Content available at: https://www.ipinnovative.com/open-access-journals

International Dental Journal of Student's Research

Journal homepage: https://www.idjsronline.com/

Review Article

Calcifying epithelial odontogenic tumor- Review of literature

Akshitha Achuthan[1], Sivaramakrishnan Muthanandam[1,*], A Santhadevy[1], Vezhavendhan N[1], Vidhyalakshmi[1], Umamaheswari G[1]

[1]*Dept. of Oral & Maxillofacial Pathology and Oral Microbiology, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidhyapeeth (Deemed to be) University, Puducherry, India*

ARTICLE INFO

Article history:
Received 18-08-2023
Accepted 05-09-2023
Available online 11-10-2023

Keywords:
Pindborg tumor
Intraosseous (central)
Liesegang rings

ABSTRACT

The Calcifying epithelial odontogenic tumour (CEOT), also known as Pindborg tumour, is a rare odontogenic neoplasm makes up 1% of all odontogenic tumours, characterized by its distinct histopathological features and challenging clinical management. CEOTs are benign epithelial odontogenic tumour that secretes an amyloid protein tending towards calcification, however they can be locally aggressive and have recurrence rates of 10% to 15%. This comprehensive review aims to provide a detailed overview of the CEOT, encompassing its epidemiology, clinical findings, radiographic features, histopathological characteristics and therapeutic strategies.

1. Introduction

A uncommon and unusual benign epithelial odontogenic neoplasm, calcifying epithelial odontogenic tumour (CEOT), also known as Pindborg tumour, makes up 1% of all odontogenic tumours. The Danish pathologist Dr. Jens Jorgen Pindborg first described the calcifying epithelial odontogenic tumour (CEOT) in 1955. The eponymous Pindborg tumour was first described in literature in 1963 by Shafer, and it was given the name Pindborg tumour in 1967. Ameloblastoma of peculiar type with calcification, calcifying ameloblastoma, malignant odontoma, adenoid adamantoblastoma, cystic complex odontoma, and a form of the solid or multicystic ameloblastoma (SMA) are a few names under which the tumour had been described prior to 1955.[1,2] Since the 1971 publication of Histological Typing of Odontogenic Tumours, Jaw Cysts, and Allied Lesions, the term "calcifying epithelial odontogenic tumour" has gained widespread acceptance and been officially recognised by the World Health Organisation (WHO). It was categorised as a benign odontogenic tumour by the World Health Organisation in 1992 because it is epithelial in origin and lacks an ectomesenchymal component.[1,3,4] CEOT is defined as a benign epithelial odontogenic tumour that secretes an amyloid protein tending towards calcification (Franklin & Pindborg, 1976; Azevedo et al, 2013; El - Naggar et al, 2017). It affects people in their fourth to fifth decades of life and has no preference for either gender. Clinically, an impacted tooth in the posterior mandibular region typically manifests as a slow-growing, painless expansile hard bony swelling.[5] This tumour has an opposite etiology. According to the literature, CEOT is caused by epithelial remnants from the dental lamina, diminished enamel epithelium, stratum intermedium, or enamel organ.[6] However, the exact cause of CEOT is still unknown. CEOT is classified as central or intraosseous (87.8%), peripheral or extraosseous (6.1%), or as a hybrid tumour when combined with an adenomatoid odontogenic tumour[7] based on the clinical presentation and histopathology. According to histopathology, CEOT

* *Corresponding author*.
E-mail address: shivarocksmds@gmail.com (S. Muthanandam).

https://doi.org/10.18231/j.idjsr.2023.023

is made up of sparse connective tissue stroma and broad sheets, islands, cords, rows, and strands of polyhedral epithelial cells. With obvious intercellular bridges and an abundance of eosinophilic granular cytoplasm, the cells have a recognisable cellular shape. These malignant cells may exhibit moderate pleomorphism and infrequent aberrant mitosis. These cancerous cells have enormous, frequently pleomorphic, hyperchromatic, and strange nuclei that are centrally placed. Round, eosinophilic, whitish lumps that resemble amyloids within the sheets of tumour cells are the hallmark feature of this tumour. This material can calcify, resulting in the concentric lamellar bodies known as Liesegang rings, because of its affinity with the mineral salt. Large pools of homogenous eosinophilic material and diffusely deposited calcium salts may be seen in the tissue around the lesion.[2,6] When stained with Congo red this amyloid-like substance shows up under polarised microscope as an apple-green birefringence. Since recurrence occurs in 15% of instances, this tumour has a propensity to do so.[7,8]

