Case Report

Clear-cell variant of oral squamous cell carcinoma: A rare entity

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Abstract

Clear-cell variant of oral squamous cell carcinoma is an extremely rare entity in the maxillofacial region. We report a case of 42-year-old female who presented with a soft-tissue growth with erythematous and nonscrapable irregular white patches on the left alveolar mucosa for the past 3 months. Histopathologic examination showed lobules and sheets of clear cells with features of malignancy extending from the surface epithelium. Periodic acid–Schiff and mucicarmine stains showed a negative reaction. Immunohistochemical study using antibody for pan-cytokeratin revealed intense positivity and negative for the markers such as S-100, smooth muscle actin and CD 117.

Keywords: Clear cells, mandibular alveolus, oral squamous cell carcinoma

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INTRODUCTION

Squamous cell carcinomas account for more than 90% of the malignancies of the oral cavity.[1] Clear-cell squamous cell carcinoma is a rare variant of squamous cell carcinoma, first described by Kuo in 1980,[2] as a tumor of skin. A predominant variant of oral carcinoma with clear cells is very rare and it is usually a salivary gland neoplasm or a metastatic tumor. Most clear-cell carcinomas of oral soft tissues represent clear-cell carcinomas "not otherwise specified" or hyalinizing clear-cell carcinomas and represent submucosal tumors of salivary gland origin. It is also referred to as hydropic squamous cell carcinoma. The clear-cell appearance may be due to hydropic degeneration of the neoplastic cells due to the accumulation of intracellular fluids and not by mucin, glycogen or lipid.

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Only six cases of clear-cell variant of oral squamous cell carcinoma (OSCC) have been reported. Here we report a rare case of clear-cell squamous cell carcinoma arising from the mandibular alveolar region.

CASE REPORT

A 42-year-old Asian Indian female patient was referred by a private practitioner to Saveetha Dental College and Hospitals who had presented with a chief complaint of pain in the lower jaw region for the past 3 months. She did not have any contributory medical history.

Intraoral examination revealed a soft-tissue growth with erythematous and nonscrappable irregular white patches on the left alveolar mucosa in relation to 35, 36 and 37 [Figure 1]. Bleeding on palpation was evident, but there was no pus

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discharge. The patient had informed that the 36 and 37 had become mobile and fell off the socket. Orthopantamogram (OPG) did not give any significant information. The provisional diagnosis of socket granuloma was given. Upon incisional biopsy, sections showed parakeratinized stratified squamous epithelium with underlying connective tissue showing dense chronic inflammatory cell infiltrate and areas of hemorrhage. The diagnosis of reactive granuloma of the alveolus was given and excision of the lesion was suggested for final diagnosis. Under general anesthesia, 34, 35 and 38 were extracted and marginal mandibulectomy with the specimen was done in relation to 35–38 regions.

The excised specimen submitted for histopathological examination revealed lobules and sheets of clear cells which were round to polygonal in shape consisting of clear cytoplasm exhibiting pleomorphism along with few squamous cells with extending from the overlying dysplastic stratified squamous epithelium into the delicate connective tissue. A few islands had areas of comedo necrosis and retraction of the tumor islands was also noted in the connective tissue. Hemorrhagic areas were evident [Figures 2-4]. Peroidic acid–Schiff (PAS) and mucicarmine staining showed a negative reaction.

Tissue sections were subjected to immunohistochemical analysis to define the tumor cell origin. Pan-cytokeratin, epithelial membrane antigen, smooth muscle actin, S100 and CD 117 were used. The tissue sections were immunoreactive for pan-cytokeratin which was suggestive of a malignancy of epithelial origin possibly a clear-cell variant of squamous cell carcinoma [Figure 5a and b]. Further biochemical investigations and whole-body scan were advised, but no significant findings were evident. Considering histopathological, histochemical and IHC examination, a final diagnosis of clear-cell variant of SCC was established.

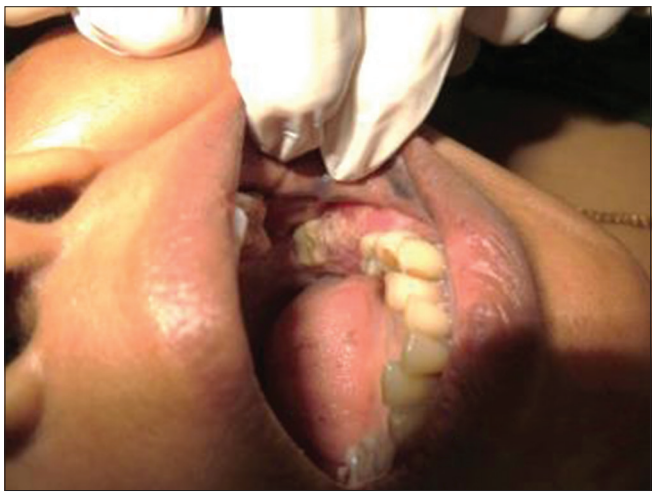

Figure 1: Intraoral picture showing soft-tissue growth with irregular white patches on the left alveolar mucosa

