Case Report

Clear cell odontogenic carcinoma with skeletal metastasis: A rare case report

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Abstract

Clear cell odontogenic carcinoma (CCOC) is a rare odontogenic malignancy with a female preponderance occurring in the adult age group. CCOC was classified as a malignant neoplasm of odontogenic origin by the World Health Organization in 2005 because of its aggressive nature, local recurrence tendency, and the potential for regional and distant metastasis. Histologically, CCOC is characterized by sheets and islands of vacuolated and clear cells. Metastasis at presentation is rare; it usually involves cervical lymph nodes and lungs, less frequently to bone. As clear cells are present in few odontogenic tumors; salivary gland neoplasms; and metastatic tumors to the jaws, especially metastatic renal cell carcinoma, the presence of clear cells in a lesion of the head and neck region poses a diagnostic challenge. So knowledge about the clinical course, histopathological pattern, and immunoprofile of CCOC helps in differentiating the other clear cell tumors.

Keywords: Clear odontogenic carcinoma, differential diagnosis, immunohistochemistry, skeletal metastasis

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INTRODUCTION

Odontogenic tumors account for approximately 9% of all tumors of oral cavity. It is a rare neoplasm with malignant potential, which was first described by Hansen *et al.*[1] in 1985 as a clear cell odontogenic tumor. Histologically, they may be confused with other clear cell carcinomas, especially metastatic renal cell carcinoma. In the same year, Waldron *et al.*[2] described similar cases and were the first to use the term "odontogenic carcinoma" to identify this pathological entity. In 1985, Eversole *et al.*[3] reviewed 17 cases and confirmed the aggressive nature of the lesion, but also concluded that there was a tendency to local recurrence after surgery and potential for regional and distant metastases. It was considered benign by the World Health Organization in 1992, but due to its high potential for regional spread and distant metastases, it was reclassified as malignant in 2005. Locoregional spread is mainly to facial skin, temporal bone, parotid gland, infratemporal fossa, retro-orbital region, and submental spaces but lymph node, and distant metastasis[4-8] to lung and bone is less frequent.

CASE REPORT

A 66-year-old known hypertensive woman presented to our institution with a 2-month history of lower tooth pain and swelling in the right lower jaw. She had

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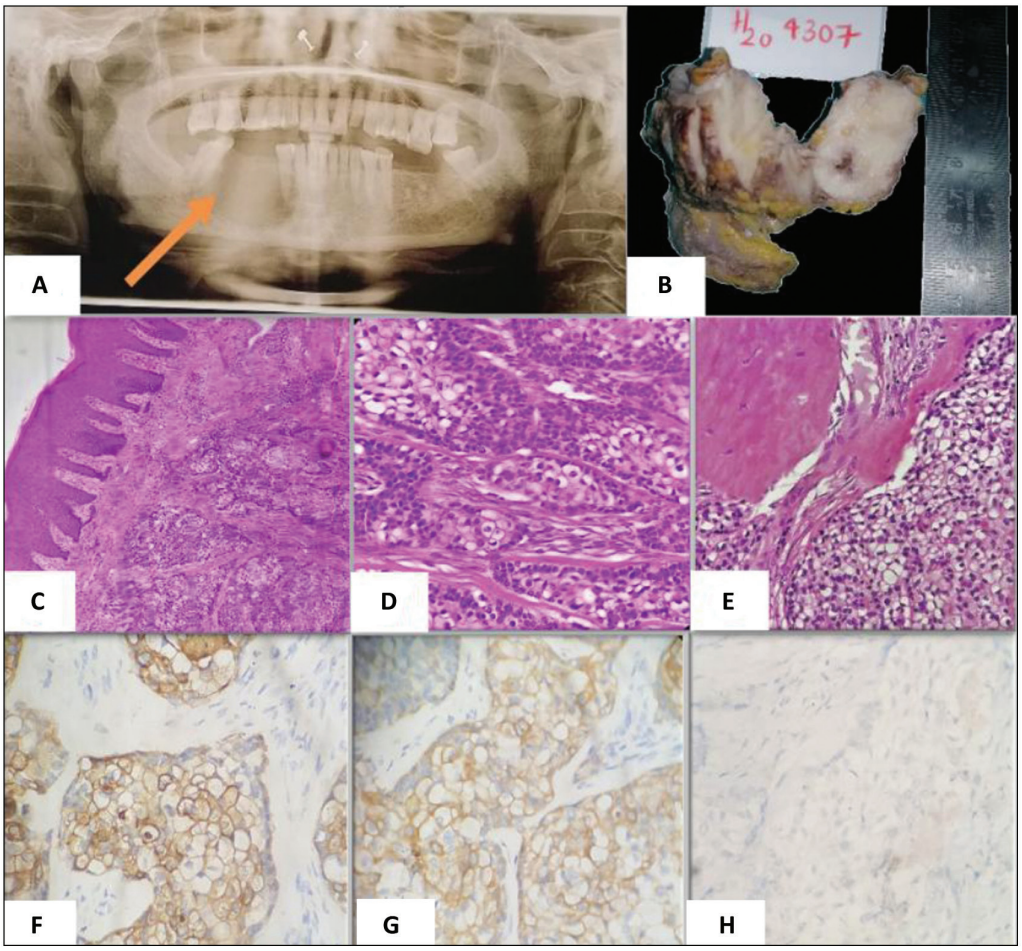

