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REVIEW ARTICLE

PERIPHERAL CALCIFYING EPITHELIAL ODONTOGENIC TUMOR: DIAGNOSTIC CHALLENGES, HISTOPATHOLOGICAL VARIANTS, AND CLINICAL PERSPECTIVES

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Abstract

Peripheral calcifying epithelial odontogenic tumor (CEOT) is a rare benign epithelial odontogenic neoplasm, accounting for only about 1% of all odontogenic tumors, with the extraosseous variant representing a small fraction of cases. Despite its rarity, this lesion can mimic various reactive and neoplastic gingival conditions, making clinical recognition challenging. The clear cell variant of peripheral CEOT is even rarer and may mimic malignant tumors in histopathology, underscoring the need for thorough clinicopathological and radiographic assessment with histopathological exclusion. Because it frequently presents as an innocuous, slow-growing gingival mass, it may be clinically misdiagnosed as hyperplasia, pyogenic granuloma, hamartoma, or salivary gland pathology. Multiple biopsies may be required for large or heterogeneous lesions. A total of 50 cases have been documented over the past five decades (1966-2025), underscoring the extreme rarity of this condition. This review synthesizes reported cases to reinforce the importance of considering peripheral CEOT in the differential diagnosis of localized gingival enlargements. Conservative surgical excision remains the preferred treatment, with low recurrence rates and an excellent overall prognosis.

Keywords: Clear cells, odontogenic tumour, pindborg tumour, peripheral calcifying epithelial odontogenic tumour

INTRODUCTION

Peripheral Calcifying Epithelial Odontogenic Tumor (P-CEOT) represents one of the rarest manifestations of the calcifying epithelial odontogenic tumor spectrum. CEOT, initially recognized as a distinct odontogenic neoplasm by Pindborg in 1955 and later described in full detail in 1958, accounts for approximately 1% of all odontogenic tumors and is best known for its locally invasive but benign behavior.[1] While the classic lesion is intraosseous and typically arises in the posterior mandible of adults in their fourth and fifth decades, an extraosseous or peripheral counterpart, first highlighted by Pindborg in 1966, is now established as an uncommon soft-tissue variant comprising only 6% of all CEOTs.[2]

P-CEOT usually presents as a slow-growing, painless gingival mass that may mimic a variety of reactive and neoplastic soft-tissue enlargements, making clinical diagnosis challenging. Although predominantly indolent, peripheral lesions may occasionally produce mild superficial or crestal bone resorption, a feature far less pronounced than in central CEOTs.[3] Most cases respond well to simple surgical excision, and recurrence appears exceedingly rare when complete removal is achieved.[4]

A critical histopathological subset is the clear-cell variant of CEOT (CCEOT), which exhibits clear-cell changes that can closely resemble mucoepidermoid carcinoma, thereby creating diagnostic dilemmas for pathologists. Although peripheral CCEOT is exceedingly uncommon, with fewer cases reported in extensive reviews, it remains clinically relevant due to concerns regarding its potentially more aggressive behavior.[5]

Recent critical analyses of reported extraosseous CEOT and CCEOT cases from 2000 to 2025 indicate a higher frequency in Asian populations and a slight male predilection, aligning with the observations of Anavi et al. (2003) but differing from Mesquita et al. (2003), who reported equal gender distribution.[6,7] Most lesions arise in the anterior gingiva, are frequently less than 2 cm, and **are predominantly benign, with minimal bone** involvement. Notably, no recurrences have been documented in the reported literature to date, further supporting the generally favorable prognosis of peripheral lesions.[4]

Given its rarity, overlapping histopathological features

and occasional clear-cell transformation, P-CEOT requires careful clinicopathologic correlation to distinguish it from other odontogenic and salivary gland neoplasms.

Histopathologically, CEOT is characterized by polyhedral epithelial cells arranged in nests, cords, or sheets, often accompanied by amyloid-like material that may calcify to form Liesegang rings, features that remain consistent in the peripheral variant.[4] Some lesions also display epithelial cells with clear or vacuolated cytoplasm, a change attributed to intracellular glycogen or related substances. This phenomenon forms the basis of the clear cell variant of CEOT, first reported by Abrams and Howell in 1967, and later recognized as an essential histologic subtype due to its potential to mimic other clear-cell odontogenic and salivary gland neoplasms.[8]

