

Calcifying Epithelial Odontogenic Tumor of Jaw; A Review (*Distinct Pathognomic Diagnostic (LRs) profile of Pindborg tumor*)

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Abstract Calcifying epithelial odontogenic tumor (CEOT) is a benign epithelial odontogenic tumor which is characterized by the presence of islands and sheets of epithelial cells, amyloid like material and calcifications. These calcifications have a concentric lamellar pattern known as “Liesegang Rings” (LRs). So far It is highlighted that LRs developed mostly in intraosseous lesions having amyloid like materials which later transformed to calcification. Many variants of histopathology discussed in this article to emphasize importance of calcification in CEOT. Although LRs are considered to be pathognomic to CEOT when it comes to odontogenic lesions, this term has sometimes been used for adenomatoid odontogenic tumor (AOT) where concentric lamellar calcifications have also been reported. However, here question arises, are LiesegangRings the misnomer in calcifying epithelial odontogenic tumor? Yes, at some aspects on basis of the different etiology, the appearance, and staining patterns. To conclude in view of literatures that phenomena of “Liesegang ring pattern of calcification” is to be more appropriate found in odontogenic tumors.

Keywords: CEOT, Liesegang Rings (LRs), calcification

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1. Introduction

Calcifying epithelial odontogenic tumor (CEOT) also known as Pindborg Tumor discovered first by Dutch Pathologist Jens Jorgen Pindborg [1] in 1958 on four unusual cases and then classified by WHO in 1992 as a rare benign odontogenic epithelial tumor. Initially Calcifying epithelial odontogenic tumor (CEOT) was described by Thonay Goldman [2] as benign tumor and placed as separate entity unusual lesion, then subsequently endorsed by Shafer et al in 1963 [3].

Its frequency of CEOT less than 1% of all odontogenic tumors which is characterized histopathological by presence of islands and sheets of epithelial cells, amyloid like material and calcification (Figure 1). Clinical this lesion is a locally aggressive benign odontogenic neoplasm arising from epithelial tissue, most commonly occurs in 4-6 decade of life and bears no gender predilection. Radiographically a well-defined radiolucency and is known to be having small radio-opacities mass within it. Differential diagnosis of CEOT including adementoid odontogenic tumor (AOT), calcifying odontogenic cyst (COC), squamous odontogenic tumor (SOT), ameloblastic fibro-odontoma and odontoma.

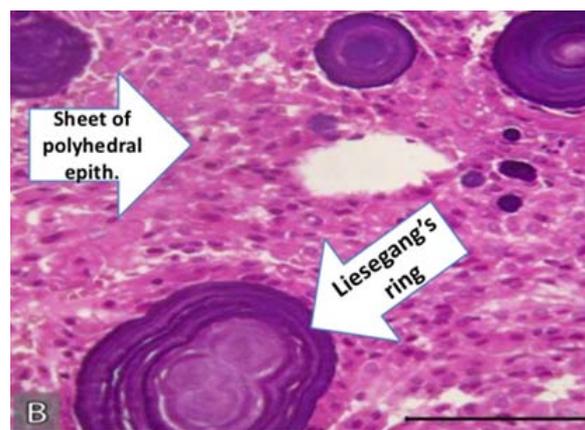


Figure 1. Histopathology slide of CEOT (taken from net)

Many variants of CEOT with calcification and without calcification but CEOT with calcification is rare pathology in maxillofacial region but non-calcifying CEOT is also unusual in other site of body. The most important striking pathognomic calcifications, from which tumor derives its name, have a concentric lamellar pattern derived from calcification of amyloid-like material and because of these known as Liesegang Rings (LRs) discovered by the German Biochemist RE Liesegang in 1896 [4].

Objective of this literature review is to highlight characteristics and diagnostic feature of "Liesegang Rings (LRs)" in relation to histopathological profile of Pindborg Tumor (CEOT).

2. Discussion

Calcifying odontogenic epithelial tumor is rare entity of maxillofacial region and an important in considering to deal with atypical histopathology. Calcifying epithelial odontogenic tumor is a painless slow-growing and locally invasive tumor in mandible mostly in 4-6 decade of life with equal distribution in both gender. Despite its odontogenic origin, its histogenesis is uncertain sometimes, a rare and atypical presentation of Pindborg tumor (CEOT) in maxillae associated with a supernumerary or permanent [5,6].

A characteristic feature of CEOT is presence of homogeneous eosinophilic 'amyloid like' material interspersed between the cells; which stains positively with Congo red and exhibit apple green birefringence under polarized microscopy. This material undergoes calcification in the form of concentric 'Liesegang Rings' that are diagnostic pathognomic entity of Pindborg tumor (CEOT). However, Liesegang rings (LRs) are concentric lamellar pattern derived from calcification of amyloid-like substance. A study documented histological variants of CEOT including CEOT with Langerhans cells (non-calcifying CEOT), CEOT with cementum and bone like material, clear-cell CEOT, combined epithelial odontogenic tumor (CEOT/AOT) and CEOT with myoepithelial cells [7].

