mass had the characteristics of osteodentin (Fig. 3e). Mixed with the calcified material there were clear cells that featured, occasionally, round eosinophilic globules consistent with "thanatosomes" (Fig. 3f). The diagnosis of clear cell cystic variant of CEOT was rendered. The patient was lost to follow-up.

Discussion

Up to now, there are only two examples of cystic CEOT [26, 27]. Table 1 summarizes the clinicopathologic features of the reported cases including the present case. Clinically, the present case is different from the other two in that, first, it was not associated with an impacted tooth and, second, it occurred in the mandible. Histogenetically, the cystic variant of CEOT in the two cases associated with impacted teeth most likely derived from reduced enamel epithelium or the lining of a cyst. The reduced enamel epithelium has been generally considered as the origin for conventional CEOT and it is well known that fifty percent of CEOTs are associated with impacted teeth [14, 15, 26]. It is also known that CEOT-like proliferations, regarded hamartomatous in nature [28], may be, infrequently, seen focally in the reduced enamel epithelial lining of otherwise pathologically unremarkable dental follicles. Interestingly, these proliferations can feature small amyloid deposits. Reduced enamel epithelium, as part of post maturation ameloblasts, has the ability to express odontogenic ameloblast-associated protein (ODAM) that is present in CEOT-amyloid [29–31]. Thus it is plausible that these proliferations may be the very early stage of CEOT.

Our case was highlighted by the presence of a clear cell epithelial lining with deposits of amyloid and the presence of osteodentin. It has been shown histochemically and ultrastructurally, that the clear cells contain PAS-positive diastase labile material consistent with glycogen [4, 5, 21, 24, 32]; however, glycogen deposition has been also ruled out [22]. The clearing is either the result of degeneration [18] or cytodifferentiation [32]. In our example, PAS diastase resistance was noted suggesting degenerative changes, since in some of the clear cells we observed cytoplasmic eosinophilic globules suggestive of thanatosomes that are reportedly diastase resistant [33, 34]. Furthermore, necrotic areas and degeneration of the epithelial

