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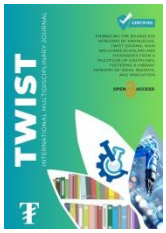

Calcifying Epithelial Odontogenic Tumor Exhibiting Clear Cell Variant

A Rare Case Report

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Abstract
Calcifying epithelial odontogenic tumor (CEOT) rarely exhibits clear cell histopathologic patterns. This unusual lesion still needs continual documentation in order to have more information regarding clinical, radiological, microscopic features and treatment with follow-up. Therefore, we present an uncommon case of the clear-cell variant of CEOT in the mandible.

Keywords
Calcifying epithelial odontogenic tumor, Microhistology, Odontology, Recurrent lesion, Hemimaxillectomy

INTRODUCTION

The term odontogenic tumors include heterogeneous entities derived from the cells that forms the tooth. They may be benign or malignant in origin. Calcifying epithelial odontogenic tumor (CEOT) is one of the rare benign neoplasms of epithelial origin, that usually has incidence of less than 1% of all odontogenic tumors [1]. Thoma and Goldman first described this CEOT as "adenoid adamantoblastoma" in 1946, but it was later acknowledged as a distinct entity by Danish pathologist Jens J. Pindborg in 1958 and is therefore also known as Pindborg tumor [2,3]. In 1971 the term "Calcifying epithelial odontogenic tumor" was generally accepted and adopted by the WHO [3,4]. This odontogenic tumor does not show a gender predilection according to most studies [5]. According to most studies, it usually affects patients between the 3rd and 4th decades of life, however a wide age range from 8 to 92 years has been reported [6].

There is nothing well known about the originating cells. Some pathologists suggested that it might be derived from the intermediate stratum layer of the enamel organ during tooth development stage, some others favored an alternative hypothesis in which, CEOT may arise from the remnants of the primitive dental lamina or sometimes from oral epithelium found in the initial stage of odontogenesis [7,8]. CEOT may be classified as intraosseous (central) or extraosseous (peripheral). Most commonly, it presents as an intraosseous lesion in the mandibular premolar/molar region [9].

The radiological features of CEOT can vary greatly and range from a uniform radiolucency to a mixed radiopaque lesion, with either poorly defined or distinct margins, and may be associated with an unerupted tooth [10,11]. Definitive diagnosis of CEOT is based on histological assessment, which in most cases is very distinctive of the tumour

[12]. The classical histopathological characteristics of CEOT comprise sheets and islands of polyhedral eosinophilic epithelial cells with calcifications as well as deposition of an amyloid-like substance; however, occasionally, focal areas of clear cells can be observed in the clear-cell variant of CEOT [10]. However, this unusual lesion still needs continual documentation in order to have more information regarding clinical, microscopic features or behavior, particularly, the potential origins of the clear tumor cells.

Surgical resection with negative margins to minimize the risk of recurrence and long-term follow-up is the treatment of choice in most of the cases. Here in this article, we report an effective management of rare clear cell variant of CEOT in an elderly female patient along with its clinical, radiographical and histological features.

CASE REPORT

A 72-year-old female presented with the chief complaint of pain and gradually increasing swelling in left lower jaw region for the past 3 months. The pain was intermittent in onset, at times radiating to left temporal region and localized in left condylar region. Patient was a known hypertensive for 3 years and it was under control with regular medication. She added the history of tingling and prickling sensation on lower lip. There was no history of difficulty in mouth opening, difficulty in swallowing, pus discharge, pyrexia, weight loss, and restriction in tongue movement.

Extra oral examination revealed that a diffuse swelling of size approximately 4cm x 2cm. Supero-inferiorly it was extending extending between ascending ramus to 1cm below inferior border of mandible. Antero-posteriorly it was extending from 2cm from angle of mouth till angle of mandible. Step deformity was noted 1cm anterior to the angle of the mandible. Swelling was firm in consistency, non-tender and non-mobile. There were no palpable lymph nodes and mouth opening was apparently normal. Left side tempero mandibular joint was non-tender and palpable.

Intra oral examination reveals a diffuse swelling of 4cm x 2cm was noted in relation to the distal aspect of 37 tooth. Supero-inferiorly it was extending between ascending ramus, retromolar region till the maxillary tuberosity. Medio-laterally it was extending from floor of mouth to buccal vestibule of 37 making the vestibule to be obliterated. There was no evidence of bleeding and pus discharge from the swelling (Figure 1).