2. Epidemiology

Epidemiological studies on odontogenic tumours conducted in different parts of the world emphasised variation in incidence and distributional pattern. According to epidemiological study conducted in Southern state of Andhra Pradesh in India, which included all the odontogenic tumours from the archives of department of oral pathology, Dental teaching and Research Institution in southern part of India from 2002 to 2014. Incidence of the odontogenic tumours was found to be 2.17%, in which Calcifying epithelial odontogenic tumour accounts1.8%. Considering the individual lesions, Ameloblastoma [49%] was found to be more frequent, followed by Keratinizing cystic odontogenic tumour [32%], Odontome [6.2%], Adenomatoid odontogenic tumour [5.5%], Odontogenic myxoma [2.4%], Ameloblastic fibroma [0.6%], Calcifying epithelial odontogenic tumour [1.8%] and Squamous odontogenic tumour [1.2%].[9] In the Brazilian survey, CEOT represented 0.03% of all samples submitted to histopathological analysis and 1. 7% of all odontogenic tumours, According to their literature review, Asian individuals were more affected by this neoplasm. Three large case series with more than 10 CEOT have been published elsewhere (Krolls & Pindborg, 1974; Ng & Siar, 1996; Azevedo et al, 2013). However, they do not provide the relative frequency among all biopsied lesions. Noteworthy, Asia usually ranks in absolute number of individuals with odontogenic cysts and tumours (Johnson et al, 2014; de Arruda et al, 2018). Nearly 131 CEOT cases affecting individuals from the Eastern world were retrieved, suggesting a predilection of the condition for this population.[10]

3. Clinical Features

Clinically, it manifests as an aggressive, locally invasive neoplasm that is slow developing and expansile. It typically affects people in their third and fourth decades of life without regard to gender. The posterior mandible is the most frequently affected region, and there are both intraosseous (central) and extraosseous (peripheral) types. When it develops intraosseously, it sometimes exhibits local invasiveness and frequently manifests as a slow-growing, painless mass. Patients may occasionally complain of nasal congestion, epistaxis, and headaches. The extraosseous CEOT or peripheral softtissue most frequently manifests as a painless, hard gingival mass with a preoperative clinical diagnostic that includes fibrous hyperplasia, peripheral giant cell granuloma, and epulis. Due to local damage after surgical excision, the underlying mucosa could develop ulcers. The origin of the Pindborg tumor's epithelial cells is still unknown, however evidence in the literature points to the stratum intermedium layer of the enamel organ as the location of these material remnants. This is supported by the idea that tumour cells share morphological characteristics with stratum intermedium cells and exhibit elevated alkaline phosphatase and adenosine triphosphate activity. The Pindborg tumor's amyloid deposits, according to the literature, are an immune system reaction to these stratum intermedium cells. According to other writers, it develops from dental lamina remnants, which are more likely to represent the genuine progenitor cell. when the condition is in the maxilla CEOT is linked to an erupted or unerupted tooth in 48% of instances.[11]

4. Radiographic Features

An irregular unilocular or multilocular radiolucent region with radiopaque masses of different sizes and opacities is the hallmark radiographic appearance, This is described as "driven snow" appearance.[12] The calcified concrements are often minute and can go undetected on radiographs, especially in tumours that have been present for a brief period of time. The radiopacities frequently occur close to the dental crown when a tumour is connected to an unerupted tooth. The radiolucent edge and normal bone may or may not be distinguished at the periphery. Some publications have cited Pindborg's original description of radio-opaque specks in the pericoronal tissues of an impacted tooth as a defining feature of CEOT. While 40% of peripheral CEOTs have adjacent bone degradation, 50% of the central lesions have signs of cortical bone perforation. Diffuse high attenuation on computed tomography (CT) scans is suggestive of ossification and/or calcification. CEOT appears as a mixed hyperintense tumour on T2-weighted images on magnetic resonance imaging (MRI) and as a hypointense tumour on T1-weighted images. The extent of the lesion may be determined using CT scans and 3D

reconstructions, which is important for surgical treatment planning.[13]

