Clinical enigma: A rare case of clear cell odontogenic carcinoma

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Abstract

Clear cell odontogenic carcinoma is a rare, aggressive neoplasm of the jaw with only 74 reported cases. It occurs predominantly in the mandibular anterior region during fifth to seventh decades of life. Clinically it manifests as intra-bony swelling with a variable degree of pain. Microscopically, it reveals nests of cells with clear cytoplasm in connective tissue stroma arranged in different patterns. It is often misdiagnosed due to the rarity of lesion and confusing histopathology. Immunohistochemical staining plays an intricate role to uncertain the native of the clear cell to reach a confirmative diagnosis. The article aims to highlight the clinicopathologic features of clear cell odontogenic carcinoma in a middle-aged man with special emphasis on its differential diagnosis.

Keywords: Biphasic pattern, clear cell odontogenic carcinoma, clear cells

Introduction

Clear cell lesions are the topic of controversy since a long time. The morphologically similar appearing clear cells are ambiguous in nature and believed to be originated from different cell lineages such as epithelial, mesenchymal, melanocytic, or hematopoietic. Clear cell odontogenic carcinoma (CCOC) is one among the rare neoplasm with only 74 reported cases in the literarure. It was first described by Hansen *et al*. and later by Waldron *et al*., in 1985, as clear cell odontogenic tumor.[1-3] In 2005, the World Health Organization (WHO) had reclassified as CCOC owing to its high rate of recurrence, local and distant metastasis, and tumor-related deaths.[4]

CCOC usually present with a variable degree of pain and mobility of regional teeth with or without the involvement of bone. Approximately 60% of patients show evidence of soft tissue involvement in the anterior portion of the mandible as lesion perforates bone.[5,6]

Radiographically, a poorly delineated, unilocular or multilocular radiolucent lesion with prominent bone destruction is observed.[4] Histopathologically, CCOC may show one or more architectural patterns such as biphasic, monophasic, and ameloblastomatous.

The undetermined source of clear cells makes the diagnosis based on conventional histology nearly impossible. They require special attention to be differentiated from other clear cell lesions either by means of special stains such as mucicarmine, Congo red and periodic acid Schiff's (PAS) or immunohistochemical staining such as cytokeratin (CK), epithelial membrane antigen (EMA), S-100 protein, and vimentin. Expression of CK-19 and EMA is a consistent finding in CCOC whereas the tumor shows negativity for vimentin, S-100 protein, desmin, and smooth muscle actin.[6,7]

This article presents another unique case of CCOC with varied clinicopathological, radiological, and histopathological findings affecting the symphyseal region of the mandible in a middle-aged patient.

Case Report

A male patient aged 46 years reported to outpatient department with the chief complain of swelling in the lower front tooth region since 4–5 months. Intraorally, firm,

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nontendered, and exophytic lesion measuring 2.5 cm × 4 cm was observed involving mandibular anterior jaw region with exfoliation of 31, 32 and 41, 42. The alveolar sockets were unhealed with no signs of lymphadenopathy [Figure 1]. The patient's personal, family, and medical histories were noncontributory. Orthopantomogram revealed the presence of an ill-defined radiolucent destructive lesion in the mandibular anterior region [Figure 2]. Computed tomography view showed well-defined hypodense area with the complete loss of buccal cortical plate and severe thinning of the lingual cortical plate in mandibular symphysis region [Figure 3].

Keeping the clinical and radiological features in view, the provisional diagnosis of squamous cell carcinoma was made. The incisional biopsy was performed after obtaining informed consent from the patient, and the tissue sections were stained with hematoxylin and eosin (H/E) for microscopic evaluation.

H/E staining of tissue sections revealed the presence of islands and sheets of round or polyhedral shaped hyperchromatic clear cells with the distinct cytoplasmic membrane. These cells were surrounded by a mature fibrous stroma with variable cellularity. The tumor cells adjacent to the fibrovascular septa were cuboidal to columnar with reversed polarity of the nucleus and eosinophilic cytoplasm whereas central cells were large, round to polygonal with clear cytoplasm. There were no signs of necrosis noted in tissue sections. Mitotic figures were insignificant without any fibrous capsule at the periphery of the tumor [Figure 4].