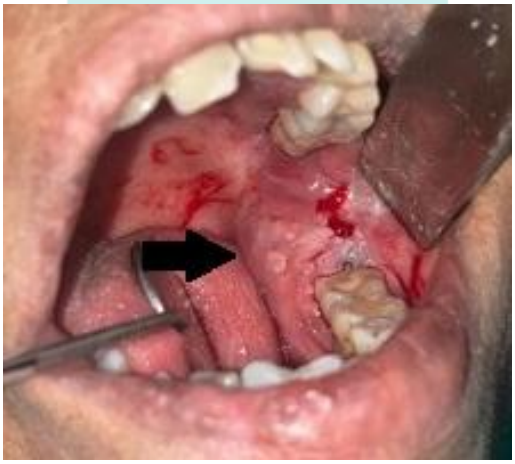

Fig. 1 Clinical intra oral image shows the swelling size and extent (*indicated by black arrow*)

Orthopantomogram revealed that an ill-defined multiloculated radiolucent lesion exhibiting soap bubble appearance. The lesion was extending from the mesial root apex of 37 medially, border of the mandible inferiorly, ascending towards the ramus of mandible till the coronoid process and condyle posterior-superiorly. Impacted mandibular left third molar was seen in the radiolucency. The inferior border of the mandible pertaining to the radiolucency is not intact (Figure 2). Axial sections of CT (Refer Figure 3) and 3D reconstruction CT (Refer Figure 4) gave better delineation of the swelling in all the dimensions. Based on these clinical and radiographical findings, ameloblastoma was considered as provisional diagnosis. CEOT and central odontogenic fibroma were added as differential diagnosis.

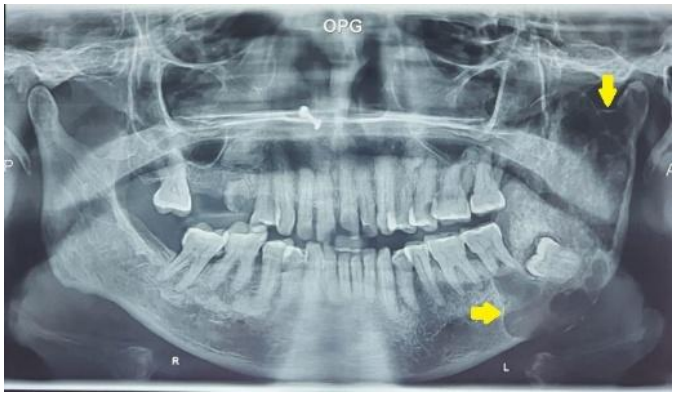

Fig. 2 Orthopantomogram reveals a multiloculated radiolucent lesion (*indicated by yellow arrows*)

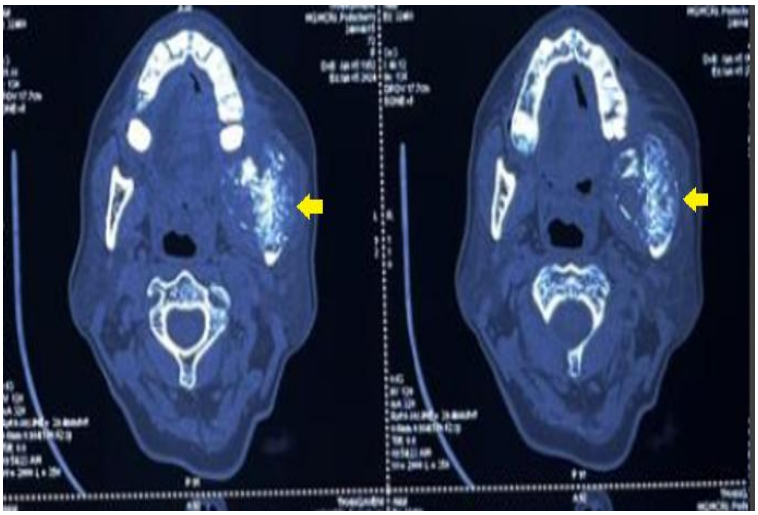

Fig. 3 CT Contrast – Axial sections reveal a hyperdense diffuse lesion in the left angle of mandible region (*indicated by yellow arrows*)

