CASE REPORT

Hyalinizing clear cell carcinoma: A rare entity

P Venkat Baghirath, J Vijay Kumar, B Hari Vinay
Department of Oral and Maxillofacial Pathology, Panineeya Mahavidyalaya Institute of Dental Science and Research Centre, Hyderabad- 500 060, India

Address for correspondence:
Dr. P. Venkat Baghirath,
Department of Oral and Maxillofacial Pathology,
Panineeya Institute of Dental Sciences,
Kamalanagar, Road No. 5, Dilshuknagar,
Hyderabad- 500 060, India
E-mail: pmvids.oralpathology@gmail.com

ABSTRACT
Hyalinizing clear cell carcinoma (HCCC) is an uncommon malignant salivary gland tumor accounting for about 1% of all intra-oral salivary gland tumors. Microscopic diagnosis of clear cell carcinoma may be challenging because of the spectrum of features which frequently overlaps with the other salivary gland tumors that contain clear cells, and thus it may be a diagnosis of exclusion. Here we, report a case of HCCC in a 36 years old female with detailed histological, histochemical and immunohistochemical discussion.

Key words: Clear cells carcinoma, clear cells, hyalinizing clear cell carcinoma, salivary gland

INTRODUCTION

Hyalinizing clear cell carcinoma (HCCC) is an uncommon malignant salivary gland tumor that was characterized only recently as a distinct entity by Milchgrub *et al.* in 1994.[1] Since then, approximately 40 additional cases have been reported in the English literature. HCCC shows a female predominance (72.7%) and older age at diagnosis (68 years mean), with the vast majority of cases (81.8%) occurring in the oral cavity, most commonly the tongue and hard palate, and less common locations include the parotid gland, nasopharynx, hypopharynx and orbit/lacrimal gland.[2] This tumor arises usually in minor salivary glands of adult women involving mainly the base of the tongue, palate and floor of the mouth. It presents as a small, painless mass that seldom ulcerates. Microscopically the diagnosis is challenging because the cohort of clear cell salivary gland neoplasms is heterogeneous. Thus, several entities should be considered in the differential diagnosis of HCCC.[1] Histologically, all cases of HCCC demostrate the features of monomorphic glycogen rich clear cells in cords, nests, islands or trabaculae within hyalinized stromal background. Fifteen cases demonstrated foci of myxoid stromal changes. A dense inflammatory infiltrate composed of lymphocytes and plasma cells was seen in five cases (9.1%), Mitotic figures were seen in 18 cases (32.7%). Necrosis was identified in one case associated with mitotic activity (O'Regan *et al.*) which had an aggressive course. Perineural invasion was identified in approximately 20 cases (36.4%) with one case showing both perineural and perivascular invasion.[2] This article presents a case of HCCC in minor salivary gland of the right palatal region. The clinical, pathological and immunohistochemical (IHC) features are described.

Access this article online
Quick Response Code:
Website: www.jomfp.in
DOI: 10.4103/0973-029X.86714

CASE REPORT

A 36 years old female patient reported to Panineeya Mahavidyalaya Institute of Dental Science and Research Centre, Hyderabad in 2010, with a chief complaint of a painless swelling in the upper right back tooth region which gradually increased in size over a period of 6 months. Intraoral examination revealed a mass measuring of about 4 × 4 cm in size in relation to right maxillary permanent first molar [Figure 1]. On palpation, the mass was non-tender, smooth, firm, fixed to the underlying structures and was associated with the expansion of buccal and palatal cortical plates. Radiographic examination revealed diffuse radiolucency in relation to 16 and 17. The lesion was clinically diagnosed as mucoepidermoid carcinoma, and incisional biopsy was done in the same area. The routine processing and hematoxylin and eosin (H and E) staining was performed.