Special stains such as mucicarmine, Congo red, and PAS were done to check the content of clear cells for mucin, amyloid, and glycogen deposition, respectively. Mucicarmine and Congo red were negative while PAS was strongly positive suggesting the glycogen content of clear cells [Figure 5]. CK-19 and EMA showed strong immunoreation to the tumor cells whereas S-100 protein and vimentin were nonreactive.

The histopathological features confirmed the odontogenic origin of tumor and diagnosis of CCOC of the biphasic pattern was made. Further, the patient was referred to oral surgery department for surgical excision of the lesion. The excised tissue showed the similar findings as that of incisional biopsy. The postoperative recovery was uneventful, and no recurrence was observed in 3 years follow-up period.

Discussion

Clear cell variant of odontogenic tumors is rare entity of jaws. Initially, it was considered to be a benign neoplasm, but later due to its aggressive nature, spread, and recurrence, it is redesignated by the WHO as CCOC in 2005.

Clear cells appear to be clear due to the presence of an intracellular accumulation of nonstaining compounds, such as glycogen, mucopolysaccharides, lipids, and mucin. The derivatives of the dental lamina or cell rests of Malassez have been suggested to be the origin of clear cells in jaws. It is believed that during late bell stage, cells of inner enamel epithelium undergo histodifferentiation to presecretory ameloblast. Electron microscope shows the presence of lysosomes, mitochondria, tonofilaments, and desmosomes. It is now known that bone morphogenetic protein (BMP-2) plays a crucial role in regulating Ms $_{\times 1}$ and Ms $_{\times 2}$ along with Dl $_{\times 2}$. The combined effect of Ms $_{\times 1}$, Ms $_{\times 2}$, and Dl $_{\times 2}$ influences Dl $_{\times 3,}$ which normally help ameloblast cell to differentiate. Absence of these two homobox genes may be due to dysregulation of BMP-2 expression affecting the terminal differentiation of ameloblast cell. In addition to this, the genomic analysis also revealed a polypoid population of cells with DNA index of 1.93 and overall S-phase of 10.2% suggesting chromosomal alterations in cases of CCOC.[8]

A wide age range from 14 to 89 years has been described with the peak incidence noted in the sixth decade of life. Females out numbers males with the ratio of 2:1. More than 80% of the lesions developed in the anterior portion of the mandible. The clinical presentation may vary from mild to extensive pain and bony swelling. Loosening of teeth and paresthesia is present occasionally.

The conventional radiological findings usually show poorly delineated, unilocular or multilocular radiolucent lesion that occurs with prominent bone destruction. The divergence of roots with or without root resorption is evident in few cases.[4]

The light microscopic features of CCOC reveal three histological patterns: Biphasic, monophasic, and ameloblastomatous. The most common biphasic pattern shows two sets of cellular population arranged in sheets and islands. Center cells are clear, round to polygonal in shape mixed with another population of cuboidal to columnar cells with eosinophilic cytoplasm at the periphery. The monophasic pattern has islands of clear cells wholly. The ameloblastomatous pattern is least common, characterized by the presence of clear cells inside the follicular network.[9,10] The degree of nuclear pleomorphism, hyperchromatism, and mitotic figures are variable. Encapsulation is rarely present. It has a higher tendency for the invasion to the medullary bone, muscle, and the neural tissue.[10]

Differential diagnoses include calcifying epithelial odontogenic tumor, mucoepidermoid carcinoma, myoepithelial carcinoma, hyalinising clear cell carcinoma, epithelial-myoepithelial carcinoma, amelanotic melanoma, and metastatic renal cell carcinoma [Table 1].[4,11-18]