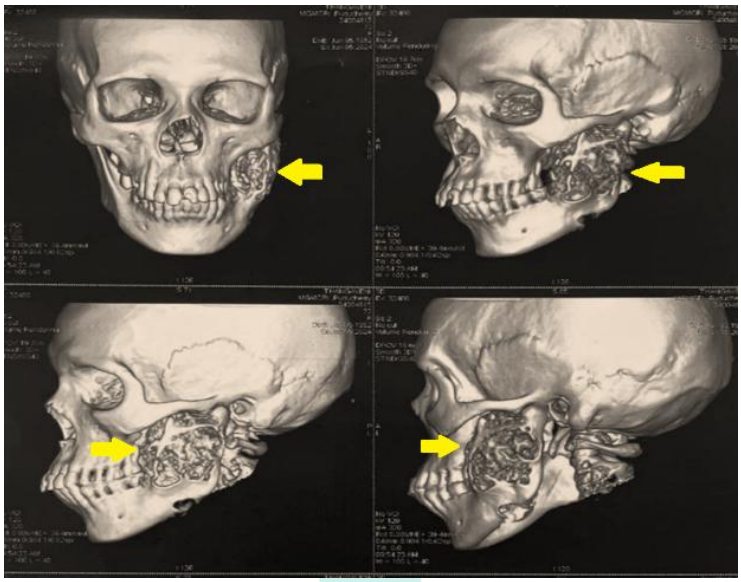

Fig. 4 3D reconstruction CT reveals exact extent and location of lesion (*indicated by yellow arrows*)

An incisional biopsy was done in the lesion site (Refer Figure 5) and sent for routine histopathological examination. H and E-stained section under microscopic examination revealed sheet of polyhedral cells with prominently eosinophilic cytoplasm, centrally placed round to oval nuclei, intercellular bridges and sparse mitotic figures. Some of the cell clusters showed scanty cytoplasm with eccentrically placed nucleus suggestive of clear cells (Refer Figure 6). Homogenous eosinophilic globular substance seen scattered among the tumour cells. Concentric globular basophilic structures mostly ovoid to round shape, few irregular in shape suggestive of areas of calcification in the form of Liesegang rings were also evident in the studied section (Refer Figure 7). Based on the above-mentioned features, a final diagnosis of "Calcifying Epithelial Odontogenic Tumor (CEOT) – Clear cell variant" was made.

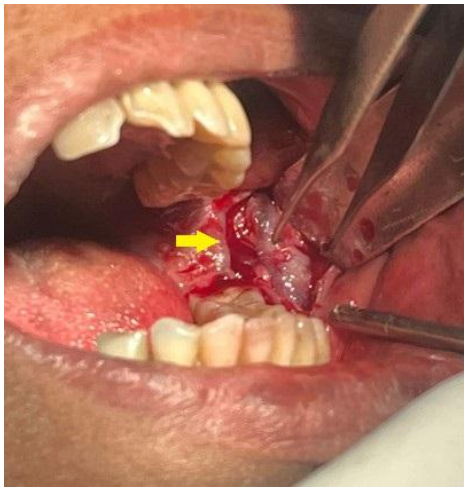

Fig. 5 Intra oral image shows the site of incisional biopsy (*indicated by yellow arrow*)

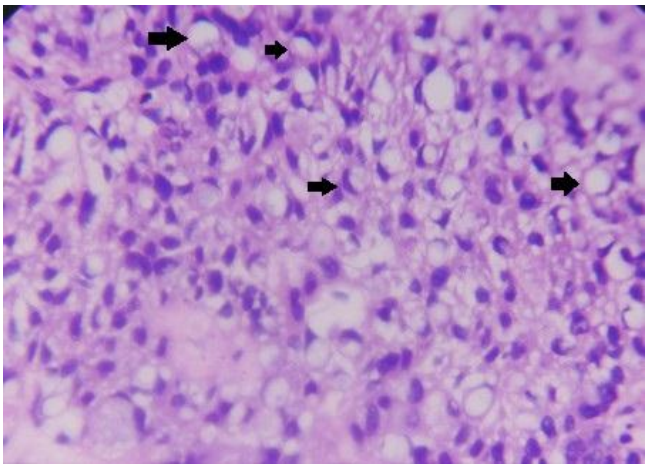

Fig. 6 Photomicrograph shows eosinophilic cells having scanty cytoplasm with eccentrically placed nucleus suggestive of clear cells. (H&E stain, 400x) (*indicated by black arrows*)