Microscopic examination revealed stratified squamous epithelium showing mitotic figures and few areas of keratin pearl formation [Figures 2 and 3]. The squamous epithelium was invading into the connective tissue. The underlying connective tissue showed islands of epithelial cells and clear cells arranged in cords or nests [Figure 4], and areas of hylanization were seen [Figure 5]. Tumors with clear cell differentiation are regarded as potentially malignant. As numerous clear cells were present in the histopathological sample of the patient, the diagnosis of mucoepidermoid

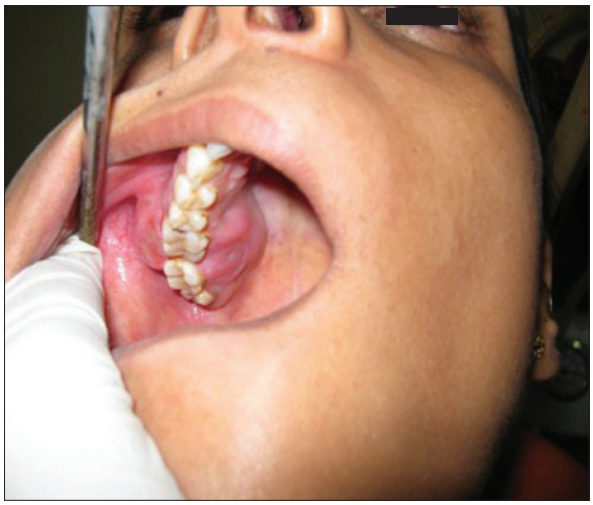

Figure 1: Intraoral examination of the patient in the case report revealing a mass measuring of about 4 × 4 cm in size in relation to right maxillary permanent first molar

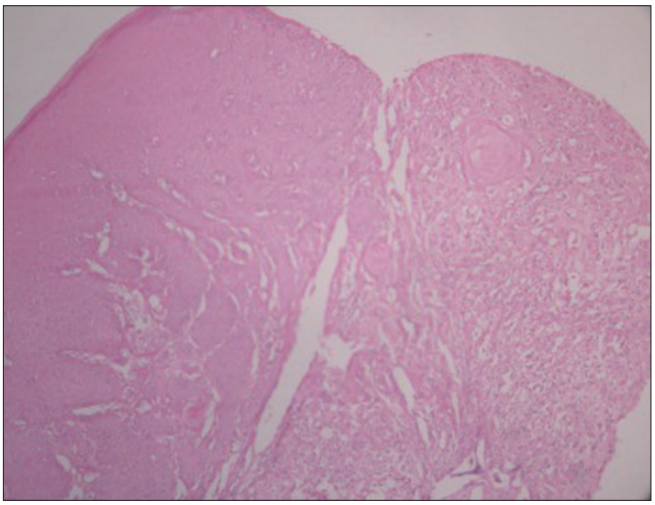

Figure 2: Histopathological examination of the lesion of the patient in the case report revealing a stratified squamous epithelium and few areas of keratin pearl formation (H and E stain, 4×)

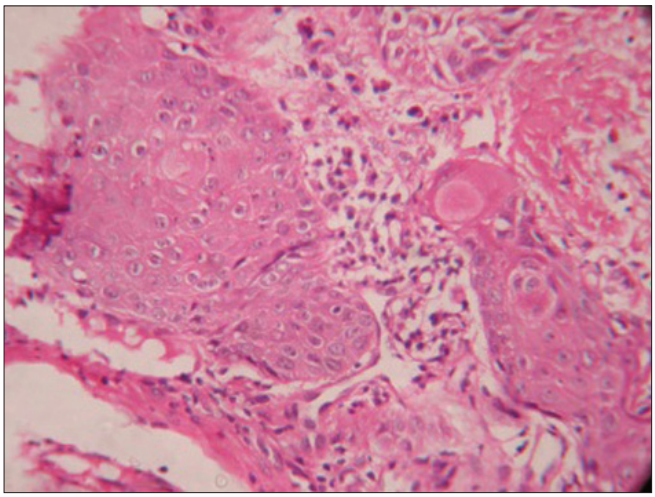

Figure 3: Histopathological examination of the lesion of the patient in the case report revealing a stratified squamous epithelium with mitotic figures (H and E stain, 40×)