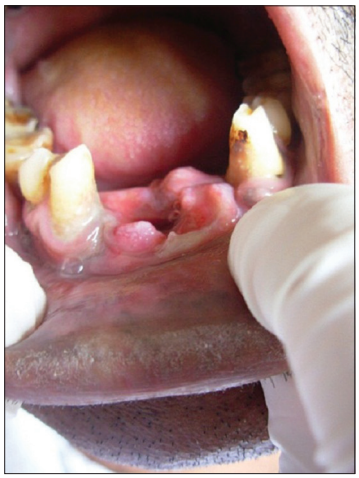

Figure 1: Intraoral view showing lesion in lower alveolar ridge

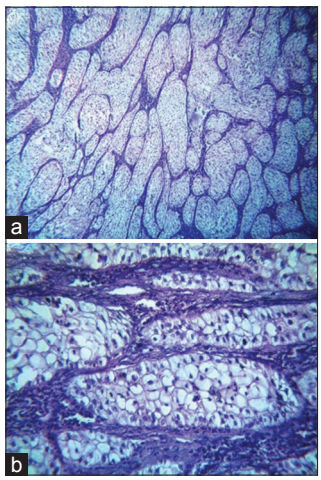

Figure 3: H and E stained section showing (a) islands of clear cells in fibrous connective tissue stroma (×40), (b) clear cells mixed with columnar cells with eosinophilic cytoplasm (×100)

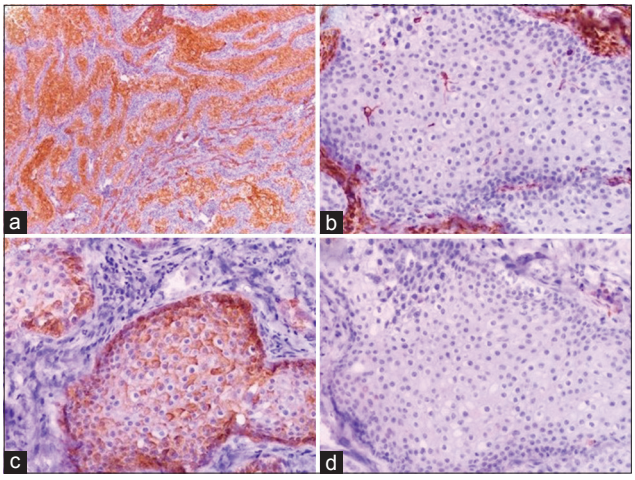

Figure 5: Photomicrograph showing (a) cytokeratin, (b) epithelial membrane antigen, (c) vimentin, (d) S-100. The tumor shows strong positivity for keratin (cytokeratin) and epithelial islands (epithelial membrane antigen). The vimentin immunoreactivity is positive for fibrous tissue stroma only while S-100 was negative

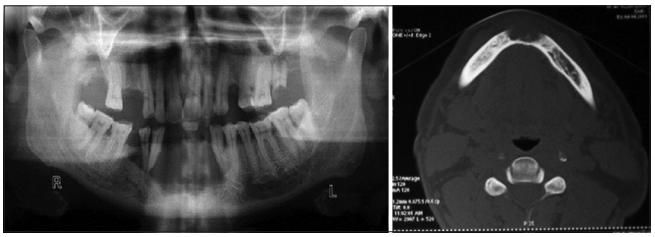

Figure 2: Orthopantomogram and computed tomography scan showing bone destruction in the symphysis region

