A rare case of clear cell variant of oral squamous cell carcinoma

Sriram Kaliamoorthy, Vijayparthiban Sethuraman, Sathish Muthukumar Ramalingam, Sandhya Arunkumar

Abstract

Oral squamous cell carcinoma with prominent clear cell differentiation is a rare occurrence. A 35-year-old female patient presented with a nonhealing ulcer persistent for 1-month involving the left lateral border of the tongue and lingual vestibule. Lobules of malignant squamous epithelial cells with abundant cytoplasm and vesicular nuclei in the connective tissue were observed following histopathology. Neoplastic cells constituting majority of lobules exhibited clear cell changes. Periodic acid-Schiff and mucicarmine stains showed negative reaction. Immunohistochemical study using antibody for cytokeratin, revealed diffuse and intense positivity. The neoplastic cells showed complete negative reaction with antibodies for vimentin, smooth muscle actin and homatropine bromide-45 antigens.

Key words: Clear cell, oral cancer, squamous cell carcinoma

INTRODUCTION

Squamous cell carcinoma (SCC) of the oral cavity is one of the most common head and neck cancer observed among tobacco users.[1] Histopathologically it is graded into well, moderate and poorly differentiated lesion, based on the keratinization and degree of anaplasia.[1] Other recognized variants of oral SCC include verrucous, spindle, adenosquamous and basaloid variants.[1] This case report describes a case of oral SCC involving the left posterior lateral border of the tongue and lingual vestibule in a 35 year old, which showed prominent clear cell changes. Previously, seven such cases are reported involving the skin[2,3] and one case in the oral cavity,[4] indicating the rarity of this oral variant.

CASE REPORT

A 35-year-old female patient presented with the chief complaint of nonhealing ulcer in the mouth for the past 1-month. No relevant past tobacco chewing/smoking history was reported. Clinical examination revealed an ulcer involving the left posterior lateral border of the tongue and lingual vestibule (2 cm × 2.5 cm in size). Surface was covered with pseudo membranous slough, with normal
tongue movement [Figure 1]. Indurated border with mild tenderness was observed on palpation. Mandibular oclusal and orthopantamogram excluded any bone involvement. An incisional biopsy was performed under local anesthesia and the tissue was submitted for histopathological examination.

Microscopic examination of the hematoxylin and eosin (H and E) stained sections indicated infiltrating lobules of malignant squamous cells, exhibiting abundant cytoplasm, and vesicular nucleus with intervening connective tissue septa. Neoplastic cells constituting plenty of lobules showed evidence of prominent clear cell changes [Figure 2a-d]. Dysplastic changes in the overlying epithelium without obvious evidence for keratin pearl formation were observed. SCC arising from an oral epithelium, amelanotic melanoma, clear cell carcinoma of minor salivary gland origin and metastatic carcinoma, most likely the renal cell carcinoma were histopathological differentials considered. Relevant clinical, ultrasound and radiographic investigations were performed and primary malignancy in kidney, large bowel, liver, and breast were ruled out. Microscopic sections stained with periodic acid-Schiff (PAS) and mucicarmine showed negative reaction.

Immunohistochemical (IHC) investigation was carried out utilizing panel of antibodies viz. cytokeratin AE1/AE3, Biogenex, USA, (Catalogue ID — RTU-AM-071-5M), Vimentin, Novocastra (Catalogue ID — RTU-VIM-V9), smooth muscle actin (SMA), Biogenex USA, (Catalogue ID — RTU-AM128-5M), homatropine bromide (HMB)-45, Dako Denmark (Catalogue ID-IS-052). Secondary antibody detection was done utilizing anti polyvalent horse radish peroxidase polymer kit, SCYCE.

The neoplastic cells showed diffuse, intense cytoplasmic positivity for cytokeratin AE1/AE3 [Figure 3a] and for vimentin antigen intense positive reaction was seen only within the tumor stroma and the neoplastic cells showed negative reaction [Figure 3b]. Antibodies for SMA antigen showed complete negative reaction with neoplastic cells, but intense positivity was seen along the blood vessel lining [Figure 3c]. Antibodies for HMB 45 antigen showed complete negative reaction for both neoplastic cells and stroma [Figure 3d]. On the basis of clinical, radiological, ultrasound, histopathological and IHC findings, a diagnosis of clear cell variant of oral SCC was made and the patient was referred to the cancer institute for the comprehensive management.

DISCUSSION

In the oral cavity, the primary malignant neoplasm with clear cell changes commonly include malignancy of salivary gland (mucoepidermoid carcinoma, acinic cell carcinoma, epithelial — myoepithelial carcinoma, clear cell myoepithelial carcinoma and hyalinizing clear cell carcinoma) and odontogenic origin (clear cell odontogenic carcinoma and clear odontogenic ghost cell tumor, with very rare occurrence of SCC and melanoma with clear cell changes). In this case, PAS and mucicarmine staining was negative, hence ruling out acinic cell carcinoma and mucoepidermoid carcinoma. Negative reaction of neoplastic cells for SMA (i.e., marker for myoepithelial differentiation), ruled out clear cell salivary gland malignancies of exclusive myoepithelial origin, such as clear cell myoepithelial carcinoma and hyalinizing clear cell carcinoma. Histopathological absence of characteristic double cell lining and negative reaction with SMA antibodies in the immunohistochemistry, excluded epithelial — myoepithelial carcinoma. We did not consider clear cell malignancy of odontogenic origin, since the tumor did not arise from odontogenic apparatus. Furthermore,
lack of glycogen, as evidenced by the PAS stain, ruled out odontogenic origin. Amelanotic melanoma was ruled out based on complete negative reaction for HMB-45.

Clear cell changes in SCC arising from the oral epithelium are highly unusual and to the best of our knowledge until to date there has been only single case report available in the English literature.[4] Optical clearance of neoplastic cells in the H and E section can be due to artifactual changes, loss of cell organelles and/or accumulation of various substances, such as glycogen, lipids, mucopolysaccharides, immature zymogen granules and water in the cytoplasm.[5] However, the cytoplasmic clearance in the clear cell variant of SCC of skin is due to hydropic degeneration and accumulation of fluid, and not due to accumulation of glycogen, mucin, and lipids.[6]

It is also likely that clear cell differentiation may result from different clonal evolution within the tumor. The prognosis of clear cell variant of SCC is not clear, mainly due to the scarcity of available literature. Of the seven cases that have been reported in the literature from skin, five had an aggressive growth feature. The single case reported from the oral cavity was a synchronous lesion and showed highly aggressive clinical feature. Current case was a single primary lesion and did not show clinical evidence of metastasis at the time of presentation. The patient was immediately referred to the cancer institute for the comprehensive management.

**CONCLUSION**

More reports on such cases should be documented, to characterize the clinical behavior and prognosis of this unusual variant of oral SCC. However, we envisage that clear cell differentiation in a lesion, due to different clonal evolution within the tumor, will result in poor prognosis.

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**REFERENCES**


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