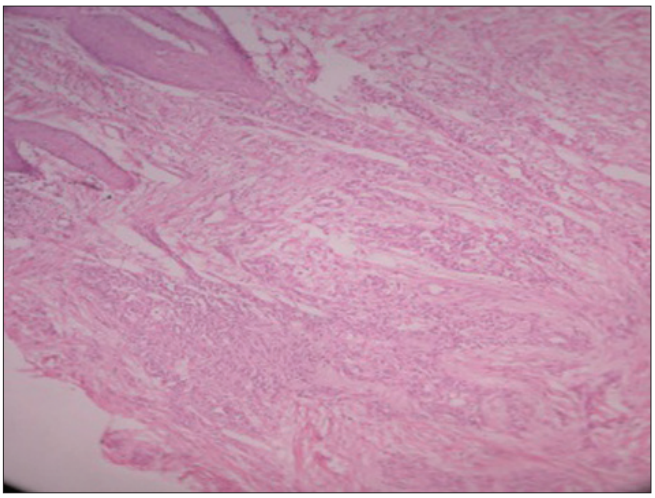

Figure 4: Histopathological examination of the specimen from the lesion of the patient in the case report revealing islands of of epithelial cells and clear cells arranged in cords or nests in the connective tissue (H and E stain, 10×)

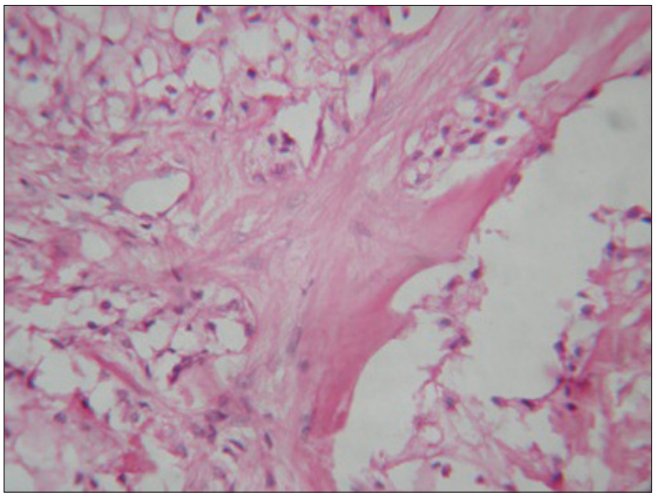

Figure 5: Histopathological examination of the specimen from the lesion of the patient in the case report revealing hyalinized areasin the connective tissue (H and E stain, 40×)

carcinoma had to be confirmed by using Periodic acid-Schiff (PAS) and Mucicarmine stains, [Figure 6] in which the clear cells were negative. Smooth Muscle Actin (SMA), S100, Vimentin and Calponin IHC testings were carried out, for which the myoepithelial cells stained negatively [Figures 7-9], whereas p63 immunoreactivity was positive [Figure 10 and Table 1] indication the lesion's proliferation potential. Thus we concluded that the tumor is of squamous origin. This was further confirmed by using pancytokeratin immunoreactivity test, where the clear cells showed positive results. [Figure 11].

Thus, the histopathological examination revealed a tumor tissue composed mainly of clear cells with round to oval nuclei. Fibrohyaline tissue separated the tumor cells which were arranged as sheets, nests and islands. IHC tests of tumor cells revealed Pancytokeratin and P63 positively while

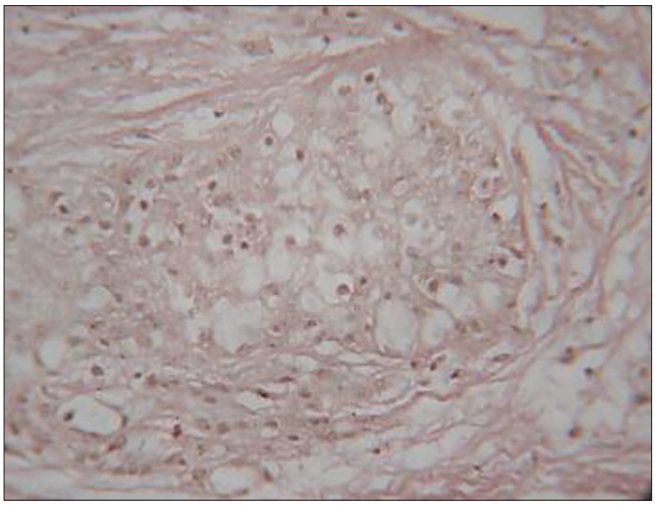

Figure 6: Histopathological examination of the specimen from the lesion of the patient in the case report showing that the clear cells stained negatively (Mucicarmine stain, 40×)