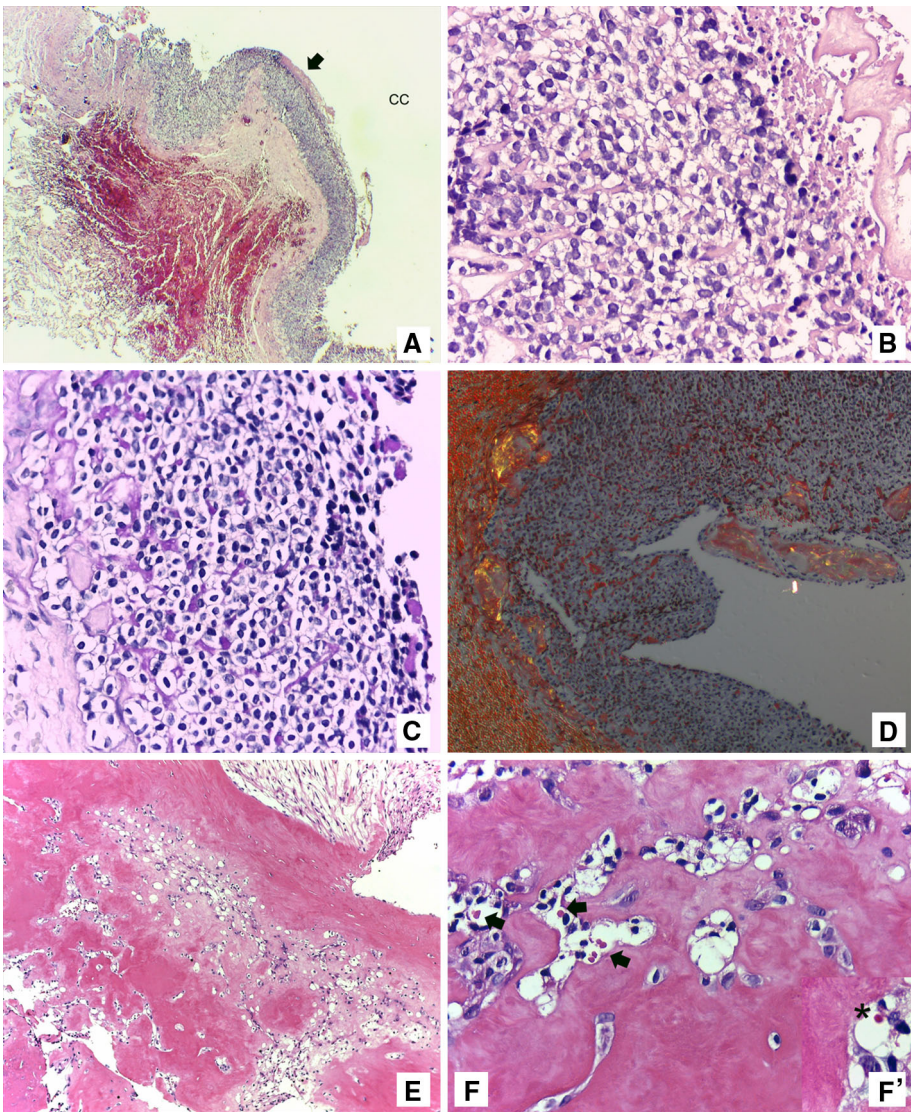

Fig. 3 **a** Cystic cavity (CC) lined by odontogenic epithelium of generally uniform thickness, with focal necrosis (*arrow*) (H&E ×40); **b** Clear cells in the cystic lining revealing intracellular and eosinophilic extracellular material (H&E ×400); **c** Positive diastase resistant deposits (PAS. diastase stain ×400); **d** Amorphous, eosinophilic hyalinized material exhibiting apple-green birefringence after polarization (*Congo red* stain ×100); **e** Calcified material with characteristics of osteodentin (H&E ×100); **f** Round eosinophilic globules consistent with "thanatosomes" (*arrows*) (H&E ×400) and f' "thanatosome" in detail (*asterisk*) (H&E ×1,000)

Table 1 Clinicopathological features of reported cases of cystic variants of calcifying epithelial odontogenic tumor (CEOT)

Case	Sex	Age (years)	Location	Radiographic findings	Histopathological findings
Gopalakrishnan et al. [26]	Male	15	Left maxilla	Unilocular radiolucency with radiopacities in association with impacted tooth #15	Cystic lining varying from focally thin, nonkeratinizing, stratified squamous epithelium to thickened epithelium with characteristics of CEOT.
Channappa et al. [27]	Male	30	Left maxilla	Unilocular radiolucency with calcifications in association with impacted tooth #13	Cyst lined by odontogenic epithelium showing a tendency towards stratification, majority with uniform thickness, with classic features of CEOT
Present case	Male	31	Left mandible	Unilocular radiopaque/lucent area, eroding the cortex and rhizolysis of teeth #17 y 18, without presence of impacted tooth	Cystic lining showed odontogenic epithelium with necrotic areas, featuring clear cells that revealed PAS positive diastase resistant deposits; and presence of osteodentin

lining was observed in the superficial aspect of the lining. Therefore, we consider that the cystic pattern observed in the tumor of our patient is the result of cystic degeneration of a solid CEOT. Conversely, Gopalakrishnan et al. [26] and Channappa et al. [27] agreed that cystic CEOT might represent neoplastic transformation of dental follicular

lining epithelium. Gopalakrishnan et al. [26] further argued that cystic CEOT could have developed from neoplastic transformation of the epithelial lining of a dentigerous cyst, since they observed in their example a cystic lining indistinguishable from that of a dentigerous cyst.

The presence of osteodentin in association with CEOT has not been described; nevertheless, osteodentin has been reported in other odontogenic tumors deriving only from odontogenic epithelium [35–37]. It is likely the result of a metaplastic process, as odontogenic ectomesenchyme is not present, and thus should not be interpreted as an induction phenomenon [38].

Differential diagnosis between clear cell variant of CEOT and other tumors showing clear cell differentiation in the jaws, such as metastatic tumors from kidney, thyroid, liver, colon, and prostate, clear cell odontogenic carcinoma and central mucoepidermoid carcinoma [4, 20, 21] is generally necessary; however, due to the histological characteristics found in our case, highlighted by the presence of amyloid, and the occurrence of osteodentin, the other tumors were excluded.

The adequacy of simple enucleation as management in patients with cystic CEOT has been suggested. Currently, conservative enucleation has been the treatment choice also for conventional CEOT [26, 27] with no recurrence reported on follow-up.

In summary, we reported a rare example of a cystic CEOT with presence of clear cells in the lining, and presence of calcified material resembling osteodentin.

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