Case Report

Clear-cell variant of squamous cell carcinoma in maxilla as primary lesion: A rare case

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Abstract

Oral squamous cell carcinoma with prominent clear-cell differentiation is a rare occurrence with incompletely understood etiology. We report a case of a 55-year-old male working in a steel factory presented with an ulcerated swelling on maxillary alveolar ridge, a rare site. Histopathology showed sheets of squamous cells with clear cell differentiation and features of malignancy. Periodic acid–Schiff and mucicarmine stains showed negative reaction. Immunohistochemical study using antibody for cytokeratin and epithelial membrane antigen revealed diffuse and intense positivity. The neoplastic cells showed complete negative reaction with antibodies for S-100 and vimentin.

Keywords: Clear cell, maxillary alveolus, oral squamous cell carcinoma, ulcerated swelling

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INTRODUCTION

Head and neck cancers represent approximately 3% of all malignancies. In the oral cavity, more than 90% of primary malignancies are squamous cell carcinomas (SCCs).[1] Histopathologically, it is graded into well, moderate and poorly differentiated lesion, based on the keratinization and degree of anaplasia. Other histologically recognized variants of oral SCC include verrucous, spindle, adenosquamous and basaloid.[2] Neoplasms with prominent clear-cell component in oral cavity are very rare and usually represent as a variant of salivary gland tumors or the result of renal metastasis.[1] Clear-cell SCC (CCSCC) is a rare entity, and a total of seven cases are reported in skin.[3] An exhaustive search on Google Scholar produced only four cases in the oral cavity till date, of which two are glycogen free, like ours indicating the rarity of this oral variant[1,2,4,5] [Table 1].

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Thus, the reported case is the third well-documented case of glycogen-free clear-cell variant of oral SCC in English literature and the first case in maxilla, and thereby being a rare entity, it is making an important contribution to the knowledge regarding this uncommon lesion in oral cavity.

CASE REPORT

A 55-year-old male presented with 6 months history of pain and swelling secondary to extraction of teeth in the left posterior region of maxilla. On examination, an ulcerated swelling extending from 23 to 28 was observed with buccal cortical plate expansion in relation to 23–25. In the posterior part of the swelling, an ulcer measuring 3–5 cm with raw floor and everted margins was present [Figure 1]. On palpation, the swelling was tender, fluctuant and compressible. Left cervical lymph nodes were palpable and

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fixed. Extraorally, the swelling in the left maxillary region caused obvious facial asymmetry.

Ultrasonography revealed hypoechoic lymph node measuring 3.6 cm × 1.7 cm in the left cervical region. Bilateral lobes of isthmus of thyroid, liver, cardiovascular system, pancreas and both kidneys were normal.

Cone-beam computed tomography exhibited superficial erosion with respect to the left-side roof of maxillary sinus, zygomatic buttress and infraorbital region. Furthermore, there was complete obliteration of left maxillary sinus and nasal cavity [Figure 2].

Fine-needle aspiration cytology from the left cervical lymph node revealed atypical cells showing pleomorphism and nuclear hyperchromasia.

Based on clinical, aspiration cytology and radiographic findings, a provisional diagnosis of SCC was made and incisional biopsy was performed under local anesthesia.

Microscopically, sections stained with hematoxylin and eosin indicated dysplastic stratified squamous epithelium exhibiting transition to an infiltrating tumor composed of lobules of malignant squamous cells separated by delicate fibrous connective tissue stroma. Sheets of clear cells were interspersed among the lobules of dysplastic epithelial cells indicating clear cell changes. The clear cells were round to polygonal having clear cytoplasm with dysplastic features such as nuclear and cellular pleomorphism, hyperchromatic nuclei and abnormal mitosis suggesting malignancy [Figure 3a-d]. Tissue sections were subjected to histochemical and immunohistochemical (IHC) analysis to know the origin of tumor cells.