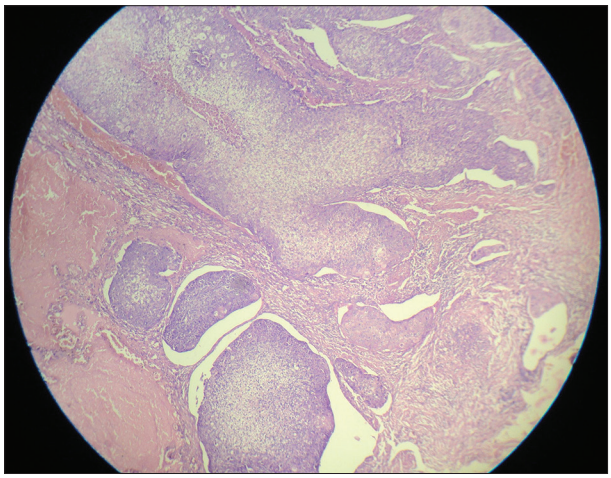

Figure 2: Histopathologic picture showing dysplastic surface epithelium infiltrating the connective tissue stroma (H&E, ×10)

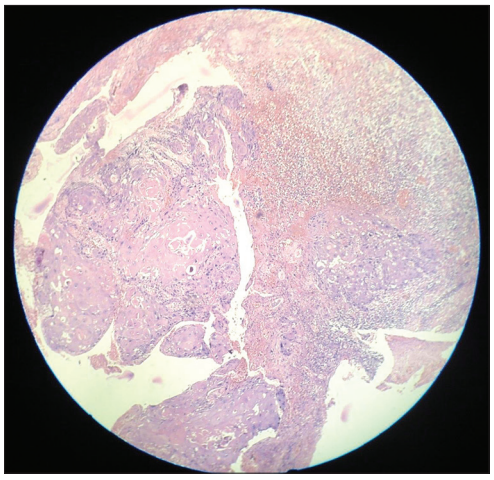

Figure 3: Histopathologic picture showing sheets of clear cells with features of dysplasia (H&E, ×10)

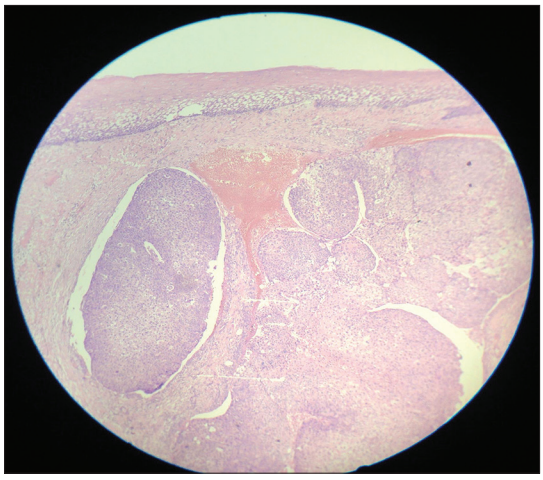

Figure 4: Histopathologic picture showing lobules of tumor cells with clear cytoplasm and centrally placed nuclei (H&E, ×10)

The patient revisited after 6 months with enlarging mass in the previous site in the left posterior mandibular region with difficulty in mouth opening [Figure 6]. Panoramic radiography revealed a pathological fracture in the left angle region [Figure 7]. A biopsy was done and the histopathological sections showed dysplastic stratified squamous epithelium exhibiting transition to an infiltrating tumor composed of lobules of malignant squamous cells separated by delicate fibrous connective stroma similar to the previous excisional biopsy and a hence a final diagnosis of clear-cell variant of squamous cell carcinoma [Figure 8]. The patient refused any further treatment and subsequently lost for follow-up.

DISCUSSION

Clear-cell variant of squamous cell carcinoma of the skin was first described by Kuo in 1980.[2] It is a rare variant of cutaneous squamous cell carcinoma which was commonly referred to as hydropic squamous cell carcinoma.

