

Clear Cell Odontogenic Carcinoma: A Case Report

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ABSTRACT

Background: Clear cell odontogenic carcinoma (CCOC) is a rare malignant epithelial odontogenic tumor of the jaws with aggressive behavior, local recurrence and distant metastases.

Case report: A 39-year-old male presented with a painful swelling and a well-defined radiolucent lesion that was comparable to an inflammatory odontogenic lesion.

Investigation: Knowledge about the clinicopathological and immunohistochemical characteristics of CCOC helps to differentiating it from other clear cell tumors.

Conclusions: CCOC is an unusual malignant odontogenic tumor with unknown etiology. A careful approach is suggested both clinically and immunohistochemically for definitive diagnosis. Long term follow up is necessary because of its potential for recurrence and distant metastasis.

Keywords: Pathology, Oral, Odontogenic tumor

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INTRODUCTION

Clear cell odontogenic carcinoma (CCOC) is a rare malignant epithelial odontogenic tumor of the jaws that was initially known as clear cell odontogenic tumor or clear cell ameloblastoma¹. Aggressive behaviour of tumor such as local recurrence or distant metastases caused CCOC to be considered as a malignant neoplasm of odontogenic origin in the WHO classification of 2005². This neoplasm tends to involve the anterior region of mandible with female predilection and a peak incidence of 5th to 7th decade of life^{1,3}. Ill – defined unilocular or multilocular radiolucency with bone destruction and tooth resorption were observed in radiographic images of most cases of CCOC. The histopathological characteristic of this tumor is the sheets or islands of large clear cells with hyperchromatic nuclei and eosinophilic cytoplasm^{4,5}.

According to latest review of literatures, only 98 cases of CCOC were reported to date. One- third of this tumor was initially misdiagnosed. Non-specific clinical and radiographical features of CCOC lead to inadequate treatment^{5,6}. In this study, we reported clinical, radiographic and histopathological features of a young patient with CCOC.

CASE REPORT

A 39 year old male was presented with a painful swelling in the anterior region of the mandible since 6 months that was referred to the Department of Oral and Maxillofacial Surgery at Isfahan Dental School, Iran. He had a history of root canal therapy of right and left mandibular central incisors and left lateral incisor of mandible due to local pain in a private clinic (Figure 1.A).

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After this treatment, he had no improvement in the symptoms and the swelling increased. The patient's medical history was not relevant. He had neither history of trauma nor any palpable lymph nodes.

Intraoral examination revealed a 3×3.5 cm painful swelling in the anterior region of the mandible which is hard in consistency with no increase in temperature or no paresthesia of the lower lip was noted. Both the buccal and lingual cortical plate expansions were observed. A panoramic radiograph showed a large, well-defined radiolucency of the lesion extending from the lower right canine to the left canine (Figure 1.B). Root divergence and resorption of the central and lateral incisors was observed

