

Clear Cell Odontogenic Carcinoma-A Review of the Literature

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Abstract

Clear cell odontogenic carcinoma is a rare jaw lesion with predominantly clear cell characteristics. Although touted as a benign lesion in the initial stages, once the aggressive nature of the lesion became evident, it was reclassified as a malignant tumor by the World Health Organization. Etiology of this lesion remains elusive, and association with any precursory lesion is yet to be proved. It may have their origins from odontogenic epithelium, salivary gland pathologies or even as metastasis from distant locations like kidneys. That the ideal treatment plan should be composite resection along with elective neck dissection, followed by reconstruction of the defect. If clinical and radiological examination of the patient reveals, extensive soft tissue invasion, perineural spread, lymph node metastasis with an extra - nodal involvement or in those where tumor-free margins are not possible, then, the use of adjuvant radiation therapy should be considered and employed at the surgeon's discretion. Even though initial tumor free margins are attained, it is emphasized that the patient should be kept under the long-term follow-up to identify recurrences

Keywords: Clear Cell Odontogenic Carcinoma; Clear Cell Odontogenic Tumor; Metastatic Clear Cell Odontogenic Carcinoma; Clear Cell Maxillary Carcinoma; Clear Cell Mandibular Carcinoma

Introduction

Hansen et al. [1] coined the term "clear cell odontogenic tumor" in 1985 when they described an odontogenic epithelial tumor with predominantly clear cell characteristics. Since all their cases were located centrally in the jaws, they contended upon the odontogenic origin of the lesion. Although previously excluded from the World Health Organization (WHO) classifications of odontogenic tumors, its tendency to recur and metastasis is, since then, well documented [2,3]. Therefore, it was agreed upon that "clear cell odontogenic carcinoma" (CCOC) is a more appropriate nomenclature, and Reichart and Philipsen, later, adopted the same in their latest classification of odontogenic tumors approved by the WHO [4]. In 1992 WHO defined CCOC as "A benign but locally invasive neoplasm originating from odontogenic epithelium and characterized by sheets and islands of uniform, vacuolated and clear cells."

Odontogenic tumors, salivary gland tumors (primary or secondary) and metastatic renal carcinomas are considered as differential diagnoses of CCOC. Based on the morphological, immunohistochemical and clinical grounds the latter two were subsequently eliminated from the list. Waldron et al. [5] first observed the resemblance of clear cell odontogenic carcinoma to

ameloblastoma due to the presence of focal palisading. In spite of their presence, no other areas exhibited typical ameloblastoma characteristics. The focal palisading later went on to justify the odontogenic origin of this lesion, more so when accompanied by inductive hyalinization of the adjacent fibrous tissue.

Normal presentations of CCOC include mild pain or tenderness, or loosening of teeth. The ragged radiolucent area with the expansion of the jaw is concomitantly seen. The first case ever was reported in Maxilla. Local recurrence, evidence of distant, metastasis, and distinct histological features accompanies the aggressive behavior of CCOC. Hence, they are currently considered as malignant [6]. Due to the rareness of the lesion, identification of risk factors is still in their nascent stages. Tumors containing the clear cell component in the head and neck region may have their origins from odontogenic epithelium, salivary gland pathologies or even as metastasis from distant locations like kidneys.

Hence, it is prudent to recommend additional specimen staining of mucin be performed, to rule out mucoepidermoid carcinoma. Lack of calcification and amyloid deposits are the markers, which, when employed, can distinguish CCOC from the clear cell variant of

the calcifying epithelial odontogenic tumor [6]. Reports of lymph node-metastasis were frequent in recurrence while the same was infrequent in the initial stages age predilection between fifth to seventh decades, with a female preponderance (Male/Female ratio, 10:17). Bang G et al. [7] reported a case, which was an exception with older age at diagnosis, more than the normal range found. Literature report that there is a prevalence in the anterior jaw regions and mandible more commonly than in the maxilla. Radiological manifestations included radiolucent lesions with irregular margins, associated with root resorption in most cases.

CCOC exhibits three distinct patterns, the most common being the biphasic pattern characterized by nests of clear cells intermixed with smaller islands of polygonal cells with eosinophilic cytoplasm. The second variant consists of epithelial islands exclusively composed of clear cells, while the least common, the third variant, is characterized by clear cell nests with an ameloblastomatous pattern. Most of the reported cases exhibited predominant clear cells arranged in smaller clusters or large islands without ameloblastic differentiation. The morphological peculiarity of these cells and their arrangement in duct-like structures further supports their odontogenic origin [8]. The exact etiology for this neoplastic occurrence remains elusive. No previous reports have indicated any association with precursory lesions [9,10].

Management

Resection with a wide margin is the mainstay treatment for the management of CCOC. Other reported modalities include curettage or enucleation, surgical resection with or without lymph node dissection, postoperative radiotherapy, and/or chemotherapy. Most of the local recurrences reported are in the form of multiple regional node involvements, and distant metastases reported are frequent [11]. Swain N et al. [12] reported cases with long-term follow-ups and observed that the overall recurrence rate was 38.35% (28/73). The author, then, went on for a breakdown of the data and noted that out of the 15 patients treated with enucleation or curettage, 86.7% had local and/or regional recurrences, four patients died with developing distant metastatic disease. By contrast, local and/or regional recurrence occurred in 26.4% of patients who underwent surgical resection.

From these data, he concluded that recurrence rate after initial treatment by resection was lower than conservative therapy (26.4 vs. 86.7%). Adjuvant radiation therapy is beneficial to patients with extensive soft tissue and perineural involvement, and in patients with extracapsular spread and/or positive nodes cases in which tumor-free margins are not possible [13]. Krishnamurthy A et al. [14], reported a case of CCOC where he performed composite resection with modified radical neck dissection and reconstruction of the defect with pectoralis major myocutaneous flap.

From the above examples, and from the extensive study of the literature available, most of the authors, including the authors of this article advocate that the ideal treatment plan should be composite resection along with elective neck dissection, followed by reconstruction of the defect [15]. Although elective neck dissection

is questioned by multiple, reports by Werle H et al. [16] & Ebert CS [17] endorse its use. They report that following neck dissection with long-term follow-up, there were no signs of recurrence. If clinical and radiological examination of the patient reveals, extensive soft tissue invasion, perineural spread, lymph node metastasis with an extra-nodal involvement or in those where tumor-free margins are not possible, then, the use of adjuvant radiation therapy should be considered and employed at the surgeon's discretion. With all the treatment modalities, even though initial tumor free margins are attained, it is emphasized that the patient should be kept under the long-term follow-up to identify recurrences in early stages and institute appropriate treatments as necessary.

Conclusion

CCOC, although rare, should be considered in the differential diagnosis of jaw tumors with prominent clear cell component. Factors such as the size, soft tissue involvement, lymph node metastasis, and the presence or absence of positive surgical margins should be considered during treatment planning. Currently, treatment aim is to achieve wide surgical resection with tumor-free margins and loco-regional control by lymph node resection and local radiation. Long-term follow-up is imperative considering the aggressive biological potential, as these tumors may recur locally or systemically.

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