Clear cell variant of intraosseous calcifying epithelial odontogenic tumor: a case report and review of the literature

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CEOT is a rare benign, but locally aggressive odontogenic tumor, and some authors have claimed that the biologic behavior of the clear cell variant is even more aggressive, with greater propensity to recur. We report a rare case of clear cell calcifying epithelial odontogenic tumor (CEOT) and discuss its possibly aggressive behavior.

A 40-year-old woman experienced an asymptomatic expansion of the left posterior mandible. After radiographic examination and biopsy, a block resection was performed. Histologic examination included analysis of Ki-67 reactivity as a marker of tumor growth activity. Ki-67 labeling was pronounced in the non–clear cell population in the tumor periphery but low in the central and clear cell portions. Clinical and radiographic follow-up 6 years after resection has not revealed any signs of recurrence. On the basis of a review of the literature and our own findings, there is no clear data to suggest that clear cell CEOT exhibits more aggressive behavior compared with conventional CEOT. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122: e125-e130)

Calcifying epithelial odontogenic tumor (CEOT) is a rare benign, but locally aggressive, odontogenic tumor first described by Pindborg in 1955.[1] It accounts for less than 1% of all odontogenic tumors[2] presenting as either an intraosseous (94%) or an extraosseous (6%) variant. Most frequently, it involves the posterior mandible and is often associated with unerupted teeth.[2,3] Intraosseous CEOTs are painless, slow-growing jaw expansions, often diagnosed as incidental findings at routine radiographic examinations in the dental office.[3,4]

Radiographically, the lesions may have different features, depending on their age. "Mature" lesions display unilocular or multilocular, "honeycombed" radiolucent areas, containing radiopaque foci of varying size and opacity that can cause a "driven-snow" pattern, whereas "earlier" lesions often appear more radiolucent.[2-4] The tumor is usually well circumscribed radiographically but may have irregular borders.[1,4]

Histologically, CEOTs are characterized by sheets, nests, or cords of polyhedral, eosinophilic epithelial cells. The nuclei are often prominent and show considerable variation in shape and size, although mitotic figures are rare.[2,5] Varying amounts of extracellular amyloid-like material are present, as well as calcified masses with a concentric Liesegang ring calcification pattern.[2,3]

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A rare variant of conventional CEOT is the clear cell type (CCCEOT). It has the classic features of CEOT but also containing a population of cells with clear, vacuolated cytoplasm. Some authors have claimed that the biologic behavior of the clear cell variant is more aggressive and that CCCEOT has a higher rate of recurrence compared with conventional CEOT.[2,6,7] However, this is still a matter of debate, since the number of well-documented tumors reported in the literature is small, and cases with long-term follow-up are few (Table I[2,5,8-28]). The aim of the current report is to describe the clinical, radiographic, and histologic findings of a case of mandibular intraosseous CCCEOT and to review its behavior.

CASE REPORT

Clinical findings

A 40-year-old woman experienced expansion of the left posterior mandible in Fall 2009 and was referred to the local Oral and Maxillofacial clinic at Sundsvall hospital, Sundsvall, Sweden. During examination, no extraoral swelling was observed. The patient had no pain, paresthesia, or loosening and deviation of teeth. Intraorally, an asymptomatic, firm swelling covered by normal oral mucosa was found on the left side of the mandible between the lateral incisor and the first molar. Radiographic examination revealed a tumorous process and was followed by a biopsy from the mid-portion of the tumor.

The patient was referred to the Departments of Oral and Maxillofacial Surgery and Ear, Nose and Throat Diseases at the Umeå University Hospital, Umeå, Sweden, for further preoperative clinical and radiographic examinations and operative treatment.

Radiographic findings

On panoramic examination, the tumor appeared as a radiolucency from the lateral incisor to the second molar and from the marginal bone to half the height of the mandible, with a

Table I. Clinical and histologic features of intraosseous clear cell calcifying epithelial odontogenic tumor (CCCEOT)

