

# Clear cell carcinoma of palatine salivary gland: A diagnostic challenge

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## INTRODUCTION

Clear cell carcinoma is a rare low-grade salivary gland malignant neoplasm which represents approximately 1% of all salivary gland tumors. These tumors occur exclusively in minor salivary gland and are characterized by an indolent growth and less aggressive biological behavior. The clarity of cytoplasm of the clear cells has been attributed to accumulation of glycogen, loss of organelles, or as fixation artifact.<sup>[1-3]</sup> As a result, the differential diagnosis of intraoral clear cell neoplasms of includes a diverse group of tumors including primary salivary gland clear cell tumors, clear cell odontogenic tumors as well as few metastatic tumors. Therefore, the diagnosis of clear cell carcinoma is of exclusion.<sup>[1,2]</sup>

## CASE REPORT


A 40-year-old female patient presented with a slow growing, painless swelling of 6–7 years' duration on the right side of the face intraorally and extraorally. Habit history revealed smoking of 10 cigarettes per day for 7 years. Intraoral examination revealed a diffuse hard swelling measuring about 5 cm × 6 cm on the maxillary right posterior region, extending from the midline of the palate, from mesial aspect of 14 to the distal aspect of 18. Orthopantomograph and occlusal radiograph showed extensive bone loss and missing 16. The computed tomography at the level of the maxilla revealed a radiodense mass extending from the 14 region up to the maxillary tuberosity and also extension of the tumor mass into the maxillary antrum. A volume-rendered

computed tomography showed erosion of the palatine bone on the right side of the maxilla [Figure 1]. Grossly, the tumor mass was yellowish cream in color with a reddish tinge, firm in consistency with an irregular surface texture. The cut surface was yellowish white with a few hemorrhagic foci at the periphery.

## HISTOPATHOLOGIC FEATURES

- Overlying orthokeratinized stratified squamous epithelium showed pseudoepitheliomatous hyperplasia, increased mitotic figures and individual cell keratinization [Figure 2]
- Connective tissue stroma showed sheets and strands of clear cells and small cells with eosinophilic cytoplasm with oval to round nucleus interspersed with dense, fibrocellular radiating collagen fibers [Figure 3]
- Some of the cells are arranged in nests and cords along with duct-like structures filled with mucoid material [Figure 4]
- Clear cells appear to be pleomorphic with prominent hyperchromatic nuclei [Figure 5]
- At the periphery, palatine salivary glands were evident [Figure 6]
- Perineural invasion was also noted [Figure 7].

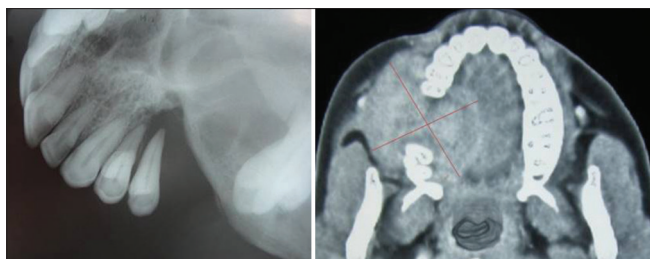
The presence of clear cells in hematoxylin and eosin sections justified the need to perform special stains and immunohistochemistry (IHC) to arrive at definitive diagnosis.