Table 1: Five reported cases of clear-cell variant of squamous cell carcinoma (2012-2016)

Authors	Year	Anatomical site	Glycogen content
John J. Frazier *et al*.	2012	Mandibular gingiva	Present
M. Romanach *et al*.	2014	Buccal mucosa	Present
Nainani P. *et al*.	2014	Buccal mucosa	Absent
Kaliamoorthy S. *et al*.	2015	Tongue and lingual vestibule	Absent
Devi *et al*.	2016	Maxillary alveolar ridge	Absent

Microscopic sections stained with periodic acid–Schiff (PAS) and mucicarmine showed negative reaction. Neoplastic cells were immunoreactive for cytokeratin (CK) and epithelial membrane antigen (EMA) [Figure 4a and b]. However, no staining occurred with S-100 and vimentin [Figure 4c and d].

Considering histopathological, histochemical and IHC examination, a final diagnosis of clear-cell variant of SCC was established. The patient subsequently underwent hemimaxillectomy with radical neck dissection of left side. The excised biopsy submitted to histopathological examination showed that the margins of excised tissue were free of tumor cells, but the cervical lymph node revealed sheets of dysplastic clear cells, obliterating its normal architecture, hence proving metastasis. During follow-up over 5 months, the patient is taking radiation therapy.

DISCUSSION

CCSCC is an extremely rare variant of SCC and was first described by Kuo in 1980. It is also referred to as hydropic SCC. The clear-cell appearance is attributable to hydropic degeneration of neoplastic cells and the accumulation of

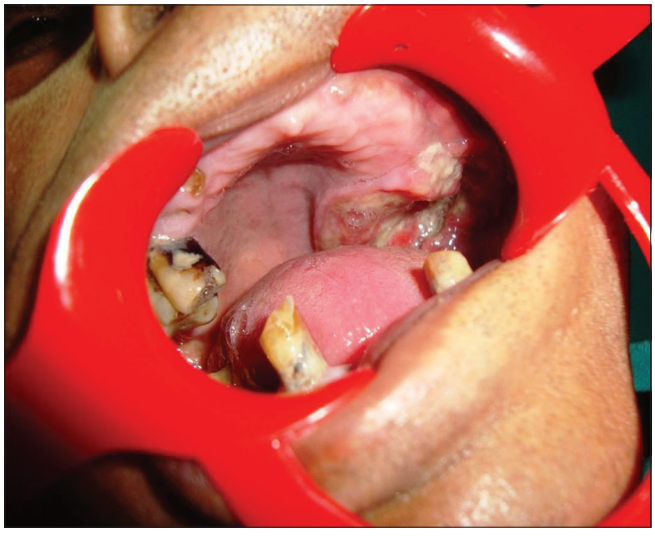

Figure 1: Intraoral picture showing ulcerated swelling on left side of maxillary ridge

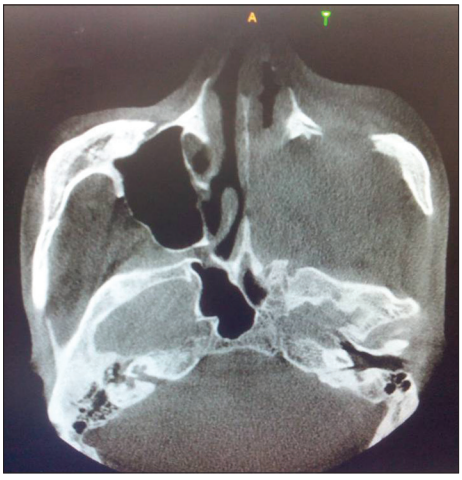

Figure 2: Cone-beam computed tomography showing superficial erosion with respect to left side roof of maxillary sinus, zygomatic buttress and infraorbital region. It also shows complete obliteration of left maxillary sinus and nasal cavity