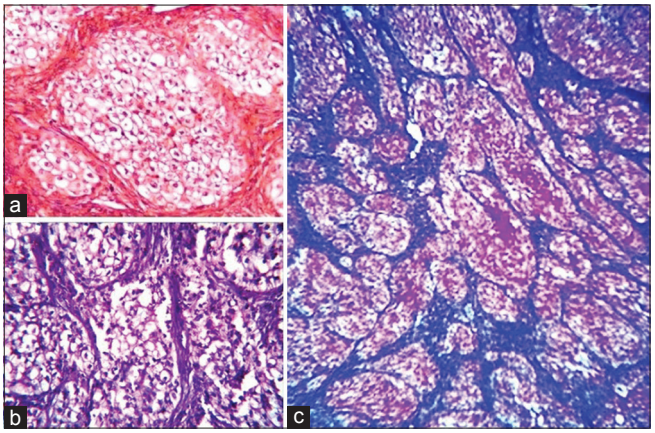

Figure 4: Photomicrograph showing (a) Congo red stain, (b) mucicarmine stain and (c) periodic acid-Schiff stain. Congo red and mucicarmine are negative while periodic acid-Schiff stain has taken up by cytoplasmic granules

We could demonstrate intracellular glycogen by means of PAS-positive, diastase-sensitive granule accumulation within the tumor cells whereas mucin and amyloid were excluded by negative mucicarmine and Congo red staining. CCOC is differentiated from calcifying epithelial odontogenic tumor due to the absence of calcifications and amyloid deposition (Congo red negative).[6] Lack of intermediate cells, squamous differentiation, and mucin (mucicarmine negative) production excluded mucoepidermoid carcinoma.[11] Metastatic lesion is differentiated from CCOC microscopically as later lacks the prominent sinusoidal vascularity and intramural hemorrhage that characterize metastatic renal carcinoma.[12] Immunohistochemically, the tumor cells showed positive staining for wide spectrum CK and EMA, but negative staining for vimentin and S-100 protein.[6] The histochemical staining profile clearly spells the odontogenic nature of neoplasm excluding the possibility of salivary gland origin.

The overall recurrence rate is as high as 55%. The treatment should aim at wide surgical resection with tumor-free margins adjunct to radiotherapy. A long-term follow-up is necessary to look for any loco-regional recurrence and distant metastasis.

Conclusion

Conspicuous nature of clear cells in CCOC poses a great challenge to a pathologist to diagnose and differentiate

Table 1: Differential Diagnosis of CCOC

Differential Diagnosis	Histopathological Features	Special and Immunohistochemical stain
Squamous cell carcinoma	Atypical squamous cell with clear cytoplasm and numerous mitotic figures.	EMA CK 8 CK 18
Calcifying epithelial odontogenic tumor	Cords, nests or sheets of polyhedral epithelial cells with nuclear polymorphism and prominent intercellular bridges with amyloid-like deposits and concentric calcified structures	Congo red stain
Mucoepidermoid carcinoma	Multiple cyst like spaces filled with mucin producing cells, epidermoid cells and intermediate cells. The clear cells are in addition to the mucocytes with pale basophilic, foamy cytoplasm.	Mucicarmine stain CK 7 CK 19
Myoepithelial carcinoma	Clear cells arranged in nodules with hypercellular areas in the periphery and myxoid or necrotic areas in the center. Pleomorphism and mitotic activity is variable.	PAS Calpolin Caldesmon
Epithelial myoepithelial carcinoma	Group of clear cells with prominent outline, centrally placed nucleus and clear cytoplasm admixed with pleomorphic cuboidal ductular epithelial cells.	Calpolin Caldesmon CK EMA
Hyalinizing clear cell carcinoma	Clear cells in cords, nests, islands or trabaculae within hyalinized connective tissue.	Pan CK
Amelanotic melanomas	Nests of polygonal, rounded or bluntly spindled cells with clear to weakly eosinophilic cytoplasm.	S-100 protein Melan A HMB-45
Renal cell carcinoma	Solid, organoid growth pattern exhibiting infiltration with little cytologic atypia and few mitosis.	Mucicarmine positive
Thyroid carcinoma	Cytoplasmic clear cell changes in papillary and follicular arrangement	Thyroglobulin

CK: Cytokeratin, EMA: Epithelial membrane antigen, PAS: Periodic acid schiff, HMB: Human melanoma black

from other clear cell lesions. The caution should be exercised to carefully determine the source of clear cells. These type of lesions demands diagnosis based on conventional histopathology adjuvant to special staining and immunohistochemistry for optimal management considering the risk of recurrence and metastases.