Figure 1: (a) Orthopantomogram showing unilocular radiolucency in the mandibular region from the first premolar to the second molar. (b) Gross photograph of mandibulectomy specimen with an ill-defined gray-white lesion involving the body of mandible. (c) Microphotograph of CCOC of mandible (H&E, 4×). (d) Microphotograph showing lobules and small nests of peripheral basaloid cells with hyperchromatic nuclei and central clear cells (H&E, 40×). (e) Microphotograph of clear cells infiltrating the rib bone. (f) Microphotograph of cytokeratin (PCK) showing strong and diffuse membranous stain (IHC stain, 40×). (g) Microphotograph of cytokeratin 5/6 showing membranous stain (IHC Stain, 40×). (h) Microphotograph of PAX 8 showing negative stain (IHC stain, 40×). H&E = Haematoxylin and Eosin

undergone tooth extraction with biopsy elsewhere. The slides were reviewed at our institution and reported as clear cell rich carcinoma. Immunohistochemistry (IHC) was done for confirmation of diagnosis and to rule out metastasis, mainly clear cell renal carcinoma. All of the markers (S100, PAX8, vimentin, and CD10) were negative [Figure 1]. Clinical examination revealed 3 × 2 cm expansile lesion involving the body of right mandible from the first premolar to the second molar. Further evaluation was done to rule out any metastasis. On positron emission tomography-computer tomography (PET–CT), apart from the primary lesion another metabolically active 2 × 1 cm lytic lesion was noted involving the left eighth rib. Along with that, level Ib and two lymph nodes were also metabolically active. Fine needle aspiration cytology (FNAC) from the rib lesion confirmed a metastatic clear cell carcinoma. Subsequently, she underwent mandibulectomy with right level I neck dissection and thoracoscopy-guided wide excision of the left eighth posterior rib lesion. She was then referred for postoperative radiotherapy.

Histopathology

The initial biopsy showed fragments of a poorly circumscribed ulcerated neoplasm composed of lobules, small islands and nests having peripheral basaloid cells with hyperchromatic nuclei, and central clear cells with abundant clear cytoplasm with well-defined borders and round-to-oval vesicular nuclei lying in a fibrous stroma.

The microscopic examination of the mandibulectomy specimen revealed an epithelial tumor with similar features as in the small biopsy. Periodic acid Schiff (PAS) stain was negative. Perineural invasion was seen. The tumor excised from the rib also showed the same morphology and was concluded as a metastatic deposit by IHC. Enlarged lymph nodes were negative for metastasis.

The tumor tissue in the mandible and the rib lesion both showed strong and extensive immunoreactivity for keratin (keratin 5/6, pankeratin) and no immunoreactivity for S-100 protein, napsin, PAX8, or SMA. So final diagnosis of clear cell odontogenic carcinoma (CCOC) was rendered.

