Clear Cell Variant of Extraosseous Calcifying Epithelial Odontogenic Tumor: Report of a Case and Review of Literature

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Abstract:
Calcifying epithelial odontogenic tumor (CEOT) is a benign epithelial odontogenic tumor which accounts for 1% of all the odontogenic tumors. The extraosseous presentation of CEOT is seen in only 6% of its cases. Histopathologically CEOT presents with sheets and islands of polyhedral cells with abundant eosinophilic cytoplasm and well-defined borders and intercellular bridges. Eosinophilic amyloid material and calcifications either focal or liesegang rings are noted in most cases. Rarely, clear cells are noted among these epithelial cells. The aim of this report was to conduct an extensive search of literature to locate, appraise, and congregate data available regarding extraosseous CEOT's with clear cells and also to report one such rare case.

Key Words: Calcifying epithelial odontogenic tumor, clear cell, extraosseous, pindborg tumor, peripheral

Introduction
Calcifying epithelial odontogenic tumor (CEOT) was first described by Dr. Jens J. Pindborg in 1955 as a separate entity and has been eponymously named as Pindborg’s tumor. It has been defined by the World Health Organization, as “a locally invasive epithelial odontogenic neoplasm, characterized by the presence of amyloid material that may become calcified.”¹ CEOTs account for about 1% of all odontogenic tumors. They are the most prevalent in patients aged between 20 and 60 years with a mean of around 40 years and have no significant sex predilection.² CEOT is most commonly seen intraosseously, but it may also present as an extraosseous lesion.¹ The classical histopathological features of CEOT include nests, cords, islands, and sheets of polyhedral epithelial cells with well-defined borders and prominent intercellular bridges. Nuclear pleomorphism is frequently encountered. Eosinophilic amorphous, homogeneous amyloid – like material and foci or large amounts of calcification in the form of liesegang rings are frequently encountered. The three main histopathological variants of CEOT are (a) conventional, (b) clear cell, and (c) hybrid. Abrams and Howell described the first case of clear cell variant of CEOT (CCEOT).³ It is ambiguous if the presence of clear cells in CEOT causes changes in biologic behavior or the prognosis of the tumor, so a detailed review of all the peripheral CCEOT cases is needed. The aim of this report was to conduct an extensive search of literature to locate, appraise, and congregate data available regarding extraosseous CEOTs with clear cells and also to report one such rare case.

Case Report
An 18-year-old male patient was referred to the Department of Oral and Maxillofacial Pathology, Saraswati Dhanwantari Dental College and Hospital, Parbhani, Maharashtra. The patient presented with the chief complaint of gingival swelling in the lower left anterior region of jaw since 6-8 months. The patient was apparently alright 6-8 months back after which he noticed a slow growing, painless gingival swelling in the lower left anterior region of the jaw. The patient had discomfort during mastication. Intraoral examination revealed a dome shaped soft tissue swelling with smooth surface on lingual side wrt 31 32 33 (Figure 1). The swelling extended superoinferiorly from the marginal and interdental gingiva wrt 31, 32, and 33 to the floor of the mouth. Drifting of 31 and 32 was noted due to the swelling extending up to the labial papilla between 31 and 32. It measured approximately 1.5 cm × 1 cm. The well circumscribed swelling was firm, sessile, and non-tender. Intraoral periapical radiograph of the lesion revealed superficial erosion of bone and alveolar crestal...
bone resorption wrt 31 and 32 (Figure 2). Clinical differential diagnosis of peripheral osteoma, peripheral ossifying fibroma, and peripheral odontogenic tumors were considered. An excisional biopsy with adequate margins was performed.

Pathology Report

Gross examination
The excised specimen consisted of grayish nodular lesional tissue along with multiple bits of marginal tissue (Figure 3).

Figure 1: Swelling over the lingual gingival region.

Figure 2: Crestal resorption noted.

Figure 3: Gross specimen showing lesional tissue and small bits of marginal tissue.

The lesional specimen was approximately 2 cm × 1.3 cm in size, with smooth superficial and deep surfaces and firm consistency.

Microscopic description
Hematoxylin and eosin stained sections revealed a well-circumscribed lesional tissue mass separated from the overlying epithelium by a thin band of connective tissue (Figure 4). The mass was made up of irregular strands, cords and nests of polyhedral epithelial cells with interspersed amorphous, homogeneous eosinophilic amyloid-like deposits (Figure 5). These epithelial cells had abundant eosinophilic cytoplasm, central round nucleus, and well-defined cell borders. Prominent intercellular bridges were noted at some places. Numerous epithelial cells showing clear, foamy, vacuolated cytoplasm were noted (Figure 6). Mild atypia and pleomorphism were noted in few areas. Few small irregular to oval calcifications were noted in focal areas (Figure 7). Staining was negative for periodic acid-Schiff. The areas showing eosinophilic material interspersed between the tumor cells were positive for Congo red stain and on observation under polarized light showed an apple green birefringence (Figure 8). A final diagnosis of Clear cell variant of Calcifying epithelial odontogenic...
tumor (CCEOT) was given. The post-operative course was uneventful and no recurrence noted at the 6 months follow-up period.