5. Histopathological Features

CEOTs have an uncommon and varied combination of odontogenic epithelium and calcified structures as their primary histologic pattern.[14] Except for the minor amount or complete absence of calcified material in the extraosseous type of CEOT, there are no major differences in the histomorphology between the two. Heterogeneous sheets of polyhedral cells with prominent intercellular bridges, amyloid-like material and calcifications make up the most typical histologic appearance. Pleomorphism, multinucleation, pronounced nucleoli, and occasionally hyperchromatism may be seen in the cells., Despite the possibility of an abnormal appearance, mitotic figures are rarely observed in these cells. In addition to the Common characteristics, a number of CEOT variants have been documented, including cystic or microcystic variants, hybrid tumours with adenomatoid odontogenic tumour or ameloblastoma, and tumours with varying proportions of clear cells, Langerhans cells, and tumours without calcification.[15] The CEOT clear cell variation has tumour cells that have transparent cytoplasm as a result of the abundance of lipid or glycogen droplets, giving them a distinctive vacuolated look. It can be difficult to detect since it resembles other clear cell tumours in some ways. However, in addition to the typical characteristics of classic CEOT, such as a sheet of polyhedral epithelial cells and varied levels of calcified material (Liesegang rings), its distinctive characteristics include the presence of transparent cells within the tumour tissue. The Langerhans cell form of CEOT is uncommon but consistent, showing tiny islands and cords of neoplastic cells with lots of amyloid material but no calcification. Combination epithelial odontogenic tumours were the designation given by Damm et al. in 1983 to the CEOT-like regions found within two cases of adenomatoid odontogenic tumours. It is uncommon for the calcifying epithelial odontogenic tumour to have a microcystic variation where the neoplastic cells exhibit microcystic pattern.[13,15]

6. Immunohistochemistry

It has been proposed that CEOTs develop from stratum intermedium or dental lamina remnants. Electron microscopy has identified two distinct cell types: polyhedral epithelial cells and myoepithelial-like cells with electron-dense bodies, tonofilament bundles, and tiny lamina dense filaments. Immunohistochemically, the polyhedral cells of CEOT express laminins 1 and 5, cytokeratins, fibronectin, and vimentin. PKK1 (specific for the 44, 46, 52, and 53 kD keratins) detectable keratins are marginally positive or negative in tumour epithelial cells, whilst KL1 (specific for the 55-57 kD keratins) and TK (41-65 kD keratins) are slightly to highly positive. Vimentin is only marginally positive but desmin is negative in the tumour epithelium. Significant findings include high alkaline phosphatase and ATPase levels localised to the cell membrane. Numerous ameloblast-associated proteins have been shown to be present in the amyloid material, with Odontogenic Ameloblast-Associated Protein (ODAM) being the most frequently observed.[13] CEOT epithelial sheets usually include dendritic cells, which are significantly positive for the S-100 and CD-1a antibodies. These dendritic cells have Birbeck's granules, which are ultrastructurally comparable to Langerhans cells, and indented nuclei. As a result, they are probably Langerhans cells and are involved in the antigen presentation from the abortive products of epithelial tumour cells.[16]

7. Treatment and Recurrence

CEOTs are mostly benign, however they can be locally aggressive and have recurrence rates of 10% to 15%. Compared to mandibular CEOTs, maxillary CEOTs are more aggressive and spread quickly, possibly involving nearby important structures. Therefore, it is recommended that maxillary CEOT be treated more aggressively, with a minimum follow-up of five years. CEOT tends to be less aggressive, despite the fact that it was initially thought that its biologic behaviour was comparable to that of ameloblastoma. Therefore, mutilating techniques, such as broad excision or mandibular hemisection, seem unnecessary given CEOT's rather passive biological behaviour. Thus, for CEOT involving the jaw, enucleation within macroscopically normal tissue is advised.

8. Conclusion

In the world of odontogenic neoplasms, the calcifying epithelial odontogenic tumour (CEOT) poses a distinctive and fascinating challenge. Due to its rarity, unusual histological characteristics, and diverse clinical manifestations, a thorough approach to diagnosis and treatment is required.

9. Source of Funding

None.

10. Conflict of Interest

None.