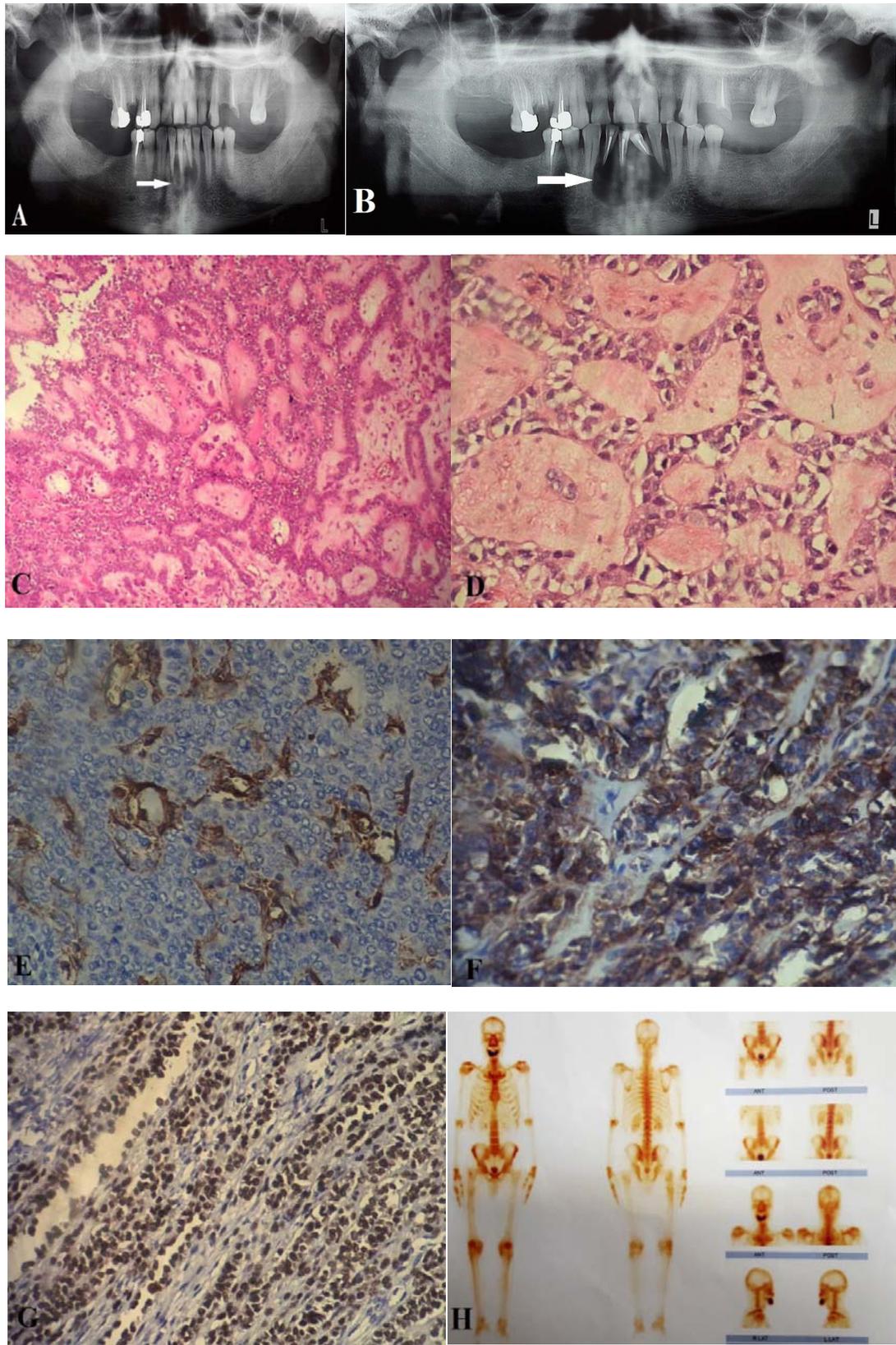


Fig 1. A: Panoramic radiograph showing a defined radiolucent lesion in the anterior mandibular region before endodontic treatment, **B:** After endodontic treatment. **C:** Photomicrograph showing a Lesion with a trabecular pattern (H&E, $\times 100$). **D:** Clear cells in histopathological examination (H&E, $\times 400$). **E:** Vimentin (IHC $\times 100$). **F:** CK14 (IHC $\times 400$), **G:** P63 (IHC $\times 100$), **H:** whole body Tc- 99m MDP bone scan shows metabolically active lesion in the anterior portion of mandible.

in occlusal radiograph. The differential diagnosis of clinical and radiographic imaging was ameloblastoma, myxoma, and early osteosarcoma.

An excisional biopsy of the lesion was done under general anesthesia. The lesion was removed with the involved teeth by partial resection and the specimen was sent for histopathological diagnosis.

Histopathological examination revealed an epithelial tumor with cells arranged in the form of islands and cords of with biphasic pattern (Fig 1.C). The tumor composes of clear cells in fibrous and hyaline stroma. Clear cells were oval or polygonal shape with dark-staining eccentric nuclei (Figure1.D). Some islands showed peripheral cell palisading. Furthermore, basaloid cells having nuclear pleomorphism and mitotic figures had been observed. Reactive calcification is also observed in some fields of histopathological sections. The differential diagnosis based on histopathological feature was CCOC, Intraosseous Mucoepidermoid Carcinoma (MEC), and metastatic lesion. In addition, the clear cells were positive for Periodic Acid-Schiff (PAS) staining, but these cells were negative for mucicarmine stain. Histochemical stains like Pan-cytokeratin, CK14, CK19, P63 were positive for clear cells. The tumor cells were nonreactive for vimentin (Figure1. E-G). Absence of amyloid deposition and liseegang's ring calcification in our case was ruled out calcifying epithelial odontogenic tumor (CEOT). The negative result for mucicarmine and Vimentin negated MEC. Intraosseous location of lesion and palisaded peripheral cells ruled out other salivary gland tumors or other adenocarcinomas such as clear cell carcinoma (CCC). The whole body scan did not reveal any metabolically active lesion except the one on the anterior portion of mandible (Figure1.H). Finally, according to histopathological and specific staining, the diagnosis of CCOC was established. Considering that the resection was performed for the patient and the lymphnodes were not palpable, only follow up was advised to patient. After a year follow up, no recurrence and distant metastasis was noted.