Although clear-cell change in odontogenic tumors has historically raised concerns about increased aggressiveness or a higher risk of recurrence, available evidence indicates that extraosseous CCEOTs exhibit indolent behavior, with no reported recurrences when adequately excised.[4,9] Nevertheless, the rarity of peripheral CEOT, particularly its clear-cell variant, makes it challenging to draw firm conclusions about biological behavior, underscoring the need for continued documentation and careful clinicopathologic correlation. Given the rarity and diagnostic challenges of peripheral CEOT, this review integrates literature from 1966 to 2025 to clarify its clinical profile, histopathologic variants and recommended therapeutic approaches (Table 1).[2,4,6-8,10-44]

Table 1- Clinical and histopathological details of reported Peripheral CEOT cases from the literature search

Author (year)	Age / Sex	Site of the lesion	Biopsy	Histopathological Findings	Follow-up; Recurrence
Kharat et al. (2023)[10]	30/F	Left maxillary posterior region	Excision with extractions	Peripheral CEOT	NA
Museedi et al. (2020)[11]	34/M	Mandibular anterior region	Enucleation	Peripheral CEOT	1 yr; No recurrence
Siriwardena et al. (2020)[12]	50/F	NA	Excision	Peripheral NCCEOT -clear cell variant	NA
	25/M	Middle to posterior mandible	Excision	Peripheral CEOT - clear cell variant	
	23/M	Anterior to Middle Maxilla	Excision	Peripheral NCCEOT clear cell variant	
	32/F	Anterior mandible	Excision	Peripheral CEOT - clear cell variant	
	47/M	Middle to posterior mandible	Excision	Peripheral CEOT - clear cell variant	
	27/F	Anterior to middle mandible	Excision	Peripheral NCCEOT	
	32/F	Anterior maxilla	Excision	Peripheral CEOT	
	34/F	Maxillary antrum	Excision	Peripheral CEOT - clear cell variant	
Feitosa et al. (2020)[13]	33/F	Gingiva of the right maxilla	Excision	Peripheral CEOT	NA
Singh et al. (2020)[14]	16/F	Left maxillary posterior vestibule.	Enucleated with the tooth	Peripheral CEOT	No recurrence
Ibituruna et al. (2019)[15]	26/M	Bilateral maxillary gingiva (canines); central tumor - left posterior mandible	Soft lesions - curettage; Hard tumor - resection	Peripheral CEOT - 2 Central CEOT - 1 (Multiple lesions)	6 yrs; No recurrence
Flores et al. (2018)[16]	21/F	Right mandibular lateral incisor to first premolar	Excision	Peripheral CEOT - clear cell variant	22 months; No recurrence
Bajpai et al. (2018)[17]	34/M	Maxillary right anterior lingual gingiva (#11, #12)	Excision	Peripheral CEOT - clear cell variant	6 months; No recurrence
de Carvalho et al.	18/M	Right mandibular posterior gingiva	Excision	Peripheral CEOT	1 yr; No recurrence

(2016)[18]					
Mitra et al. (2016)[19]	47/M	Right nasal polyp from the lateral wall	Polypectomy	CEOT - Nasal Polyp	NA
Gadodia et al. (2016)[20]	18/M	Left mandible anterior lingual gingiva (#31,32,33)	Excision	Peripheral CEOT - clear cell variant	6 Months; No recurrence
Shetty et al. (2016)[21]	47/F	Left mandibular anterior (lateral incisor to first premolar) lingual gingiva.	Excision	Peripheral CEOT	6 Months; No recurrence
Shetty et al. (2014)[22]	41/F	Maxillary anterior gingiva, extending from the right to the left canine	Anterior maxillectomy	Peripheral CEOT	2 yrs; No recurrence
Afrogheh et al. (2014)[2]	37/F	Mandibular anterior gingiva	Excision	Peripheral LC CEOT - clear cell variant	1.5 yrs; No recurrence
Marino et al. (2013)[23]	37/F	Left maxillary premolar gingiva	Conservative surgery with extraction	Peripheral CEOT	2 yrs; No recurrence
Afroz et al. (2013)[24]	20/F	Right maxillary lateral incisor mucosa	Excision	Peripheral NCLCCEOT - Clear cells	6 months; No recurrence
Studart-Soares et al. (2011)[8]	28/M	Anterior mandibular gingiva	Excision	Peripheral CEOT	4 yrs; No recurrence
Etit et al. (2010)[25]	62/F	Maxillary molar gingiva	Excision	Peripheral CEOT - Ameloblastoma	No recurrence
Habibi et al. (2009)[26]	70/F	Left maxillary anterior (lateral incisor to canine) gingiva	Excision with 5-mm safety margins	Peripheral CEOT - clear cell variant	No recurrence
de Oliveira et al. (2009)[4]	43/F	Maxillary premolar and left mandibular incisor region.	Excision	Peripheral CEOT - clear cell variant (2)	1 yr; No recurrence
Abrahão et al. (2009)[27]	40/F	Mandibular first premolar gingiva - Bilateral	Excision	Bilateral Peripheral CEOT	Initial 1 yr; recurrence - Excision; after 3.5 yrs; No recurrence
Wang et al. (2006)[28]	39/F	Left maxillary premolar vestibule and the gingiva	Excision	Peripheral NC CEOT - clear cell variant	2 yrs; No recurrence
Shetty et al. (2006)[29]	22/F	Left mandibular anterior gingiva (lateral incisor to canine)	Excision	Peripheral CEOT - clear cell variant	NA
Buchner et al. (2006)[30]	71/F	NA	Excision	Peripheral CEOT	NA
Patiño et al. (2005)[31]	67/F	Alveolar border of the right maxillary gingiva	Excision	Peripheral CEOT	4 yrs; No recurrence
Manor et al. (2004)[32]	19	Mandible retro-molar region	Excision	Peripheral CEOT	No recurrence