**Review of Literature**

**Strategy employed for literature search**

The present review was based on electronic database search through International English Language Literature from the year 1958 to 2015 for all histopathologically confirmed cases of peripheral CEOTs with clear cells in the tumor in any amount. The cases with detailed demographic data, complete clinical, radiographic, and histopathological findings were retrieved. All the details were tabulated. After an extensive search of international literature, we noted that clear cell variant of peripheral CEOT is a very rare form and only 13 cases have been reported till date worldwide. The review conducted by Habibi et al. on clear cell variants of peripheral CEOT enlists the case of Kumamoto et al. under peripheral variant, but we found that the case was an intraosseously located CCEOT and thus excluded from our study.

**Results**

A total of 14 cases have been reported (including the present case) from the year 1958 till date. Table 1 shows the demographic details, and Table 2 shows clinical, radiographic, and treatment details of all the cases.

**Age**

The age ranged from 18 to 70 years. The mean age of 35.64 years is in concurrence with the review by Anavi et al.13

**Gender**

The male to female ratio was 4:3 for extraosseous CCEOT. This was in concurrence with the previous review by Anavi et al.13

**Clinical presentation**

All the cases presented as a swelling over the gingiva. Only the case reported by de Oliveira et al. presented with 2 lesions one in the maxillary premolar region and one in the mandibular incisor region. All the other 13 cases presented with a single lesion. Among these 13 cases, 38.46% presented in the maxillary anterior region, 7.69% in the maxillary posterior region, 30.77% in the mandibular anterior region, and 23.08% cases in the mandibular posterior region, demonstrating that the extraosseous CCEOTs have almost equal predilection for maxilla and mandible. It was observed that extraosseous CCEOTs are seen more commonly anterior to the bicuspid in concurrence with the previous articles, but the most common site of occurrence was maxillary anterior region in contrast to the previous conception they occur in the mandibular anterior region.5,13,14 The size of the lesion ranged from 0.5 to 5 cm, with most cases, i.e., 4 cases having a size of 1-1.5 cm, 3 cases with a size of 1 and 2 cm each, and only 1 case with a size of 5 cm. No details regarding size were mentioned in 3 cases.

**Radiographic**

On analyzing, the radiographic details reported in all the 14 cases including the case reported by Oliveira et al.; since the two lesions presented with similar radiographic picture, it was noted that no bony involvement was noted in 50% (7) cases, unilocular radiolucency was noted in 14.29% (2) cases, and crestal resorption and superficial erosion were noted in
28.57% (4) cases each. One case report had no details on the radiograph.

**Treatment details**

A total of 12 of the cases reported were excised, except two cases which required resection and partial resection, respectively.

**Discussion**

CEOT is a slow growing benign odontogenic tumor accounting for only around 1% of all odontogenic tumors. Extraosseous presentation of CEOT is seen in only 6% of all the CEOTs. The tumor presents with typical polyhedral cells with round central nucleus and prominent intercellular bridges. Nuclear hyperchromatism and pleomorphism are commonly reported. Few cases present with clear cells in tumor in varying amounts, such cases are diagnosed as CCEOT.1,3,5

The present case is a rare entity because clear cells have been noted in the extraosseous CEOT. The lesional tissue showed cords and islands of cuboidal to polyhedral cells with central round nucleus and prominent intercellular bridges in many areas. These cells were interspersed with abundant eosinophilic material confirmed to be amyloid-like material on subjecting the section to Congo-red staining and viewing under polarizing microscope. Thus, the case was diagnosed as extraosseous CEOT - clear cell variant based on histopathological features and the staining characteristics.

On critical analysis of the cases of extraosseous CCEOTs documented from 1958 to 2015 in the English-language literature, we noted that the occurrence of extraosseous CCEOT’s is a more common in Asia. A slight predilection for males was noted in concurrence with review by Anavi et al.,13 but in contrast to review by Mesquita et al.,4 which showed equal predilection. All the cases presented with a swelling in the gingival region more commonly anterior to bicuspid. The most cases presented with a small size of ≥2 cm except 1 case with a large lesion measuring 5 cm. We noted that the peripheral CCEOT’s show an indolent behavior in the majority of the cases with either no bony involvement or mild superficial or crestal resorption. Only two cases showed a unilocular radiolucency, but none showed cortical bone perforation which is considered important factor considered for commenting on the aggressive behavior of the tumor.1,5 Most of the cases required sheer complete excision with only 2 cases requiring complete or partial resection and no recurrence has been reported till date, further emphasizing its indolent nature.

The occurrence of clear cells has always been observed with suspicion. Literature shows that clear cells may confer more aggressive behavior to the lesion, higher tendency

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<th>Country</th>
<th>Age (year)</th>
<th>Sex</th>
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<th>Site</th>
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<th>Bone involvement</th>
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for recurrence and a more radical surgical approach.\textsuperscript{16-20}
Extraosseous CCEOTs have neither shown aggressive behavior nor recurrence, as can be noted here. The reason probably could be that extraosseous location permits early diagnosis and treatment. However, the role of clear cells in extraosseous CEOTs is still obscure since very few cases have been reported to date to reach a precise conclusion regarding the impact of clear cells on the biologic behavior of the tumor.

**Conclusion**
In the present case and the review of literature, reinforces the importance of accurate diagnosis based on complete investigations, histopathological features along with the use of auxiliary methods such as special stains and examination under polarized light. It is important to identify clear cells in the tumor even when their number is small. We also emphasize the need for correct management of gingival overgrowths and swellings.

**References**