DISCUSSION

CCOC is an unusual odontogenic tumor with unknown etiology.⁷ Some literatures suggest that clear cell of jaw tumors originate from dental lamina and rest of malassez.⁸ Literature reviews reported that CCOC commonly occurred in the sixth decade of life with an age range from 14 to 89 and has a female predilection with male/female ratio= 1:2.¹ Furthermore, mandible has more frequency than maxilla with Mand: Max ratio of 3:1.^{1,4} The anterior region of the jaws is most frequently affected.⁹ In the present case, we reported a rare case of CCOC in 39 year old male. It is inconsistent with the usual demographic finding (age and gender) of CCOC. The usual clinical symptoms of this tumor is a painless swelling,¹⁰ however pain, tooth mobility, paresthesia, ulceration of soft tissue, cortical destruction have been observed in other cases.^{5,11} In this case, the patient had pain before the swelling occurred. Because of the absence of swelling, the case was misdiagnosed as periapical inflammatory lesion in a private clinic and it's late diagnosis.

Radiographic assessment showed unilocular or multilocular radiolucency with or without well-defined margins. Although, few cases reported with mixed radiolucent-radiopaque lesion.^{1,6,11} In this case, a well-defined unilocular radiolucency was observed in early stage, but 3 months after root canal, radiological view showed divergence and resorption of involved teeth and increase of lesion

size. The possibility of misdiagnosis of CCOC is relatively high. A radiolucent jaw lesion with increase swelling and loosening teeth should be considered to possibly a malignant lesion. Furthermore, the diagnosis of CCOC is difficult by considering only the histopathological feature because of the presence of clear cells in other odontogenic tumors.^{2,12} CCOC demonstrates one or more of three patterns like biphasic, monophasic, and ameloblastomatous are patterns. Biphasic pattern is the most common pattern that comprises of clear cell and basaloid cell. The clear cell have abundant clear to faintly eosinophilic cytoplasm with distinct cell membrane central/eccentric uniform dark staining nuclei which lacks nuclear pleomorphism and mitotic activity.^{4,5} Basaloid cells with scant eosinophilic cytoplasm were seen. The monophasic pattern consists only of clear cells. Ameloblastomatous pattern consists of the nest of cells showing central cystic change, squamous differentiation and peripheral nuclear palisading with reverse polarity.³ Our case is the biphasic pattern of tumor growth. Although, ameloblastoma pattern was observed focally. Presence of clear cell in CCOC are hallmark but not the pathogonomic feature because in many other odontogenic tumors (CEOT, Clear cell ameloblastoma), Salivary gland tumors (Mucoepidermoid carcinoma, Clear cell carcinoma, Epithelial- myoepithelial carcinoma, Acinic cell carcinoma), Amelanotic melanoma, Metastatic tumors (Renal cell carcinoma, thyroid, parathyroid, breast prostate, lung, colon tumor), Perivascular epithelial carcinoma it can be observed.¹⁻⁵ The presence of palisading cells and hyalinization in stroma can be help to diagnosis of odontogenic tumor.⁷ In addition to morphological and immunohistochemical pattern of tumors with clear cell changes, the location is the most important factor for these tumors.¹³ However, when a case is doubtful to CCOC, search for any metastatic lesional site is recommended.⁵ In this case, the metastatic lesion was not detected. For definitive diagnosis of CCOC, immunohistochemical staining is also necessary. This malignant neoplasm may be having aggressive behavior such as local recurrence, regional or distant metastasis.⁷ According to studies, 41% of all patients have recurrence and 31% have distant metastasis.¹⁰ Zharg et al reported that rate of recurrence was 41.8% to 86.7% in curettage treatment and 29.8% with resection method.¹⁴ 17% of patients with recurrence lesion had distant metastasis. The initial treatment methods and the extent of the tumor invasion have a important roles in recurrence rate. According to result of other studies, conservative methods such as curettage and enucleation, soft tissue involvement were related to higher recurrence rate. Furthermore, the degree of nuclear pleomorphism and hyperchromatism may be related to metastatic potential of the tumor.^{5,6} According to new documents, the CCOC is considered a high grade malignant odontogenic tumor.⁴

Surgical resection with wide margins is the ideal treatment method for CCOC. In addition, adjuvant radiotherapy and elective neck dissection along with the lymph nodes for patients with perivascular or perineural invasion should be considered. There no sufficient studies for evaluating the benefits of these treatments. In our case, the initial clinical findings were similar to inflammatory periapical lesion, the reasons for delayed treatment of CCOC. Additional reports have showed that many cases of CCOC are misdiagnosed. Since our patient had neither palpable lymph nodes nor metastatic lesions, partial resection of the mandible was performed, no adjunct radiotherapy and chemotherapy was required.

CONCLUSION

CCOC is an unusual malignant odontogenic neoplasm with unknown etiology. A careful approach is necessary both clinically and immunohistochemically for definitive diagnosis. In this report, we discuss a patient that presented with a painful periapical lesion. Similar cases should be considered for the possibility of malignant lesions for early diagnosis and better prognosis. A long term follow up is crucial for understanding the biological behavior of this tumor.

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