



Non-calcifying Langerhans Cell-Rich Variant of Calcifying Epithelial Odontogenic Tumor: A Distinct Entity with Predilection for Anterior Maxilla

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Received: 10 July 2018 / Accepted: 10 August 2018 / Published online: 14 August 2018
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Abstract

Calcifying epithelial odontogenic tumor (CEOT) is an uncommon locally invasive epithelial odontogenic tumor of the jaws associated with amyloid production. Intraosseous presentations are most common and they frequently occur in the posterior mandible. A non-calcifying Langerhans cell-rich variant of CEOT (NCLC CEOT) has been described with predilection for the anterior maxilla. Interestingly, all reported cases of NCLC CEOT have occurred in Asian population. We present a case of a 43-year old Caucasian female with a large radiolucent lesion involving the left anterior maxilla with histologic features of NCLC CEOT. This is the first reported case of this rare variant of CEOT in a Caucasian individual.

Keywords Calcifying epithelial odontogenic tumor · Anterior maxilla · Non-calcifying variant · Langerhans cells

Introduction

Calcifying epithelial odontogenic tumor (CEOT), also known as Pindborg tumor, is an uncommon odontogenic epithelial neoplasm, associated with amyloid material and initially reported by Pindborg in 1958 [1]. Prior to its recognition, CEOT was often misdiagnosed as ameloblastoma with unusual forms of calcification [1]. This tumor predominantly occurs intraosseously, although peripheral or extraosseous presentations have been reported. Clinically, CEOT may present as a painless slow growing mass and about two-thirds of cases arise in the posterior mandibular region. Radiographic features include a unilocular or multilocular radiolucency, often with variable sizes of radio-opaque calcifications and in association with impacted tooth [2].

Microscopically, the classic lesions exhibit sheets, strands or nests of polyhedral, occasionally pleomorphic epithelial cells with prominent intercellular bridges. The prototypic CEOT usually has large areas of amorphous congophilic eosinophilic material that may calcify to form concentric rings (Liesegang rings) which can coalesce to form larger dystrophic calcifications. Despite its name; however, calcification is not always identified in CEOT. The nature of the eosinophilic amyloid-like material seen in CEOT has been extensively studied [2]. A few histologic variants of classic CEOT have been described including: clear cell type, Langerhans cell-rich type and myoepithelial cell-rich type as well as combined lesions with adenomatoid odontogenic tumor and recently, microcystic type [3–7]. In spite of more than 200 cases of CEOT published in the English language literature, only a few cases of the above mentioned microscopic variants have been published [3, 8–13]. We report a case of non-calcifying Langerhans cell-rich (NCLC) CEOT in a 43-year old Caucasian female and review the pertinent literature to increase awareness on the unique clinical and histopathologic features of this rare variant of CEOT.

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Case Report

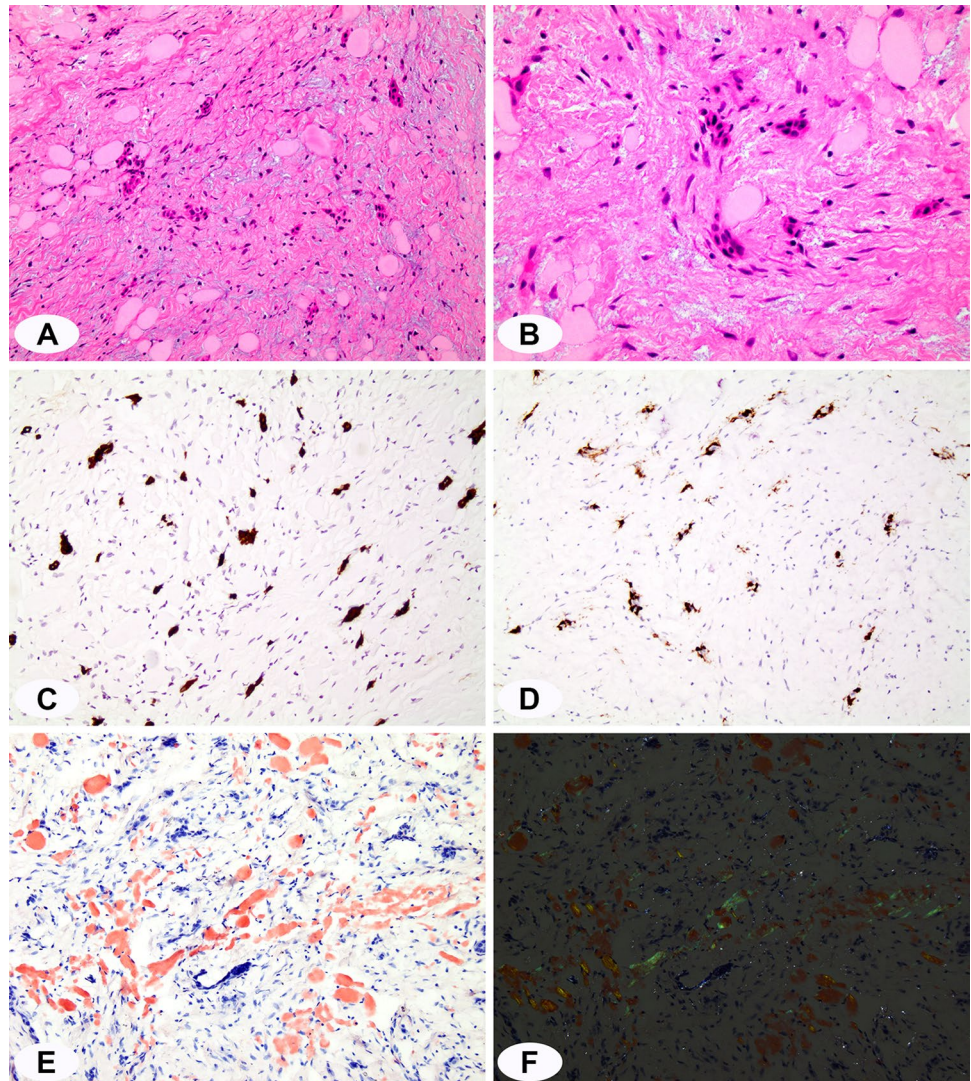
A 43-year-old Caucasian female was referred from a local dentist for evaluation of a large radiolucent lesion involving the left anterior maxilla. Review of medical records