The clear-cell lesions of the oral cavity can be broadly categorized as salivary gland origin, odontogenic origin and metastatic lesions in which salivary gland and odontogenic lesions alone contribute to about 90% in the head-and-neck region.[3] Premalatha *et al.* classified the clear-cell tumors occurring in the head-and-neck region based on their origin like odontogenic lesions, salivary gland tumors, metastatic tumors, keratinocytic and melanocytic tumors, bone and cartilaginous tumors and adipocytic and skin adnexal tumors.[4]

The origin of clear cells is either epithelial or mesenchymal which has a pale or clear cytoplasm with a distinct centrally placed nucleus. The clear cytoplasm may be due to artifactual changes, accumulation of water, glycogen, mucopolysaccharides, lipids, mucin, intermediate filaments and immature zymogen granules, phagocytosed foreign-body material or hydropic degeneration of organelles.[5,6] Physiological evidence of clear cells in dental lamina sometimes gives rise to pathological conditions like odontogenic cysts; likewise, melanocytes and adipocytes give rise to melanoma and lipoma or liposarcoma, respectively. Pathological clear

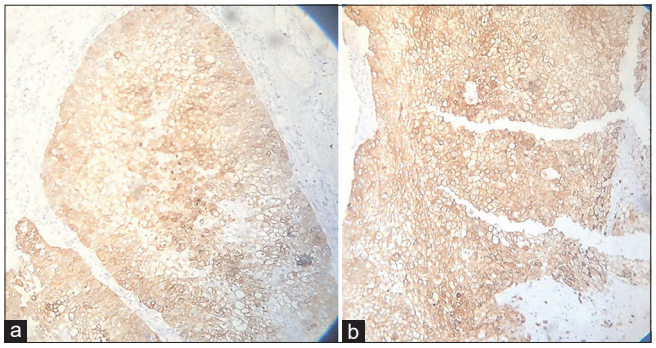

Figure 5: (a) Immunohistochemical picture showing clear cells with strong immunoreactivity for cytokeratin. (b) Immunohistochemical picture showing clear cells with strong immunoreactivity for cytokeratin

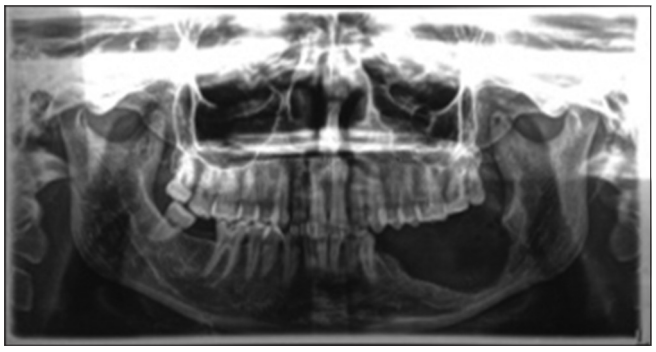

Figure 7: OPG showing pathologic fracture in the angle of the mandible on the left side

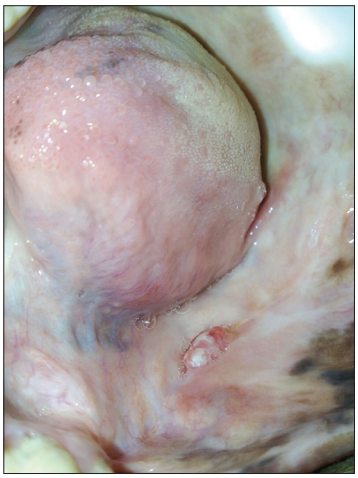

Figure 6: Intraoral picture showing recurrence in the left mandibular alveolar region

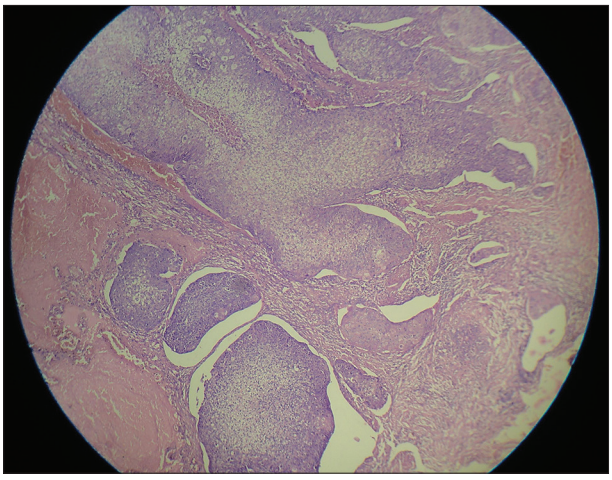

Figure 8: Histopathologic picture showing sheets of tumor cells with clear cytoplasm and centrally placed nuclei (H&E, ×40)

cells include koilocytes seen in human papillomavirus infections.

