

CASE REPORT

CLEAR CELL CARCINOMA OF MINOR SALIVARY GLAND ORIGIN: A CASE OF MISTAKEN IDENTITY

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ABSTRACT

Clear cell carcinoma (CCC) of salivary gland origin is an extremely rare low-grade carcinoma. It occurs in the minor salivary glands. This is a recent addition to the World Health Organisation (WHO) classification of salivary gland tumours and defines it as a malignant epithelial neoplasm with single monomorphic population of cells having optically clear cytoplasm on standard Hematoxylin & Eosin (H & E) stain. We hereby, report an interesting case of CCC of minor salivary gland origin initially misdiagnosed as squamous cell carcinoma and have drawn the comparisons from other salivary gland tumours with a minor clear cell component.

Keywords: Clear cell, carcinoma, salivary gland

INTRODUCTION

CCC is an extremely rare salivary gland tumour, representing 1% of malignant tumours of salivary gland.¹ Most common site of origin is the minor salivary gland, mainly the palate. Tonsillar sulcus, parotid, oral mucosa and jaw are uncommon sites. This entity has been recently included in the WHO classification of salivary gland tumours.² It is a slow growing low grade carcinoma, usually asymptomatic, hence reaches considerable dimensions before being diagnosed.³ Recurrence rates are low and distant metastasis is exceptional.⁴ It has an excellent prognosis. No deaths have been reported so far.

Clear cell component can be seen in a variety of benign and malignant salivary gland tumours such as oncocytoma, sebaceous adenoma, muco-epidermoid carcinoma, acinic cell carcinoma, epithelial adenoma and sebaceous carcinoma.³ But the predominant histopathological features help in the diagnosis.

CASE REPORT

A 36 year old female, presented in the surgical OPD, with the history of a slow growing painless mass in the tonsillar region, for the past four years with no significant history of dysphagia, hoarseness of voice or excess salivation. She was a non-smoker with no history of tobacco chewing. On eliciting further history, a previous biopsy which was done outside, reported the lesion as squamous cell carcinoma. On examination, a large ulceroproliferative lesion involving the left tonsil, floor of mouth and left side of tongue was visualised. Few enlarged, palpable ipsilateral cervical lymph nodes of level

II and III were present. On CECT (Contrast enhanced computed tomography) of the head and neck, the extent of the tumour was seen with no evidence of bony erosion. A provisional diagnosis of advanced squamous cell carcinoma of the oral cavity was offered.

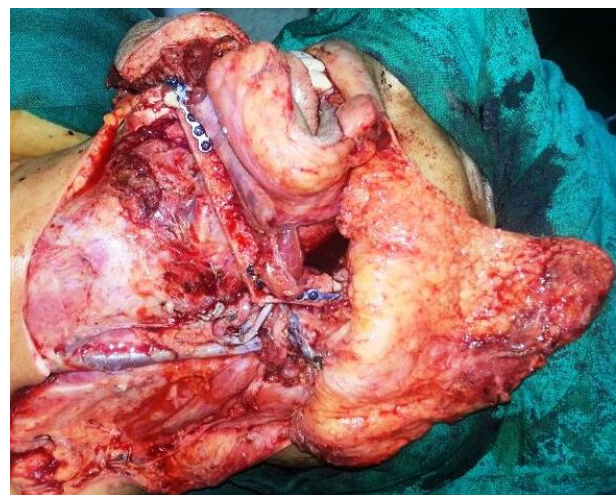


Fig 1: Intra-operative photograph showing en block removal with radical neck dissection.

A planned surgery i.e left tonsillar commando operation en block removal with radical neck dissection (RND) (Figure 1) was performed and the specimen was sent for histopathology. Gross examination of the specimen showed a firm grey white solid tumour mass measuring 4.5x3x 1.8 cm involving the base of tongue, left tonsillar sulcus and the tonsil. Multiple sections taken from the

growth, showed clear cell tumour throughout. Tumour cells were arranged in sheets, nests and trabeculae formation.

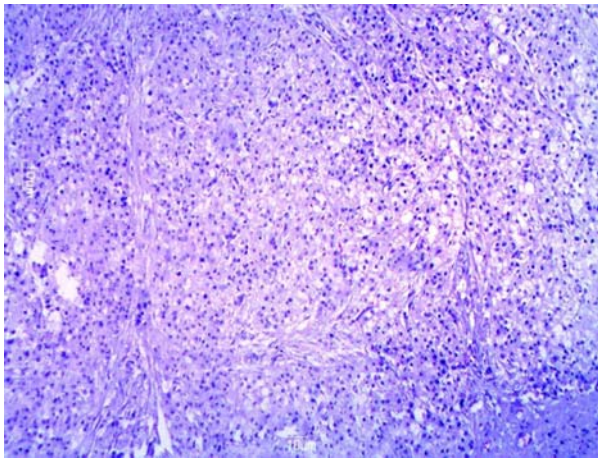


Fig 2: Microphotograph showing tumour with clear cells & areas of fibrosis (H&E,20 X)

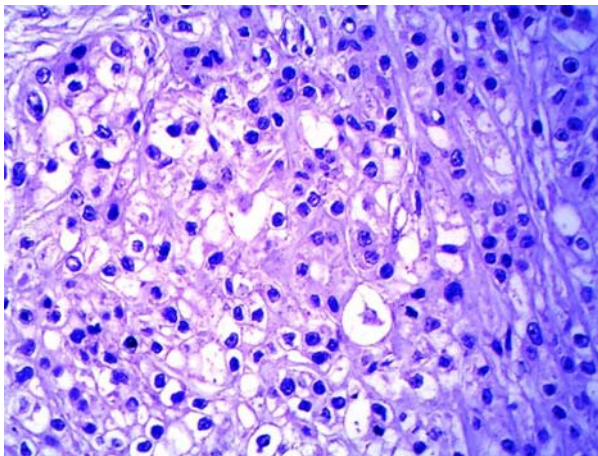


Fig 3: Microphotograph from tumour showing polygonal monotonous cells with clear vacuolated cytoplasm and small nuclei. (H& E, 40X)