DISCUSSION

CCOC is a rare odontogenic tumor. The histogenesis of CCOC is unclear, and the literature suggests that clear cells in jaw lesions originate from dental lamina or cell rests of Malassez.[9] It is suggested that the presence of clear cells is an attempt to recapitulate the presecretory phase of ameloblast with the accumulation of glycogen.[10]

A review of literature of the 43 cases reported by Ebert *et al*.[11] showed that the male:female ratio was 3:1 with mean age of 58 years at the time of presentation (range 17–89 years), the average period of follow-up was 5.5 years (range 0.5–21 years), and mandible was the most common location (84%). The overall recurrence rate for these tumors was 55% and local recurrence rates were higher (80%) for curettage alone than for resection alone (43%). Lymph node metastasis on initial presentation was rare (10%) but rapidly increased in those with recurrent disease (33%). Factors such as size of the lesion, soft tissue involvement, lymph node metastasis, and most importantly, the presence or absence of positive surgical margins should be considered when developing the treatment strategy. The classic clinical presentation of CCOC is a painful anterior mandibular swelling in an elderly woman. There may be loosening of adjacent teeth, and a roentgenogram shows a well or poorly demarcated radiolucent mass that can be either unilocular or multilocular, most often in a premolar location.[12] Our patient was an elderly female who presented with pain in the mandibular region with a well-defined, well-corticated, unilocular radiolucency with dislocation of the associated tooth.

Histopathologically, CCOCs show one or more of three architectural patterns: biphasic, monophasic, and ameloblastomatous. The most common pattern is biphasic pattern where tumor growth comprises nests of cells with clear cytoplasm admixed with cells containing eosinophilic cytoplasm. The monophasic pattern comprises only clear cells, whereas the ameloblastomatous pattern resembles the growth pattern of ameloblastoma with nests of cells showing central cystic change and squamous differentiation, and peripheral nuclear palisading with reverse polarity.[13]

The differential diagnosis of jaw tumors with prominent cytoplasmic clearing includes intraosseous salivary gland tumors (epithelial–myoepithelial carcinoma, in which the clear myoepithelial cells are immunoreactive for S-100 protein, vimentin, smooth muscle actin, and calponin, and the other is mucoepidermoid carcinoma (MEC), which is distinguished by its triphasic architecture comprising mucin-positive mucous cells, squamoid cells, and intermediate cells) and metastatic tumors from kidney (classic clear cell renal cell carcinoma, which can be identified by its characteristically rich vascular pattern and its immunoreactivity for cytokeratins and vimentin and lack of reactivity for S-100 protein, and amelanotic melanoma, which reacts for HMB-45, S-100 protein, and other melanoma markers). Other odontogenic tumors may also show clearing of their constituent cells. Such tumors include calcifying epithelial odontogenic tumor and clear cell ameloblastoma. The former can be identified by the presence of psammomatous calcifications and amyloid deposits; the latter is actually difficult to distinguish from CCOC. In fact, some authors think that clear cell ameloblastomas and CCOCs may represent a clinicopathological continuum of a single neoplastic entity.[14]

The absence of amyloid and psammomatous calcification in the present case negated the possibility of clear cell variant of calcifying epithelial odontogenic tumor. Lack of mucin and negative staining for S100, alpha SMA, vimentin, and calponin ruled out clear cell variant of MEC. Intraosseous location of tumor with central bone destruction, presence of palisaded peripheral cells, differentiated the case from clear cell carcinoma (CCC). The absence of sinusoidal vascularity, intramural hemorrhage, and non-contributory findings of ultrasonography (USG abdomen, chest radiographs, and IHC ruled out the possibility of a metastasis, particularly from renal cell carcinoma.[15-17]

CONCLUSION

CCOT is a rare jaw tumor that should be considered in the differential diagnosis of clear cell tumors. Radical resection with tumor-free margins is needed as recurrence and metastases are inevitable. Local radiation is essential in cases with extensive soft tissue invasion, perineural spread, lymph node metastasis with extra nodal involvement, or where tumor-free margins are not possible. A long-term follow-up is essential as these tumors may recur locally or present with late distant metastases. Our patient underwent resection of primary lesion and metastasectomy of the rib lesion, and her follow-up is uneventful for over 1 year now.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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