References

1. Malik S, Alam M, Shahina M, Siddique S, Prabhu V. Calcifying epithelial odontogenic tumor. *Bangladesh J Med Sci*. 2014;13:14–23.
2. Chen Y, Wang TT, Gao Y, Li TJ. A clinicopathologic study on calcifying epithelial odontogenic tumor: With special reference to langerhans cell variant. *Diagn Pathol*. 2014;9:37. doi:10.1186/1746-1596-9-37.

3. Lim I, Mallari R, Lacsamana N, Paz D, Villafuerte A. Recurrent calcifying epithelial odontogenic tumor (Pindborg tumor): A case study. *Oral Oncol Extra*. 2005;41:259–66.
4. Sri KK, Vinod V, Venkateswarlu M, Sridevi K, Reddy P. Pindborg tumor: Review of literature and case reports. *J Indian Acad Oral Med Radiol*. 2011;23(4):660–3.
5. Pereira OG, Carvalho LPB, Junior V, de Figueiredo CV. Calcifying epithelial odontogenic tumor. *Case Rep Pathol*. 2013;p. 725380. doi:10.1155/2013/725380.
6. Singh N, Sahai S, Singh S, Singh S. Calcifying epithelial odontogenic tumor (Pindborg tumor). *Natl J Maxillofac Surg*. 2011;2(2):225–7.
7. Misra SR, Lenka S, Sahoo SR, Mishra S. Giant pindborg tumor (calcifying epithelial odontogenic tumor): An unusual case report with radiologic-pathologic correlation. *J Clin Imaging Sci*. 2013;3(Suppl 1):11. doi:10.4103/2156-7514.124056.
8. Gotmare SS, Pereira T, Shetty S, Kesarkar KS. Pindborg tumor: Pathology with special stains. *Indian J Pathol Microbiol*. 2018;61(2):239–41.
9. Nalabolu GR, Mohiddin A, Hiremath SK, Manyam R, Bharath TS, Raju PR, et al. Epidemiological study of odontogenic tumours: An institutional experience. *J Infect Public Health*. 2017;10(3):324–30.
10. De Arruda J, Abreu LG, Silva LV, Schuch LF, Monteiro JL, Arantes DA, et al. Calcifying epithelial odontogenic tumours: collaborative study of 32 cases and review of literature. *Oral Dis*. 2019;25(1):192–205. doi:10.1111/odi.12958.
11. Belmonte R, Torres D, Mayorga F, García-Perla A, Infante P, Gutiérrez JL, et al. Calcifying epithelial odontogenic tumor (Pindborg tumor). *Med Oral*. 2002;7(4):309–15.
12. Caliaperoumal SK, Gowri S, Dinakar J. Pindborg tumor. *Contemp Clin Dent*. 2016;7(1):95–7.
13. Siriwardena BS, Speight PM, Franklin CD, Abdelkarim R, Khurram SA, Hunter KD, et al. CEOT Variants or Entities: Time for a Rethink? A Case Series with Review of the Literature. *Head Neck Pathol*. 2021;15(1):186–201.
14. Lee SK, Kim YS. Current Concepts and Occurrence of Epithelial Odontogenic Tumors: II. Calcifying Epithelial Odontogenic Tumor Versus Ghost Cell Odontogenic Tumors Derived from Calcifying Odontogenic Cyst. *Korean J Pathol*. 2014;48(3):175–87. doi:10.4132/KoreanJPathol.2014.48.3.175.
15. Reichart P, Philipsen HP. Odontogenic Tumors and Allied Lesions. 1st Edn.. vol. 148. London: Quintessence; 2004.
16. Lee SK, Kim YS. 2014.

Author biography

Akshitha Achuthan, 1st Year Post Graduate https://orcid.org/0009-0009-1225-4394

Sivaramakrishnan Muthanandam, Reader https://orcid.org/0000-0002-3251-9814

A Santhadevy, Professor and Head https://orcid.org/0000-0003-2452-3837

Vezhavendhan N, Professor https://orcid.org/0000-0003-1608-0984

Vidhyalakshmi, Professor https://orcid.org/0000-0001-6556-4518

Umamaheswari G, Senior Lecturer https://orcid.org/0000-0003-4172-3654

Cite this article: Achuthan A, Muthanandam S, Santhadevy A, Vezhavendhan N, Vidhyalakshmi, Umamaheswari G. Calcifying epithelial odontogenic tumor- Review of literature. *International Dental Journal of Student's Research* 2023;11(3):103-106.