Fig. 1 Panoramics showing a radiolucent defect spanning from teeth #9 to #12

did not indicate that the patient had any multi-racial ethnic background. The radiolucent defect was noted on a routine panoramic radiograph affecting the maxillary alveolar bone in the area of teeth #9–12 (Fig. 1). The patient was asymptomatic with no bony expansion or paresthesia, and teeth in the area tested vital to thermal sensitivity testing. Following informed consent, surgical excision of the tumor with intraoral osteotomy was performed. Microscopically, the lesion consisted of a paucicellular collection of bland odontogenic epithelial cells admixed with amorphous eosinophilic globules (Fig. 2a, b). No calcified material was identified. By immunohistochemistry, the epithelial cells were strongly and diffusely positive for Pancytokeratin-MNF-116, (Fig. 2c). Scattered CD1a- and Langerin-positive Langerhans cells were present (Fig. 2d). The amorphous eosinophilic globules were reactive with Congo red stain, producing an apple-green birefringence noted under polarized light (Fig. 2f, g). The overall histopathologic features were

Fig. 2 **a** Photomicrograph showing amorphous eosinophilic globules admixed with paucicellular odontogenic epithelial cells without any calcifications (H&E, original magnification $\times 100$). **b** High power showing prominent eosinophilic globules in between paucicellular odontogenic epithelial cells (H&E, original magnification $\times 200$). **c** Epithelial clusters are strongly positive for Pancytokeratin-MNF116 (original magnification $\times 200$). **d** CD1a highlights the scattered Langerhans cells are present (original magnification $\times 200$). The Langerin stained similarly as the CD1a (not shown). **e** Eosinophilic amyloid like material shows congophilia with Congo red stain (H&E, original magnification $\times 200$). **f** Congophilic areas shows apple green birefringence under polarized light microscopy (original magnification $\times 200$)



consistent with the NCLC variant of CEOT. Follow-up at 18 months showed no evidence of recurrence.

Discussion

While classic CEOT represents a mere 1–2% of odontogenic neoplasms, NCLC CEOT is even less common, with only 9 cases previously reported in the English literature to date [14]. A summary of these previously reported cases with the present case is shown in Table 1. The age of patients ranged from 20 to 58 years and out of 10 cases, six cases occurred in females and four in males. Eight cases occurred intraosseously, while 2 cases presented as extraosseous soft tissue swellings. Similarly, the maxilla was the site of origin for 8 cases, while 2 cases arose in the mandible. Radiographically, all 10 cases presented as a radiolucent defect without detectable radiopaque calcifications. Follow-up information was available for 7 cases and none showed evidence of recurrence.