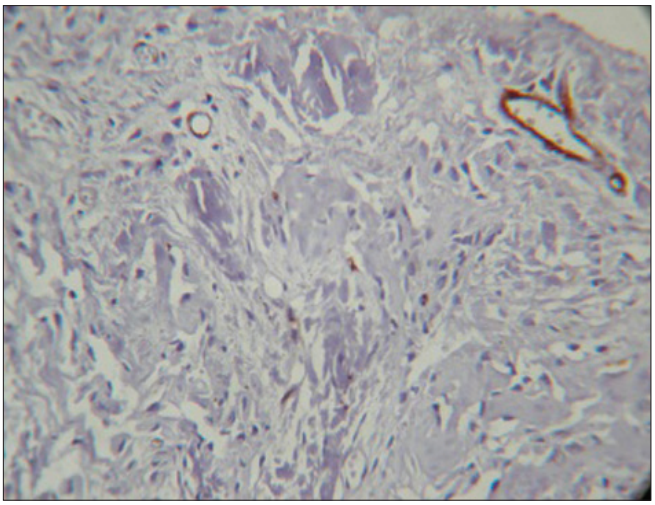

Figure 7: Immunohistochemical testing for smooth muscle actin (SMA) showing negative reactivity of the clear cells (10×)

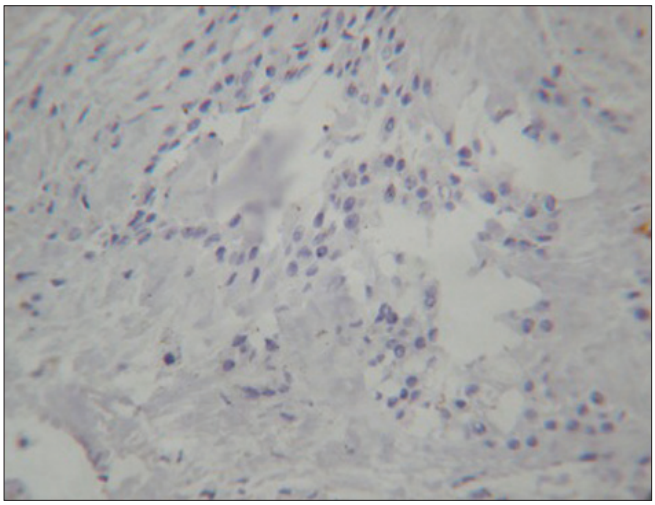

Figure 8: Immunohistochemical testing for S-100 showing negative reactivity of the clear cells (10×)

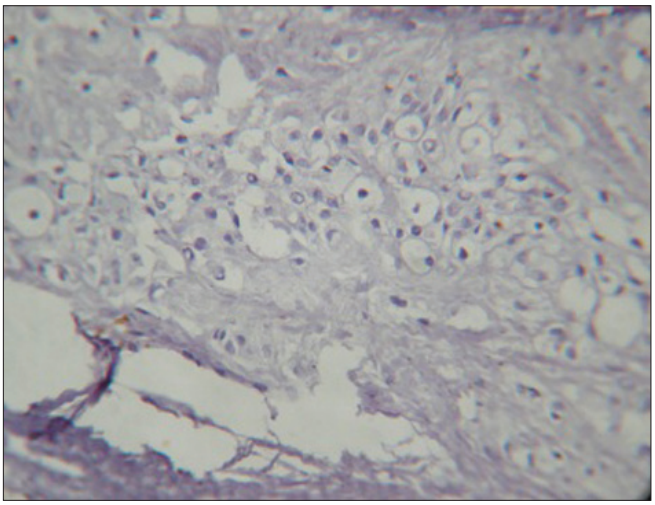

Figure 9: Immunohistochemical testing for Calponin showing negative reactivity of the clear cells (10×)