Anavi et al. (2003)[6]	27/M	Left mandibular canine and first premolar lingual gingiva	Excision	CEOT - clear cell variant	1 Yr; No recurrence
Mesquita et al. (2003)[7]	48/F	Right maxillary anterior (canine) gingiva	Excision	Peripheral CEOT - clear cell variant	2.5 yrs; No recurrence
Orsini et al. (2000)[33]	32/M	Maxillary anterior (lateral incisor to canine) gingiva	Excision	Peripheral CEOT - clear cell variant	4 yrs; No recurrence
Houston, Fowler et al. (1997)[34]	64/M	Maxillary premolar gingiva	Excision	Peripheral CEOT - clear cell variant	4 yrs; No recurrence
	27/M	Right mandibular premolar (#44, 45) gingiva	Excision	Peripheral CEOT - clear cell variant	4 yrs; No recurrence
KH Ng et al. (1996)[35]	52/M	Maxillary canine-premolar gingiva	Excision	Peripheral CEOT	No recurrence
Ledesma et al. (1993)[36]	21/F	Maxillary anterior (#21) gingiva	Excision	Peripheral CEOT - AOT	1 yr; No recurrence
Takeda et al. (1983)[37]	31/F	Right upper posterior (#16,17) gingiva	Resection with removal of adjacent bone	Peripheral CEOT	2 yrs; No recurrence
Ai-Ru et al. (1982)[38]	32/F	Mandibular premolar - molar gingiva	Partial resection	Peripheral CEOT - clear cell variant	2 yrs; No recurrence
	47/F	Mandibular canine-premolar gingiva	Resection	Peripheral CEOT - clear cell variant	2 yrs; No recurrence
Wertheimer et al. (1977)[39]	20/M	Maxillary lateral incisor to premolar gingiva	Excision	Peripheral CEOT - clear cell variant	No recurrence
Krolls and Pindborg (1974)[40]	60	Mandibular anterior gingiva	Excision	Peripheral CEOT	No recurrence
Patterson et al. (1969)[41]	12/M	Mandibular anterior (#41, 31) gingiva	Excision	Peripheral CEOT	No recurrence
Decker and Laffitte (1967)[42]	40/M	Mandibular premolar gingiva	Excision	Peripheral CEOT	No recurrence
Abrams and Howell (1967)[43]	16/F	Mandibular anterior (#41,42) gingiva	Excision	Peripheral CEOT - clear cell variant	3 yrs; No recurrence
Pindborg (1966)[44]	29/F	Maxillary anterior (#22) gingiva	Excision	Peripheral CEOT	No recurrence
	16/F	Mandibular anterior (#41, 42) gingiva	Excision	Peripheral CEOT	No recurrence

CEOT - Calcifying epithelial odontogenic tumor; AOT – Adenomatoid odontogenic tumor; NCLCCEOT - Non-calcifying Langerhans Cell-Rich Variant of Calcifying Epithelial Odontogenic Tumor