Table 2: Differential diagnosis of clear cell squamous cell carcinoma

Differential diagnosis	Clinical and histologic features	Special stains and immunohistochemical profile
Clear-cell odontogenic carcinoma	Lobulated pattern, nonencapsulated monophasic or biphasic	PAS-positive, diastase-sensitive cytoplasmic granules CKs 8, 13, 18 and 19 positive clear cells
Mucoepidermoid carcinoma	Triphasic architecture comprised of mucin-positive mucous cells, squamoid cells and intermediate cells Mucous pools present	PAS-positive, diastase resistant granules in cytoplasm of mucous cells. Mucicarmine, alcian blue positive mucous cells CKs 7, 8 and 13 positive in epidermoid cells CK-14 positive in epidermoid andintermediate cells CK-19 positive in epidermoid and mucous cells
Calcifying epithelial odontogenic tumor	Psammomatous calcifications, amyloid deposits	Hyaline droplets either stain positive with Congo red (amyloid) or keratin or enamel proteins
Acinic-cell carcinoma	Acinar differentiation	CKs 7 and 8 positive
Epithelial-myoepithelial carcinoma	Biphasic differentiation	Clear cells are S-100, vimentin, SMA and calponin positive
Hyalinizing clear-cell carcinoma of salivary glands	Extraosseous location and salivary gland swellings Hyalinized stroma intervening between the tumor islands	Negative for high molecular weight CK SMA positive
Myoepithelial carcinoma	Spindle cells, plasmacytoid, clear or epidermoid cells in sheets	Clear cells are S-100, vimentin, SMA and calponin positive
Sebaceous carcinoma	Cells with bubbly cytoplasm	Sudan III positive
Amelanotic melanoma	Large nests of polygonal, rounded or spindle cells	S-100 and HMB-45 positive
Metastatic renal-cell carcinoma	Intratumoral hemorrhage and sinusoidal vascularity	Clear cells positive for renal cell carcinoma antigen and vimentin
Metastatic tumor from liver, prostate and thyroid	Usually poorly differentiated	A-fetoprotein, thyroglobulin and prostate-specific antigen positive
Metastatic tumor from lung		CK (CK 7+, CK20−) and TTF-1

PAS: Periodic acid-Schiff, SMA: Smooth muscle actin, HMB-45: Human melanoma black-45, CKs: Cytokeratins, TTF-1: Thyroid transcription factor-1

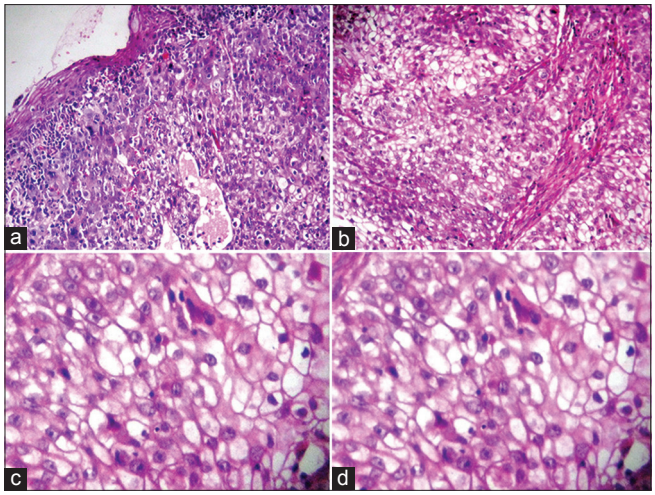

Figure 3: (a) Histopathologic picture showing dysplastic surface epithelium containing cells with large, pleomorphic and hyperchromatic nuclei, infilterating the connective tissue stroma (H&E, ×4). (b) Sheets of clear cells with features of dysplasia (H&E, ×10). (c) Tumor cells with clear cytoplasm and centrally placed nuclei (H&E, ×20) and (d) (H&E, ×40)