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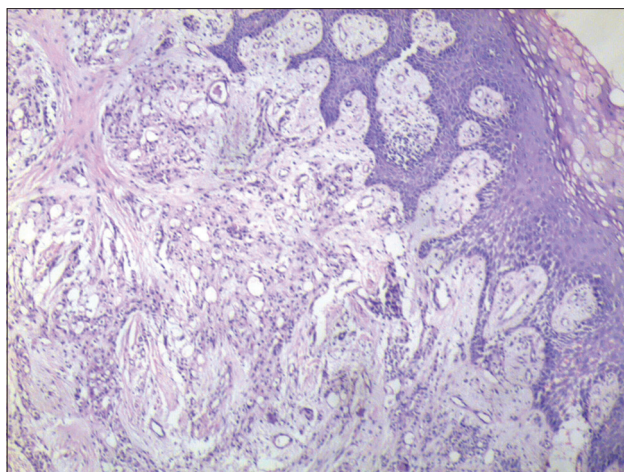
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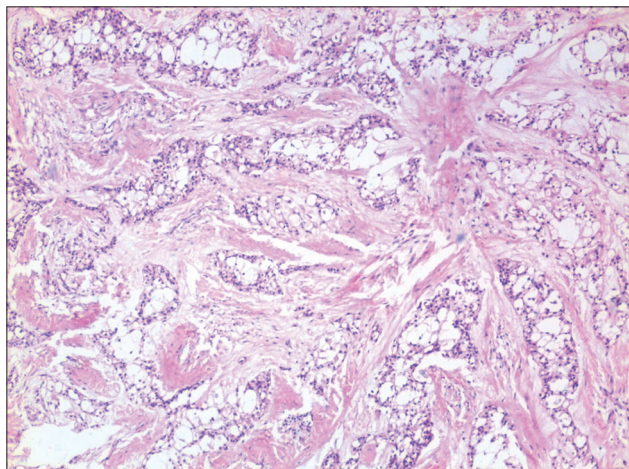
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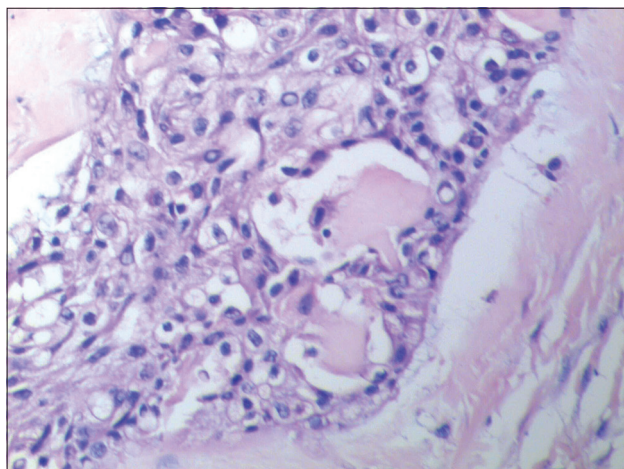
**Figure 1:** Occlusal radiograph (left) superficial erosion of the palatine bone, computed tomography (right) revealed the extent of the tumor mass



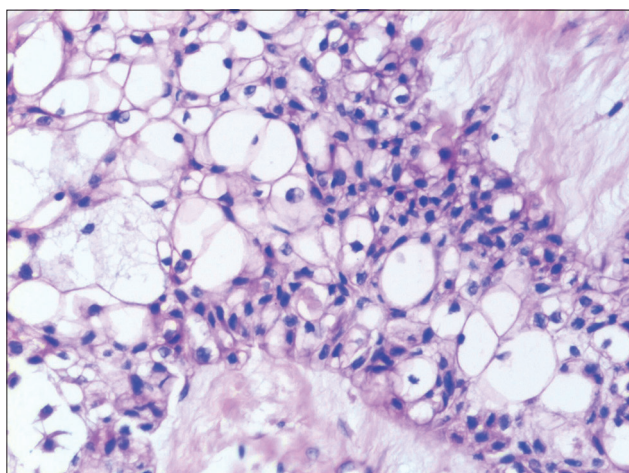
**Figure 2:** Photomicrograph of overlying palatine epithelium with underlying connective tissue showing clear cells (H&E, x40)



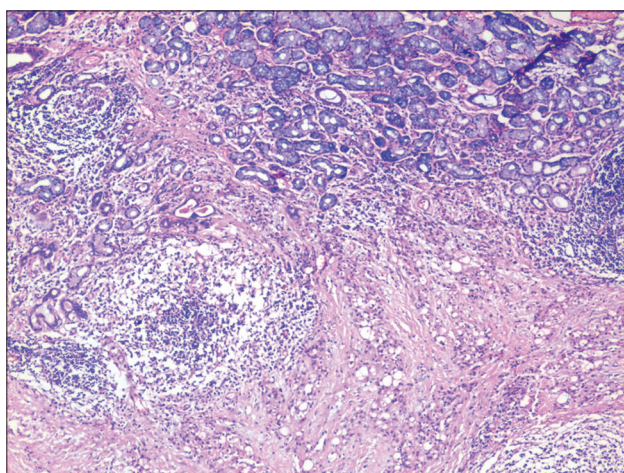
**Figure 3:** Photomicrograph of clear cells and small eosinophilic cells in sheets and islands separated by fibrocellular connective tissue septa (H&E, x40)



**Figure 4:** Photomicrograph of island of clear cells and eosinophilic cells with duct-like structures (H&E, x200)



**Figure 5:** Photomicrograph of island of pleomorphic clear cells and eosinophilic cells (H and E, x200)



**Figure 6:** Photomicrograph of palatine salivary gland at the periphery of the mass (H&E, x40)

### SPECIAL STAINS

- Mucicarmine (residual salivary glands at the periphery showed positive stain) [Figure 8], alcian blue, periodic acid–Schiff reagent (PAS), phosphotungstic acid

hematoxylin (PTAH), Congo red and oil red O stain showed a negative reaction for the tumor.