DISCUSSION

Peripheral calcifying epithelial odontogenic tumor (P-CEOT) is an uncommon odontogenic neoplasm, accounting for only a small proportion of calcifying epithelial odontogenic tumors, which in turn represent <1% of all odontogenic tumors.[45] The compiled cases in the table demonstrate that P-CEOT occurs across a wide age range (12–71 years), though the most common presentation remains in young to middle-aged adults. Traditionally, P-CEOT has been described as more frequent in the third and fourth decades of life, with a predilection for the anterior gingiva. While historical literature emphasizes female predominance, the present review shows a substantial number of male patients, supporting recent claims of shifting or variable gender predilection.[12,22] Findings from the present review further reveal a broader demographic and anatomic distribution, reinforcing observations from recent studies that have noted variable patterns and frequent involvement of the mandibular canine-premolar region.[21,22]

Anatomically, most lesions in the present review involve the anterior to middle gingival quadrant, particularly the maxillary and mandibular canine–premolar region, consistent with reports suggesting an origin from gingival epithelial remnants, such as the rests of Serres or basal epithelium.[32,46] Several maxillary cases, including those involving the antrum and nasal cavity and rare bilateral lesions, highlight the broad clinical spectrum previously described in the literature.[19,27] Clinically, P-CEOT typically presents as a slow-growing, painless gingival swelling that may mimic reactive lesions such as pyogenic granuloma, peripheral ossifying fibroma, or fibrous hyperplasia.[32,33,47] The cases summarized in the present review frequently describe an asymptomatic soft-tissue mass, emphasizing the importance of considering P-CEOT in the differential diagnosis of innocuous-appearing gingival enlargements. Atypical presentations, including the bilateral lesions documented by Ibituruna et al. (2019) and Abrahão et al. (2009), further expand the known clinical spectrum of this tumor.[15,27]

Radiographically, P-CEOT may show no detectable osseous changes or may present as a mixed radiolucent–radiopaque lesion depending on the degree of internal calcification.[44,46] Many reported cases required only simple excision, indicating minimal bone involvement, which aligns with descriptions in the literature of superficial cortical erosion or mild tooth displacement without root resorption.[48] Such subtle or absent radiographic findings highlight the essential role of histopathology, particularly when lesions resemble fibro-osseous conditions such as cemento-ossifying fibroma or cemento-osseous dysplasia.[49]

Histopathology remains the cornerstone of diagnosis, characterized by polyhedral epithelial cells, eosinophilic or clear cytoplasm, intercellular bridges, and amyloid-like material that may exhibit Liesegang ring calcifications.[7,50] A notable trend in the review is the high frequency of clear cell variants, paralleling evidence in the literature that describes multiple peripheral clear-cell CEOTs but suggests no greater aggressiveness than central clear-cell lesions.[48] Congo red staining, demonstrating apple-green birefringence, supports the presence of amyloid, although older or heavily calcified lesions may yield negative results.[51] Immunohistochemical findings such as CK14/CK19 positivity and S-100 negativity assist in differentiating P-CEOT from salivary gland and metastatic clear cell tumors.[21,52] Hybrid histologic patterns, including CEOT with AOT-like features,[36] further reflect the pluripotent potential of odontogenic epithelium.[38,53]

Management across nearly all reported cases involved simple local excision, reinforcing the consensus that P-CEOT is a benign, slow-growing soft-tissue tumor.[4,21,33] Follow-up data demonstrate extremely low recurrence, with most patients remaining disease-free for 6 months to 6 years. Recurrence occurred only in rare cases with bilateral involvement or incompletely excised tumors, consistent with the reports of Mesquita et al. (2003) and Abrahão et al. (2009).[7,27] This behavior contrasts with intraosseous CEOT, which presents a higher recurrence risk and often requires more aggressive surgical approaches such as marginal or segmental resection.[52] The absence of malignant transformation in peripheral lesions, even in clear cell variants,[2] is in agreement with the predominantly indolent behavior observed in the reported cases. Advanced imaging modalities, including CT, improve visualization of calcifications and cortical involvement. Molecular findings such as PTEN and CDKN2A alterations further support the neoplastic nature of CEOT.[48] Overall, integrating clinical assessment, imaging, histopathology, immunohistochemistry, and molecular diagnostics remains crucial for accurate diagnosis and individualized treatment planning.[54]

CONCLUSION

Peripheral CEOT should be routinely considered in the differential diagnosis of asymptomatic anterior gingival swellings. Comprehensive clinical assessment, appropriate imaging, histopathological examination, and, when necessary, advanced diagnostic methods are critical for accurate diagnosis and optimal management. Continued reporting and molecular characterization of cases will enhance understanding of their clinical behavior, epidemiology, and optimal therapeutic strategies, ultimately improving patient outcomes.

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Conflict of Interest

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