Two histological variant of Liesegang Rings including one is Classic Liesegang Rings (CLRs) which are acellular, laminated structures known to occur in cystic, hemorrhagic, inflammatory, and necrotic processes. These rings characteristically have central amorphous cores which are surrounded by peripheral concentric layers with radial cross striations, located in other sites of body [8,9]. Second type of LR is restricted to calcifying epithelial odontogenic tumors (CEOT) are called CEOT-LRs which are the concentric lamellar structure [10]. Under hematoxylin and eosin stain CEOT-LRs are basophilic in nature while CLRs are eosinophilic. Calcification in CEOT are of dystrophic type wherein the calcification occurs around degenerating epithelial cells. On the other hand, Classic LR, have been reported to consist more of organic matrix and the presence of calcium in these rings have yielded varied results, even staining negative for Von Kossa. [11]. However, in brief CLRs are known to be negative for amyloid while CEOT-LRs are frequently found to be arising in the amyloid areas.

Regarding discussion of uncertainty of histogenesis, the study [7] reviewed biological profile of 181 interosseous variant cases of CEOT from literatures and concluded the tumor cells originate from other sources than reduced enamel epithelium of unerupted tooth according to Pindborg 1958 [12,13]. Later study [14] explained that tumor cells exhibit morphologic characteristics of squamous epithelium, and even this histochemical studies support that CEOT arises from the stratum intermedium.

A study [15] found five cases of the combined epithelial odontogenic tumor comprising primarily areas

of adenomatoid odontogenic tumor intermixed with foci of calcifying epithelial odontogenic tumour which were retrieved from the files of the Division of Stomatology, Institute for Medical Research, Kuala Lumpur, however variation in CEOT in jaws may be evident.

Another study 2005 [16] designed on series of 4 cases from literature review, revealed CEOTs are unencapsulated infiltrating tumor and calcification of eosinophilic amyloid-like materials in concentric lamellar pattern (Liesegang Rings) within sheets of tumor cells as characteristic feature. In all cases, eosinophilic material has an apple-green birefringence under polarized light after staining Congo red.

A study [17] reported first case of CEOT associated with SOT (Squamous Odontogenic Tumor) revealed same meticulous clinical, radiographically and histological findings with lamellar calcification (LRs). Another study [18] documented 2 clinico-topographic variants; intraosseous (central) and extraosseous (peripheral) in mandible. The study concluded that it is an aggressive and also rapidly progressive in short duration, and positive histologically most characteristic findings are the presence of amyloid-like substances followed by calcified concentric Liesegang Rings.

A case report [19] revealed areas of concentric lamellated calcification in histopathological finding of 50 years old patient, even CT revealed an osteolytic lesion with foci of calcification. An old study documented on reviewing 113 cases and another colleague in his study reported cases with CEOT in young adult age group (mean 40 years) concluded the diagnosis on basis of histopathological examination presenting an eosinophilic homogeneous materials amyloid which is a characteristic of this tumor with concentric calcific deposits called Liesegang Rings (LRs). The cases described also depicted foci in abundance with fused amorphous calcified aggregates [20,21].

Another case report [22] reported 30 years old patient with CEOT in maxilla, which is sometimes rare tumor site, solitary diffuse swelling extending from right maxillary lateral incisor to second molar on intraoral examination. The hematoxylin and eosin stained sections revealed sheets of epithelial cells with prominent intercellular bridges, nuclear pleomorphic and hyperchromatic interspersed with eosinophilic amyloid like material and basophilic irregular to concentric calcification (LRs).

Three recent case reports published CEOT without calcification (CLRs), one in 2012 [23]; second in 2017 [24] and third one in 2013 [25]. The study in 2013 noticed one case among four cases (intraosseous) documented CEOT with clear cells (Langerhans cells) as extraosseous. [23,24,25]

An interesting study in 2010 [26] explained in comparing with interosseous ameloblastoma, CEOT is rare than Ameloblastoma. Both are mostly similar in demographic and nature, and also localized generally in mandible. Another two studies documented an unusual case of CEOT occurring respectively in posterior mandible with impaction molar and posterior maxillary region with involving the maxillary sinus, displacement of third molar to lateral wall of nose and root resorption associated with lesions. However, there was no evidence of calcification [27,28].

CEOT is rare benign local invasive tumor and exclusively epithelial in its tissue of origin, Histopathological findings revealed neoplastic cells are interspersed by prominent homogeneous hyaline acellular material with area of concentric lamellated calcifications. CBCT confirmed boundaries of the neoplasm and revealed an osteolytic lesion with foci of calcifications (Liesegang Rings-LRs). In view of extensive involvement, resection of involved portion of jaw followed by reconstruction. However, classic Liesegang rings seen in other extragnathic sites although have a lamellated pattern but different in composition as well as appearance. CLRs are known to be negative for amyloid while LR of CEOT are frequently found to be arising in the amyloid areas. This brief communication aims to highlight the key differences between liesegang rings seen in other lesions with that of those seen in CEOT.

3. Conclusion

Liesegang Rings (LRs) is an important feature to diagnose CEOT which is particular related for Oral Histopathologists. So far Intraosseous lesions have mostly the tendency to develop calcification unlike peripheral (Extraosseous) having less tendency. Many other oral lesions have such type of controversial clinical and histopathological issues to diagnose which can be discussed in future intention.

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