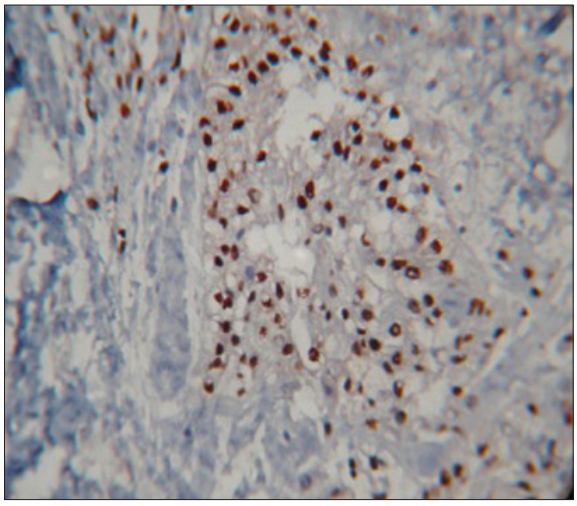

Figure 10: Immunohistochemical testing for P63 showing positive reactivity of the clear cells (10×)

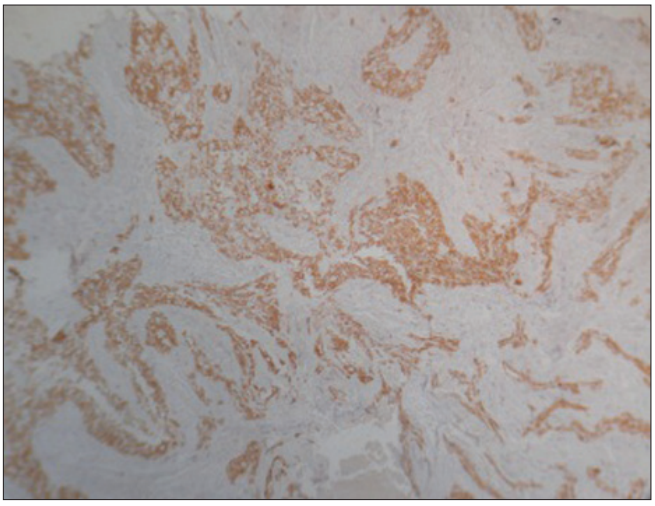

Figure 11: Immunohistochemical testing for Pancytokeratin showing positive reactivity of the clear cells (10×)

Table 1: Special stains and immunohistochemical of the present case

PAS	Mucicarmine	SMA	S100	Vimentin	Calponin	PCK	P^{63}
-	-	-	-	-	-	+	+

Table 2: Differential diagnosis with special stains and IHC markers for clear cell lesion in the oral cavity

	PAS	Mucicarmine	PCK	P^{63}	SMA	S100	Calponin
Mucoepidermoid carcinoma	+	+	+	N/A	-	-	NA
Epithelial myoepithelial carcinoma	-	-	-	+	+	+	+
Clear cell myoepithelioma	-	-	+	+	+	+	+
Acinic cell carcinoma	+	-	+	+	+	-	N/A
Clear cell odontogenic tumor	N/A	N/A	+	+	+	-	N/A
Metastatic Tumor	+	-	+	+	-	+	N/A
Hyalinizing clear cell carcinoma	+/-	-	+	+	-	-	-

Vimentin, S100 and SMA were negative. These features were consistent with a Hyalinizing clear cell carcinoma of minor salivary gland.

DISCUSSION

Clear cells create diagnostic dilemmas and controversies in the classification of clear cell salivary gland neoplasms, and hence correct classification is a challenge in their presence. The entire range of salivary gland neoplasms that presents with a high proportion of clear cells includes [Table 2]: clear cell variants of well recognized salivary gland tumors; clear cells mucoepidermoid carcinoma; epithelial myoepithelial carcinoma; acinic cell carcinoma; some odontogenic tumors; and, metastatic clear cell tumors.[1] In most of the cases they constitute only a minor component of cellular constituency and appropriate classification of the tumor is easily established on the basis of typical features that are apparent. In some tumors they constitute the major cellular component and it is in this situation that the diagnostic challenge is the greatest.[3] It is important to differentiate HCCC from other tumors with clear cell features because of their differences in treatment and clinical outcome.