## IMMUNOHISTOCHEMISTRY

- Tumor cells showed positivity for cytokeratin panel CK, CK5/6 (CK5-basal cell marker with myoepithelial markers CK6) [Figure 9]
- P63-small eosinophilic cells showed positive reaction indicative of proliferation, whereas clear cells showed no reaction [Figure 10]
- Eosinophilic cells showed S100-positive reaction [Figure 11]
- Negative reaction for CK8, CK19, smooth muscle actin (SMA), CD10 (metastasis) and Vimentin markers.

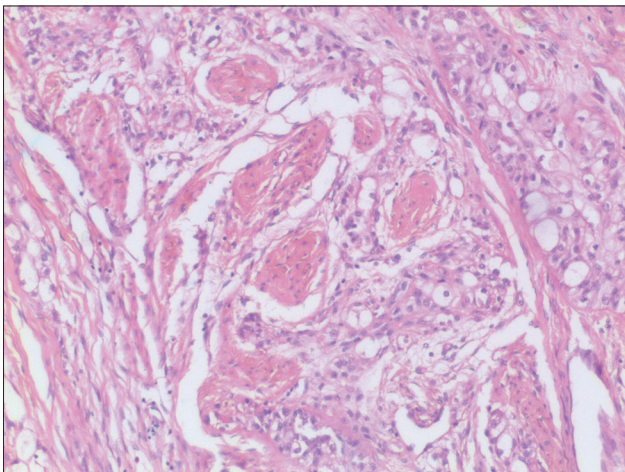
## DIFFERENTIAL DIAGNOSIS

### Clear cell variants of primary salivary gland tumors

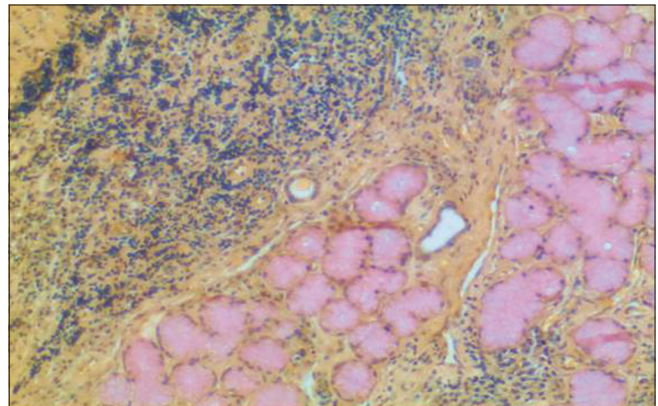
- Mucoepidermoid carcinomas – they show PAS positive, diastase-resistant cytoplasmic granules. Mucous cells demonstration by mucicarmine,

alcian blue and IHC staining for MUC5AC helps in diagnosis<sup>[2,3]</sup>

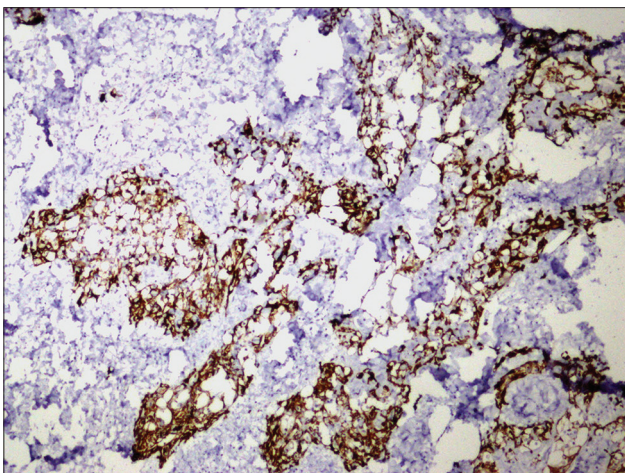
- Acinic cell carcinoma – degenerative clear cell changes account for < 95% of tumor cells. They show PAS positive, diastase-resistant cytoplasmic granules, negative with mucicarmine and alcian blue. IHC staining for CK7 and CK 8 positive<sup>[2,3]</sup>
- Oncocytoma – positive with PAS and PTAH (blue cytoplasmic granules under oil immersion). Negative with digested PAS and Alcian blue<sup>[2]</sup>
- Epithelial-myoepithelial carcinoma – characteristic biphasic pattern with inner cell expressing epithelial markers (low-molecular-weight cytokeratin Cam 5.2, European medicines agency and AE1/AE3), surrounded by an outer layer of cells showing positive staining with myoepithelial markers such as SMA, calponin, vimentin and S-100. PAS-positive basement membrane separating the tumor island from stroma<sup>[1-3]</sup>
- Myoepithelial carcinomas – clear cells negative with mucicarmine staining. Myxoid matrix is positive with