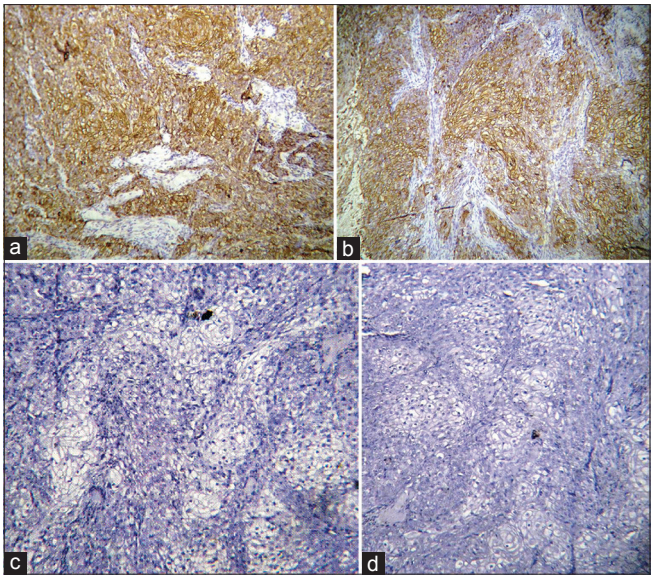

Figure 4: (a and b) Immunohistochemical picture showing clear cells with strong immunoreactivity for cytokeratin and epithelial membrane antigen. (c and d) Clear cells with negative results for S100 and Vimentin

intracellular fluid, not the accumulation of glycogen, lipid or mucin. All cases of CCSCC have been found in head and neck region, with mandible being the most common site whereas ours is the only case which is present in maxilla. It commonly appears as a nodule or mass that may occasionally be ulcerated.[6,7]

The possible etiological factors include immune suppression, arsenic exposure, radiation and chronic ulceration.[6] As the present case occurred in a patient working in steel factory, radiation can be the cause, but more number of cases should be published to support this assumption.

Clear-cell tumors constitute a heterogeneous group of lesions and can be broadly classified into three main categories (odontogenic, salivary glands and metastatic), according to their presumed origin which were considered as differentials for the present case [Table 2].[4]

Clear-cell odontogenic tumors are clear-cell variant of calcifying epithelial odontogenic tumor (CCCEOT), clear-cell odontogenic carcinoma (CCOC) and clear-cell odontogenic ghost cell tumor (CCGCOT).[8] CCCEOT lacks the characteristic calcifications and amyloid deposition.[9] CCGCOT can be ruled out on acount of presence of ghost cells. PAS-positive, diastase sensitive cytoplasmic granules and CKs 13,18 and 19 positive clear cells must be present to rule out Clear cell odontogenic carcinoma.[10]

Salivary gland tumors including epithelial myoepithelial carcinoma, hyalinizing clear-cell carcinoma, clear-cell acinic cell carcinomas and clear-cell mucoepidermoid carcinoma can be considered in differential diagnosis of clear cell tumors. Lack of presence of glycogen, mucin and negative staining for S-100 ruled out epithelial myoepithelial carcinoma, mucoepidermoid carcinoma and clear-cell acinic cell carcinomas. Furthermore, epithelial-myoepithelial carcinoma reveals duct-like structures composed of an inner cuboidal cell layer and outer clear myoepithelial cell layer. These bilayered ductal structures were not seen in our case. Clear-cell variant of acinic-cell carcinoma presents neoplastic cells with serous acinar differentiation which was also not seen in present case. Hyalinizing clear-cell carcinoma was ruled out on account of the lack of dense fibrous stroma.[1,4]

The metastatic deposits containing clear cells may morphologically mimic salivary gland tumors as well as odontogenic tumors, but renal-cell carcinoma is characterized by a prominent sinusoidal vascular component with hemorrhagic foci.[9] General physical examination, chest X-ray and ultrasonography ruled out distance metastasis. Melanocytic tumors stain was positive for S-100. The present case showed negative results for S-100 and vimentin and strong positivity for CK and EMA.

Frazier *et al*.[1] studied numerous case series on SCC, but no cases of CCSCC were identified. Same way, in our institute also, we did not find any case of CCSCC between 2011 and 2016. Although SCC is the most common tumor of oral cavity, its clear-cell variant as primary lesion in oral mucosa is very rare.

CONCLUSION

CCSCC is a rare malignant neoplasm of oral cavity and ours is the only reported case in maxilla. As only few cases in oral cavity have been reported in English literature, more reports on such cases should be documented for better understanding of its etiology, clinical behavior and prognosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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