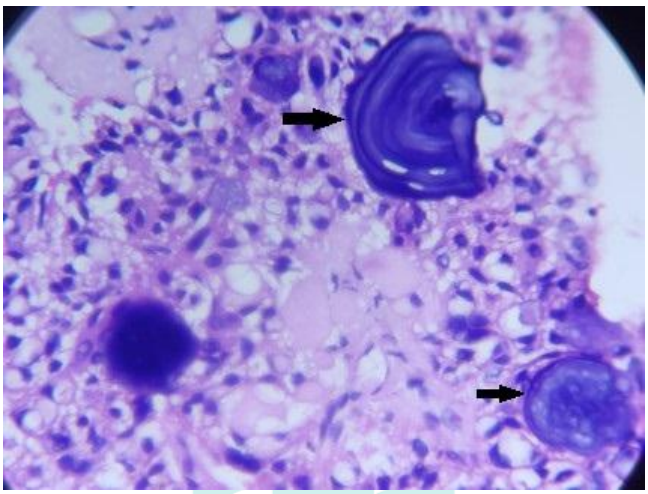

Fig. 7 Photomicrograph shows round to ovoid areas of calcification in the form of Liesegang rings (H&E stain, 400x) (*indicated by black arrows*)

After the patient was declared fit for surgery under general anesthesia, resection of the lesion with a 1 cm clearance and the defect bridged using reconstruction plate. Through Risdon's submandibular approach, the lesion was exposed. As the tumor had fully eroded on all the surfaces of mandible, segmental resection was performed (Refer figure 8) distal to mandibular left canine and a portion of condyle was left after the tumor removal to ensure the fixation of reconstruction plate. The patient was followed up on the intervals of one week, one month, three month and sixth month. The follow up period was uneventful till date and patient is still in the follow up to check for any incidence of recurrence.

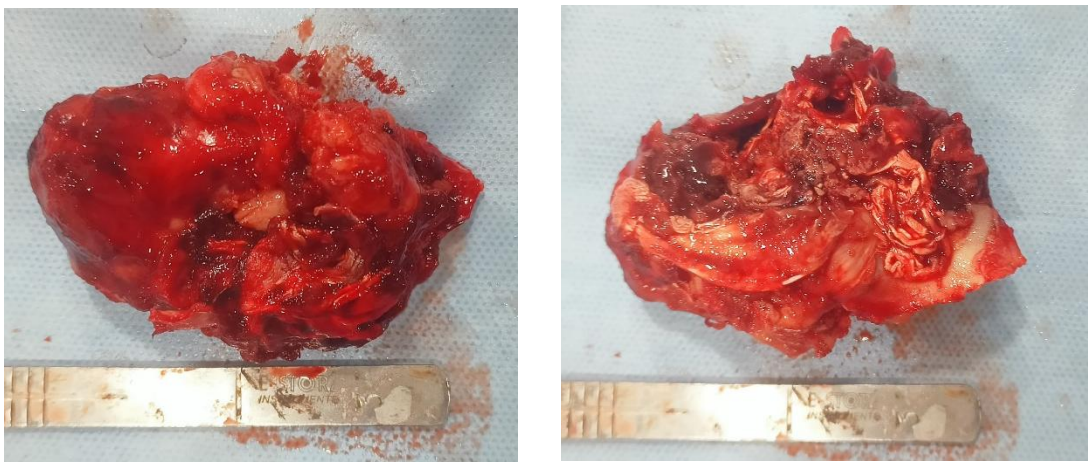

Fig. 8 Photomicrograph shows round to ovoid areas of calcification in the form of Liesegang rings (H&E stain, 400x) (*indicated by black arrows*)

DISCUSSION

CEOT is a rare benign odontogenic tumor, described in 1955 by Pindborg and also known as Pindborg tumor. This lesion represents about 0.4-3 % of all odontogenic tumors.[10] The intraosseous CEOT most often presents as a painless mass with slow growth. The most frequent presenting symptom of CEOT is swelling or expansion (72%); 22% of cases are

asymptomatic and 13% complained of pain or discomfort.[11] In our case, pain and swelling were increased gradually in left mandibular molar ramus area.