Some features of the NCLC variant of CEOT appear to be unique when compared with classic CEOT. All reported cases of the NCLC variant have occurred in individuals of Asian descent, except in our case. NCLC variant of CEOT tends to be more common in anterior-premolar region of maxilla rather than the posterior mandible. Most cases have shown very sparse odontogenic epithelial cells with eosinophilic amyloid globules, substantial numbers of Langerhans cells and no calcification. In contrast, classic CEOT is

seen more commonly in the posterior mandible and is more often associated with impacted teeth. They usually consist of large sheets of polyhedral epithelial cells with lamellar calcification of the amyloid globules (Liesegang rings). Large numbers of Langerhans cells are uncommon in the classic CEOT. The contrasting features of classic and NCLC variant of CEOT are summarized in Table 2. The principal differential diagnosis of NCLC variant of CEOT includes odontogenic neoplasms such as central odontogenic fibroma. A few sentinel reports of central odontogenic fibromas with Langerhans cells have been documented in literature [15, 16]. However, pancytokeratin and Congo red stains are useful in differentiating NCLC CEOT from other histological mimics.

The histologic hallmarks of NCLC CEOT includes: thin strands or small nests of odontogenic epithelial cells, amyloid deposits, scattered Langerhans cells and minimal/absent calcifications. Various case reports have investigated the correlation between amount of calcification and behavior of the CEOT [8, 17]. None of the reported cases, which had follow-up information available, exhibited recurrence. It is possible; however, that the follow-up period may not be long enough to draw sufficient conclusion about its full biologic potential [8, 17]. The role of Langerhans cells in this neoplasm and their effects on tumor behavior remains to be resolved. Langerhans cells, a part of the mononuclear phagocytic system, act as antigen-presenting cells to T cells [18]. They are usually present in the skin, oral mucosa, lymph node and thymus. Given that oral ectoderm is the precursor

Table 1 Previously reported non-calcifying Langerhans cell-rich CEOT along with present case

Citations	Age/sex	Location	Clinical features	Radiographic appearance	Treatment/follow-up
Asano et al. [3]	44/F	Maxilla: #3–#9	Asymptomatic	Unilocular radiolucency	Partial resection of maxilla No information on follow-up
Takata et al. [8]	58/M	Mandible: #11–#13	No swelling; bone resorption with mobile teeth	Unilocular radiolucency	Surgical enucleation No recurrence after 10 years
Wang et al. [9]	38/M	Mandible: #28-ramus	Painful swelling	Radiolucency	Partial resection of mandible No recurrence after 2.5 years
	39/F	Maxilla: Gingiva-left premolar	Painless gingival swelling	Extra-osseous	Surgical excision No recurrence after 2 years
Wang et al. [10]	52/F	Maxilla: #6–#8	Painless palatal depression	Unilocular radiolucency	Partial resection of maxilla No information on follow-up
Afroz et al. [11]	20/F	Maxilla: Gingiva-right lateral incisor	Painless gingival swelling	Extra-osseous	Surgical excision No recurrence after 6 months
Chen et al. [12]	40/F	Maxilla: #8–#12	Painful palatal depression with mobile teeth	Unilocular radiolucency	Curettage No recurrence after 5 years
	58/M	Maxilla: #3–#11	Painless swelling	Multilocular radiolucency	Partial resection of mandible No recurrence after 10 years
Tseng et al. [13]	24/M	Maxilla: #11–#13	No swelling; Pain with mobile teeth	Unilocular radiolucency	Complete excision No information on follow-up
Present case	44/F	Maxilla: #9–#12	Asymptomatic	Unilocular radiolucency	Surgical excision No recurrence after 18 months

Table 2 Contrasting features between classic and non-calcifying Langerhans cells-rich variant of CEOT

Features	Classic variant	Non-calcifying Langerhans cell-rich variant
Location	Posterior mandible	Anterior-premolar maxilla
Association with impacted teeth	50% of the cases	None of the cases reported
Radiographic features	Radiolucency with radiopaque calcifications	Radiolucency
Odontogenic epithelial cells	Large sheets or islands with pleomorphic features	Small nests or thin strands with no pleomorphism
Calcifications	Present with Leisegang rings	Absent
Langerhans cells	Absent or very small amount	Substantial amount

for both oral and odontogenic epithelium, Langerhans cells could also migrate to odontogenic epithelial rests from the bone marrow [10]. In the case of CEOT, amyloid globules may be recognized as foreign antigens by Langerhans cells. As Langerhans cells play a major role in the regression of certain skin lesions such as halo nevi, keratoacanthomas and benign lichenoid keratoses, more studies are needed to determine if their presence in CEOT has any effect on prognosis or even tumor regression [19].

In summary, we present a case of NCLC CEOT, a distinct Langerhans cell-rich, non-calcifying odontogenic neoplasm with marked predilection for the anterior maxilla. Due to its rarity, NCLC variant of CEOT may pose a diagnostic challenge to pathologists who may be unaware of this clinical and histopathologic presentation.

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