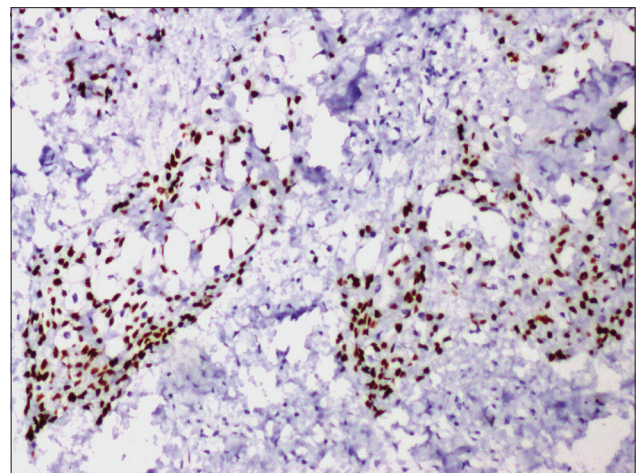
**Figure 7:** Photomicrograph of infiltration of nerve fiber bundles at the periphery of the tumor (H&E, x100)



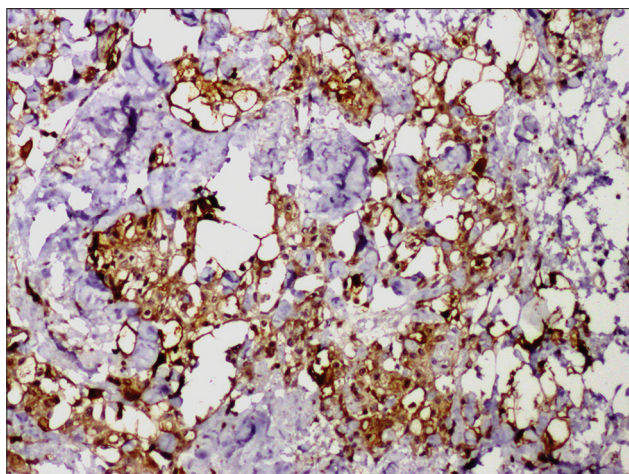
**Figure 8:** Photomicrograph of negative mucicarmine staining of the clear cells except the palatine salivary (H&E, x40)



**Figure 9:** Photomicrograph of immunostaining of the clear cells by the cytokeratin 5/6 (x100)



**Figure 10:** Photomicrograph of immunostaining of the small eosinophilic cells by the proliferative marker P63 (x100)



**Figure 11:** Photomicrograph of immunostaining of the clear cells by the s100 (x100)

alcian blue staining. Tumor cells are positive with myoepithelial markers calponin, vimentin, SMA, S-100, CK7 and CK14.<sup>[1-3]</sup>

#### Clear cell lesions of odontogenic origin

- Clear cell odontogenic carcinoma shows lobulated growth pattern, presence of osteodentin, and more likely to be intraosseous in origin. The clear cells are PAS positive with diastase sensitive cytoplasmic granules. They are negative with mucin, vimentin and muscle actin. Positive with CK8 and CK19<sup>[4]</sup>
- Clear cell variants of calcifying epithelial odontogenic tumor – presence of calcifications – Liesegang rings and Congo red stain positive for amyloid deposition in connective tissue.<sup>[4]</sup>

#### Metastatic clear cell lesions

- Renal cell carcinoma shows pronounced cellular atypia, vascularity of the lesions, demonstration

of intracytoplasmic fat, positivity with CD10 and vimentin.<sup>[2,3]</sup>

#### FINAL DIAGNOSIS

Based on clinicoradiological findings and immunohistochemical profile of the microscopic features, the diagnosis of clear cell carcinoma of minor salivary gland of hard palate was given.

#### 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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