Most of the authors agree that intraosseous CEOT is usually located in the premolar and molar regions, with a mandibular to maxillary ratio of 2:1 or 3:1.[10] The majority of CEOTs are associated with impacted or unerupted teeth.[13] The age of the patients affected by this tumor ranges from 8 to 92 years, with a mean age of 40.[14] In this case report, it was a 72 year old female patient with a swelling in relation to the mandibular angle region with an impacted or unerupted tooth.

Radiographically, according to a study by Kaplan et.al.[11] 58% of CEOTs are unilocular, 27% multilocular, and 15% nonloculated. The periphery of the tumor may demonstrate a fine sclerotic rim, and internal aspect frequently contains mineralized structures that appear as amorphous radiopacities of varying sizes. The tumor in this case was seen mainly as multilocular radiolucencies with amorphous opacification and a sclerotic rim. The bigger lesions can be multilobulated, imitating an ameloblastoma, mainly if we do not observe intramural calcifications.[15]

There are different school of thoughts within the oral and maxillofacial pathologists regarding the degree of differentiation of the odontogenic epithelium which forms the basis for tumour pathogenesis. Few researchers suggest that the epithelial cells of the CEOT are reminiscent of the sequestered cells in the stratum intermedium layer of the enamel organ. This idea is based on the morphological similarity of the tumour cells to the normal cells of stratum intermedium and a high activity of alkaline phosphatase and adenosine triphosphate.[16] In our case, the impacted tooth in the mandibular angle region might cause disruption of ectomesenchyme signalling in that region, that possibly turned to be CEOT.

It has been suggested that amyloid deposition within CEOT is an immunologic response to these stratum intermedium cells. Others insist that it arises from remnants of the primitive dental lamina found in the initial stage of odontogenesis, and these epithelial rests are the more likely true progenitor cell. However, the exact aetiology is unknown.[16] Mutations in tumour suppressor genes such as PTEN, CDKN2A, PTCH1 and other oncogenes like JAK3, MET were identified in CEOT. Till date, none of these do not contribute to clinical properties or treatment decisions substantially.[17]

The histopathology of CEOT, in its classic pattern, comprises sheets of polyhedral epithelial cells with well-defined cell borders and distinct intercellular bridges; these neoplastic cells may demonstrate pleomorphism, but only rarely typical mitoses. Additionally, the other most characteristic findings are the presence of amyloid-like substances and calcified concentric Liesegang rings. To date, five histopathologic patterns of CEOT have been documented: [18,19] (i) strands/ sheets/islands of polyhedral cells with intracellular bridges; (ii) a cribriform arrangement with many spaces containing an eosinophilic (amyloid-like) substance; (iii) densely-populated neoplastic cells with interspersed multinucleated giant cells; (iv) nests of epithelial cells similar to neoplasm of the salivary gland; and (v) prominent clear-cell arranged in a pseudo glandular manner.[20] The last pattern is referred to as the clear-cell variant of CEOT, and the histopathological findings of the current case were consistent with this pattern, showing abundant clear cells arranged in a pseudo glandular pattern containing an amyloid-like material.

This tumor still has an unpredictable clinical behavior, and can force an aggressive surgical treatment when the local behavior is not benign, or we have a recurrent lesion.[15] Methods of treatment have ranged from simple enucleation or curettage to hemimandibulectomy or hemimaxillectomy.[21] Some authors consider however, that conservative surgery is treatment of choice.[10] In view of the biological behavior of the CEOT, mutilating procedures, such as wide resection or hemiresection of the mandible, seem unwarranted. Enucleation with a margin of macroscopic normal tissue is, therefore, the recommended treatment for lesions involving the mandible. CEOT of the maxilla, however, should be treated more aggressively, as maxillary tumors, in general, tend to grow more rapidly than their mandibular counterpart and do not usually remain well confined. [10,13] Treatment should, however, be individualized for each lesion because the radiography and histologic features may differ from one lesion to another. [10] The prognosis of the CEOT is good with infrequent recurrence. Although malignant behavior is extremely rare, five years follow-up of the operated patients should be recommended to assess the healing for this tumor. [22,23]

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