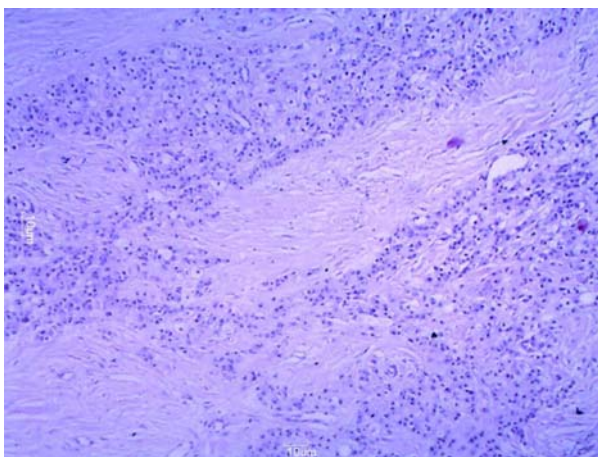


Fig 4: Microphotograph showing nests of tumor cells separated by fibrous septae (H& E,20X)

Cells were polygonal with monotonous morphology, distinct cell borders, clear cytoplasm and a centrally placed small, round nuclei (Figure 2,3). Tumour cells were seen infiltrating the skeletal muscle and reaching upto the resected margin. Intervening fibrous stroma was seen separating nests of cells.(Figure 4) Minimal mitosis and focal areas of hyalinisation were also seen. The resected margins of tongue, salivary gland as well as the bony cut margin were free from tumour involvement. A total of 21 lymph nodes were isolated from the specimen out of which four showed tumour deposits. A final diagnosis of CCC (NOS) of minor salivary gland origin was made. The post-operative period was uneventful and the patient was free from local or distant disease in the follow up.

DISCUSSION

CCC is a low grade carcinoma, recently included in WHO classification² It is found primarily in the minor salivary gland, especially the palate and less commonly in other intraoral sites. They account for approximately 1% of the primary tumours of all types of salivary glands.^{5,6}

By definition, CCC contains a significant proportion of clear cells. These clear cells are thought to be originating in the intercalated duct cells or the myoepithelial cells.⁷ The cytoplasm is clear due to glycogen and reacts variably with Periodic Acid Schiff (PAS) stain, hence a negative PAS stain does not preclude the diagnosis of clear cell carcinoma. The cytoplasmic clearing may also result from loss of organelles, storage of substances or fixation artefacts.⁸ Various salivary gland tumours show clear cell component, hence a differential diagnosis of muco-epidermoid carcinoma, acinic cell carcinoma, epithelial-myoeplithelial carcinoma, clear cell oncocytoma, sebaceous adenoma and sebaceous carcinoma, having a salivary gland origin should be considered.⁹

Although diagnosis CCC is usually apparent on routine H & E stained sections but sometimes special stains and immunohistochemistry may be required to differentiate from other tumours with similar morphology and conclude the diagnosis. Clearing due to hydropic degeneration in the squamous component may be seen in mucoepidermoid carcinoma. However, it is positive for alcian blue and mucicarmine stains. Sebaceous adenoma as well as carcinoma have clear cells with a foamy cytoplasm due to lipid droplets, positive for fat stains. Clear cells of oncocytoma contain glycogen but can be differentiated by being well circumscribed and non-infiltrating with foci of characteristic oncocytic cells.³ Epithelial-myoeplithelial carcinoma has a biphasic cell population i.e. ductal cells surrounded by large polygonal clear cells immunoreactive for S-100 and SMA (smooth muscle specific actin) which are myoeplithelial markers, consistently negative in clear cell carcinoma.

Another important differential diagnosis is metastatic lesion from clear cell variant of renal cell carcinoma (RCC). A high degree of vascularity, pronounced atypia

and lack of hyaline stroma is generally regarded as hallmark of RCC.¹⁰ IHC including vimentin, CD10 are positive in RCC while clear cell carcinoma shows immunoreactivity for cytokeratin (CK7), High molecular weight keratin (HMWK) and Carcinoembryonic antigen (CEA). Combined imaging and clinical findings are instrumental in provisional diagnosis of RCC. Clear cell tumors of other sites such as the lung, thyroid and female genital tract are also potential sources of metastasis.

Clear cells on morphology along with lack of evidence of other salivary gland malignancies, are important criteria for concluding the diagnosis. In our case, a predominant clear cell component was seen on histopathology along with inconspicuous mitotic activity. Hence, the diagnosis of clear cell carcinoma (NOS) was made. For most clear cell carcinoma, wide excision is the treatment of choice^{11,12,13} although neck dissection and radiotherapy have been performed in a few cases.¹³ Multiple recurrences to local nodal or distant disease have been seen in some of the reported cases¹⁴ The presence of positive margins, high grade histology, invasion (vascular or neural) or positive neck nodes. are some of the deciding factors for lymph node dissection or radiotherapy.¹⁵ Since this was a low grade tumor, no post-operative radiotherapy was considered after RND, instead a close follow up was adopted.

CONCLUSION

Most common site of origin of CCC of the oral cavity is the minor salivary gland, mainly the palate. Clear cell component is a common feature in a number of salivary gland tumours. Hence, a thorough clinical and histological examination along with awareness of this recent entity is essential to achieve a final diagnosis.

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