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Conflicts of interest
There are no conflicts of interest.

References

1. Hansen LS, Eversole LR, Green TL, Powell NB. Clear cell odontogenic tumor – A new histologic variant with aggressive potential. Head Neck Surg 1985;8:115-23.
2. Waldron CA, Small IA, Silverman H. Clear cell ameloblastoma – An odontogenic carcinoma. J Oral Maxillofac Surg 1985;43:707-17.
3. Kramer IR, Pindborg JJ, Shear M. WHO Histological Typing of Odontogenic Tumors. 2nd ed. Berlin, Germany: Springer Verlag; 1992.
4. Reichart PA, Philepsen HP. Odontogenic Tumors and Allied Lesions – Clear Cell Odontogenic Carcinoma. London, UK: Quintessence Publishers; 2004. p. 239.
5. Neville BW, Damm DD, Allen CM, Bouquot JE. Odontogenic cysts and tumors. Oral and Maxillofacial Pathology. 3rd ed.. Philadelphia, UK: WB Saunders; 2009. p. 712-3.
6. Li TJ, Yu SF, Gao Y, Wang EB. Clear cell odontogenic carcinoma: A clinicopathologic and immunocytochemical study of 5 cases. Arch Pathol Lab Med 2001;125:1566-71.
7. Bilodeau EA, Hoschar AP, Barnes EL, Hunt JL, Seethala RR. Clear cell carcinoma and clear cell odontogenic carcinoma: A comparative clinicopathologic and immunohistochemical study. Head Neck Pathol 2011;5:101-7.
8. Panda S, Sahoo SR, Srivastav G, Padhiary S, Dhull KS, Aggarwal S. Pathogenesis and nomenclature of odontogenic carcinomas: Revisited. J Oncol 2014;2014:197425.
9. Dahiya S, Kumar R, Sarkar C, Ralte M, Sharma MC. Clear cell odontogenic carcinoma: A diagnostic dilemma. Pathol Oncol Res 2002;8:283-5.
10. Swain N, Dhariwal R, Ray JG. Clear cell odontogenic carcinoma of maxilla: A case report and mini review. J Oral Maxillofac Pathol 2013;17:89-94.
11. Maiorano E, Altini M, Viale G, Piattelli A, Favia G. Clear cell odontogenic carcinoma. Report of two cases and review of the literature. Am J Clin Pathol 2001;116:107-14.
12. Mosqueda-Taylor A, Meneses-García A, Ruíz-Godoy Rivera LM, de Lourdes Suárez-Roa M. Clear cell odontogenic carcinoma of the mandible. J Oral Pathol Med 2002;31:439-41.
13. Kumar K, Shetty DC, Wadhwan V, Gupta P. Synchronous oral squamous cell carcinomas with unusual histopathological feature. J Oral Maxillofac Pathol 2012;16:420-4.
14. Varma S, Shameena P, Sudha S, Nair RG, Varghese IV. Clear

cell variant of intraosseous mucoepidermoid carcinoma: Report of a rare entity. J Oral Maxillofac Pathol 2012;16:141-4.
15. Gupta A, Manipadam MT, Michael R. Myoepithelial carcinoma arising in recurrent pleomorphic adenoma in maxillary sinus. J Oral Maxillofac Pathol 2013;17:427-30.
16. Munot PC, Ganvir SM, Dolas RS, Hazarey VK. Epithelial myoepithelial carcinoma of palate: A case report. J Oral Maxillofac Pathol 2003;7:54-6.
17. Baghirath PV, Kumar JV, Vinay BH. Hyalinizing clear cell carcinoma: A rare entity. J Oral Maxillofac Pathol 2011;15:335-9.
18. Busam KJ, Jungbluth AA. Melan-A, a new melanocytic differentiation marker. Adv Anat Pathol 1999;6:12-8.