Reference	*Age/gender*	*Treatment*	*Follow-up*	*Size*	*Treatment recurrence; follow-up*	*Ki-67*	*Clear cells*
Abrams & Howell[8]	50 M	Enucleation	3 yr	1.2 cm			(+)
Anderson et al.[9]	68 F	Curettage	4 mo*	3 cm	Block resection; NR		(+)
Wallace & McDonald[10]	65 M	Excision	22 mo	NR			?†
Greer & Richardson[11]	37 F	Enucleation	13 mo	0.5 cm			+
Oikarinen et al.[12]	36 F	Enucleation	2 yr	10 cm			+†
Yamaguchi et al.[13]	36 M	Partial resection	2 yr	2.5 cm			+
Ai-Ru et al.[5]	64 F	Partial resection	2 yr	2 cm‡			+†
Asano et al.[14]	44 F	Partial maxillectomy	NR	NR			(+)
Schmidt-Westhausen et al.[15]	38 M	Resection	2 yr	2.5 cm			+
Hicks et al.[2]	59 F	Resection	3 yr	3.8 cm			
Kumamoto et al.[16]	14 F	Partial resection	13 yr*	NR	Partial maxillectomy; 1 yr†		+
Anavi et al.[7]	27 M	Excision	1 yr	1 cm		Low	+
Germanier et al.[17]	44 F	Enucleation	1 yr	NR			? †
Motasham et al.[18]	18 M	Excision	NR	3.5 cm			? †
Rangel et al.[19]	65 M	Excision	2 yr	1.5 cm			(+)
Sahni et al.[20]	52 M	Partial maxillectomy	3 yr	3 cm			(+)
Badrashetty et al.[21]	36 F	Curettage	10 mo*	3.5 cm	Partial maxillectomy; 2 yr		? †
Chen et al.[22]	59 F	Excision	2 yr	3 cm		Low	+
Azevedo et al.[23]	6 cases	NR	NR	NR			(+)
Urias Barreras et al.[24]	31 M	Excision	NR	3 cm			+
Mutalik et al.[25]	27 M	Incision biopsy	NR	2 cm‡			? †
Mariano et al.[26]	51 F	Enucleation	8 yr	4 cm‡			(+)
Afrogeh et al.[27]	37 F	Excision	18 mo	2 cm			§
Turatti et al.[28]	25 F	Curettage	2 yr	3 cm		2%	(+)
Present case	40 F	Block resection	6 yr	4 cm		10%	+

+, Significant number of clear cells; *(+)*, few clear cells; *?*, portion of clear cells not stated; *NR*, not recorded.
*Recurrence.
†Inadequate documentation.
‡Size estimated, inadequate documentation.
§Possibly artefact.

total size of approximately 4 × 2.5 cm (Figures 1A−1D). Within the radiolucency, there were numerous small radiopacities with a "driven-snow" appearance. Cone beam computed tomography revealed a unilocular lesion with multilobular borders expanding both cortices. Although the lesion was mostly well circumscribed, it had focal perforations involving both the buccal and lingual cortical borders, and there was also a suspected extraosseous extension into soft tissue. The canine tooth had signs of root resorption.

In the preoperative analysis after confirmed diagnosis, the tumor was identified on the intraoral radiographs that had been taken by the patient's regular dentist 14 years ago. At that time, the size of the tumor had been approximately 0.8 × 1 cm (Figure 2). Numerous small radiopacities had been present, but both the density and the extension of the calcifications had been less pronounced than they were at the time of discovery.

Surgical procedure

The surgical procedure was performed with the patient under general anesthesia. A soft tissue vestibular and lingual incision was made from the median incisor to the second molar, and a mucoperiosteal flap was reflected. Special care was taken to identify the mental foramen. The tumor was well defined within the alveolar process and separated from the mental foramen.

The resection, using a surgical saw, was performed with macroscopic tumor-free margins superior to the mandibular canal to avoid damage to the inferior alveolar nerve. Macroscopically, there was no sign of direct contact between the tumor and the alveolar nerve. A reconstruction plate was applied to increase the strength of the mandible. The soft tissue incision was subsequently closed with resorbable sutures.

Initially, the postoperative healing was uneventful, with only slight reduction in sensitivity in the left inferior alveolar nerve. Histopathologic examination of the specimen showed that the tumor had been completely removed. The patient was initially planned to undergo reconstruction of the alveolar process with free iliac crest bone graft and titanium implants for a fixed supraconstruction in a two-stage procedure. However, postoperative infection destroyed the bone graft, and a new alveolar bone reconstruction with local bone grafts from the mandible was performed. The left mandible was reconstructed with four titanium implants and a screw-retained fixed supraconstruction, and no signs of recurrence have appeared after 6 years. The patient has been closely monitored with annual clinical and radiographic examinations, including cone beam