A thorough search of the English literature revealed only six cases of clear-cell variant of SCC in the head-and-neck region, predominantly involving the mandible [Table 1]. The clinical presentation is usually a nodule or mass that may be ulcerated occasionally. The current case presented as a soft-tissue growth in the left alveolar mucosa. Mostly females without any adverse habits such as tobacco chewing or alcohol consumption are affected in the cases reported so far which seems to be matching with our case. Immune suppression, arsenic exposure, radiation and chronic ulceration might be the possible etiological factors associated with it.[13]

Histologically, Kuo further classified the six cases of clear-cell carcinoma reported by him into three major types: type I keratinizing, type II nonkeratinizing and type III pleomorphic.[2] In all types, there was a negative staining for PAS and mucin indicating the absence of glycogen and mucin. In our present case, clear cells show strong positivity for CK 8 and 18 and negative for PAS and mucicarmine and thus fit wells in the diagnosis of clear-cell squamous cell carcinoma.

Clear cells in the clear-cell odontogenic carcinoma are negative for mucicarmine, Alcian blue, Congo red and Sudan Black but are positive for PAS due to the presence of glycogen. Our case also shows PAS negativity which ruled out odontogenic origin.

Another differential diagnosis includes intraosseous mucoepidermoid carcinoma (MEC) in which the clear-cell component accounts for about 10% of the cell population. If the clear-cell component is large, it is designated as a clear-cell variant of MEC which accounts for 7.5%.[14] Clear cells in MEC show positivity for PAS and mucicarmine stain and immunoreactive to calponin, S-100 and vimentin. However in our case, the clear cells were negative for these markers, thus ruling out the possibility of MEC.

The oral amelanotic melanoma accounts for only 1% of all reported primary melanomas of the oral cavity,[15] in which the clear-cell component shows immunoreactivity for S-100 and HMB45. However, our case showed no reactivity for these markers.

Very rarely, metastases to the oral cavity can be seen. Renal cell carcinoma (RCC) is one of the most common tumors after lung and breast cancers to metastasize to the head-and-neck region. RCCs show multiple metastases to the head-and-neck region in almost 15% of cases.[16] Clear cells in RCC show the presence of glycogen by its positivity for PAS which was again negative in our present case. Clear-cell differentiation within other population of the tumor indicates different clonal evolution which may suggest a poor prognosis.[10]

CONCLUSION

The clear-cell variant of OSCC is a very rare entity which has to be diagnosed with thorough knowledge of histopathological features and a specific use of immunohistochemistry markers. Prognosis of clear-cell SCC is not very clear due to the paucity of cases. Further documentation of such cases will help us better understand the etiology, clinical behavior, prognosis and treatment.

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.

Table 1: Table showing author and case details including clinical, histopathological (special stains) and immunohistochemical profile described in previous literature

Author	Age	Gender	Clinical presentation	Site	Special stains and IHC profile	
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Frazier *et al*., 2012[7]	59	Female	Pain and swelling, exophytic mass	Left posterior mandible	PAS (diastase labile)	Mucicarmine
Romañach *et al*., 2014[8]	60	Female	Ulcerated swelling	Posterior buccal mucosa extending to the soft palate	PAS, CK AE1/AE3 and p63	Vimentin and CD10
Nainani *et al*., 2014[9]	52	Male	Ulcero-proliferative lesion	Left buccal mucosa	Cytokeratins 8 and 18	PAS, mucicarmine, oil red O, vimentin and S-100
Kaliamoorthy *et al*., 2015[10]	35	Female	Nonhealing ulcer	The left posterior lateral border of the tongue and lingual vestibule	Cytokeratin AE1/AE3	SMA, HMB 45, PAS and mucicarmine
Devi *et al*., 2017[11]	55	Male	Ulcerated swelling	Left posterior region of the maxilla	CK, EMA	PAS and mucicarmine
Khoury *et al*., 2017[12]	66	Female	Large painful mass that showed ulcerations	Left lateral tongue	Cytokeratin 5/6, PAS (diastase labile-glycogen rich)	S-100, calponin, smooth muscle actin and HMB45

SMA: Smooth muscle actin, PAS: Periodic acid-Schiff, EMA: Epithelial membrane antigen, CK: Cytokeratin, IHC: Immunohistochemical, hmb-45 - Human Melanoma Black - 45

The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed

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Self.

Conflicts of interest

There are no conflicts of interest.

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