Histopathological examination and IHC testing form the basis for differentiating between different types of tumors containing clear cells. Mucoepidermoid carcinoma, the most common neoplasm of salivary gland has characteristically demonstrated three morphologically distinct cell types on histopathological study, which include: mucin producing cells that can have the appearance of foam cells and goblet cells; and, epidermoid cells and intermediate cells that have eosinophilic cytoplasm with round nuclei. The clear cells are in addition to the mucocytes in these tumors which typically have pale basophilic, foamy cytoplasm as revealed on H and E staining. Mucicarmine stain can be very helpful for highlighting the mucocytes and distinguishing them from the other clear cells.[4]

Epithelial myoepithelial carcinoma is rare and the tumor cells tend to show duct like growth with a biphasic appearance. Clear cells contain glycogen which is positive to PAS staining and negative with mucicarmine staining. Architecture of this tumor varies from sheets to organoid nodules to discrete tumor nests, and they may be solid or cystic.[1,3,5] Stroma varies from loose fibrous to hyalinized tissue. The epithelial cells show positivity for cytokeratin and epithelial membrane antigen (EMA) immunoreactivity, whereas clear cells stain positively for myoepithelial markers such as calponin, and also S100 and SMA.[6]

Acinic cell carcinoma is often infiltrative and shows different cellular growth patterns including solid, papillary, microcystic and follicular and usually more than one cell type. The cells are positive for PAS staining.[7] Clear cell odontogenic carcinoma is an aggressive tumor and is morphologically characterized by islands of mostly clear cells surrounded by fibrous stroma. These are positive for cytokeratin, EMA and S-100 immunoreactivity.[8] Metastatic tumors like renal cell carcinoma are associated with haemorrhage and necrosis and are positive for renal cell carcinoma antigen, cd10 and cytokeratin.[9]

CONCLUSION

HCCC should be considered in the differential diagnosis of tumors with a histology marked by monomorphic clear cells arranged in cords, trabecular or in clusters, and surrounded by hyalinized stroma. Special stains and IHC tests help in diagnosing this type of carcinomas. Hence HCCC is a diagnosis of exclusion.

REFERENCES

1. Dardick I, Leong I. Clear cell carcinoma: review of its histomorphogenesis and classification as a squamous cell lesion. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:399-405.
2. O'Sullivan-Mejia ED, Massey HD, Faquin WC, Powers CN.

Hyalinizing clear cell carcinoma: report of eight cases and review of literature. Head Neck Pathol 2009;3:179-85.
3. Ellis GL. Clear cell neoplasm in salivary glands: clearly a diagnostic challenge. Ann Diagn Pathol 1998;2:61-78.
4. Lai G, Nemolato S, Lecca S, Parodo G, Medda C, Faa G. The role of immunohistochemistry in the diagnosis of hyalinizing clear cell carcinoma of the minor salivary gland: a case report. Eur J Histochem 2008;52:251-4.
5. Sun ZJ, Zhao YF, Zhang L, Zhang WF, Chen XM, He SG. Hyalinizing clear cell carcinoma in minor salivary glands of maxillary tuberosity. Oral Oncol Extra 2005;41:306-10.
6. Solar AA, Schmidt BL, Jordan RC. Hyalinizing clear cell carcinoma case series and comprehensive review of the literature. Cancer 2009;115:75-83.
7. Said-Al-Naief N, Klein MJ. Clear cell entities of the head and neck: a selective review of clear cell tumors of the salivary glands. Head Neck Pathol 2008;2:111-5.
8. O'Regan E, Shandilya M, Gnepp DR, Timon C, Toner M. Hyalinizing clear cell carcinoma of salivary gland: an aggressive variant. Oral Oncol 2004;40:348-52.
9. Félix A, Rosa JC, Nunes JF, Fonseca I, Cidadão A, Soares J. Hyalinizing clear cell carcinoma of salivary glands: a study of extracellular matrix. Oral Oncol 2002;38:364-8.

How to cite this article: Baghirath PV, Kumar JV, Vinay BH. Hyalinizing clear cell carcinoma: A rare entity. J Oral Maxillofac Pathol 2011;15:335-9.
Source of Support: Nil. **Conflict of Interest:** None declared.