CASE REPORT

An unusual case of palatal swelling – Hyalinizing clear cell carcinoma: a case report

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Abstract

Hyalinizing clear cell carcinoma is an uncommon malignant salivary gland tumour that appears almost exclusively in the minor salivary glands of the oral cavity.1,2 It is an indolent tumour with little metastatic potential, and therefore, it is important to distinguish it from other, more aggressive, clear cell lesions such as metastatic renal cell carcinoma.3 We present the case of a 48-year-old woman who presented with a 2-year history of a mass on her soft palate. The clinical history, imaging and histopathological features are described and discussed.

Introduction

Hyalinizing clear cell carcinoma (HCCC) is a rare neoplasm, first described by Milchgrub et al2; it accounts for less than 1% of all salivary gland tumours4, with around 300 cases documented in the literature5. It is almost exclusively found in the minor salivary glands of the oral cavity; however, the literature does report occurrence at other sites, such as the major salivary glands and the larynx6. HCCC presents as a small, painless, submucosal mass arising primarily in the palate or tongue. It predominantly presents in the seventh decade of life, although it has been shown to occur in a wide age range with a female predilection7.

HCCC continues to be classified as a ‘Clear Cell Carcinoma, Not Otherwise Specified’ by the World Health Organisation (WHO)8 and was previously always considered a diagnosis of exclusion in order to distinguish it from other clear cell lesions, as clear cells are present in many benign and malignant head and neck tumours. Many differential diagnoses may be considered including clear cell variants of other primary salivary carcinomas, such as myoepithelial carcinoma, epithelial-myoepithelial carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma and metastatic renal cell carcinoma9. Clear cell odontogenic lesions should also be considered when abutting bone, but can often be excluded by detailed imaging and radiography. Recent molecular studies have shown that 82% of HCCC demonstrate an EWSR1 rearrangement, with the majority showing an EWSR1-ATF1 translocation10,11. This translocation may be useful in distinguishing HCCC from other clear cell salivary gland lesions.

Case report

A 48-year-old Caucasian woman was referred by her general dental practitioner to the Oral and Maxillofacial Surgery Department in Monklands Hospital, North Lanarkshire. She presented with a 2-year history of a slow growing palatal swelling, which was interfering with the placement of her upper denture. The patient felt that the growing lesion on her palate was making her denture ‘loose’, and she was unable to wear her denture while eating, due to its instability. The patient had no relevant medical history and
took no prescribed medication. The extra-oral examination did not demonstrate any lymphadenopathy, swelling or asymmetry.

Intra-oral examination revealed a soft exophytic pedunculated mass at the midline of the palate, extending to the junction of the hard and soft palate (Fig. 1).

Magnetic resonance imaging (MRI) showed a 3 cm diameter palatal tumour eroding bone situated towards the left aspect of the hard palate and extending through the floor of the left nasal cavity (Fig. 2). Computed tomography (CT) revealed no evidence of metastatic disease.

Microscopic examination of an incisional biopsy revealed an epithelial tumour comprising islands and strands of clear cells infiltrating through a fibrocellular stroma. Towards the deep aspect of the specimen, islands of epithelial cells, consistent with intermediate cells, were noted. A differential diagnosis of clear cell carcinoma, a clear cell variant of a myoepithelial lesion, clear cell mucoepidermoid carcinoma and clear cell odontogenic carcinoma was considered. Clear cell odontogenic carcinoma was excluded on the imaging, as the lesion was not arising from within the bone, and on the lack of typical histological features, such as strands of basaloid cells within the lesion. Following multidisciplinary team meeting agreement, the patient underwent wide local excision of the tumour with a left-sided selective neck dissection.

Final diagnosis was made following microscopic and immunohistochemical examination of the whole specimen. The specimen margins were shown to be clear of tumour, and no positive neck nodes were identified. Microscopic examination showed lobules and cords of rounded and polygonal cells, with clear or pale eosinophilic cytoplasm, separated from the surrounding fibrous stroma which featured prominent hyalinised collagenous strands (Fig. 3). No evidence of epidermoid or mucous differentiation was identified. The clear cells were glycogen rich, demonstrated by diastase-sensitive, PAS-positive cytoplasmic staining. Immunohistochemical staining for cytokeratin CK7 (Dako, GA61961) was positive, consistent with a lesion of salivary gland origin. Staining for SMA (Dako, M085101) and S100 (Dako, GA50461) was negative, indicating a lack of myoepithelial cells. However, CK14 (BD Biosciences, 550953) was positive, suggesting the basal cells were of ductal origin (Fig. 4).

Markers for renal cell carcinoma (RENCA [Dako, M3632]) were also negative. Histological and immunohistochemical findings allowed a definitive diagnosis of HCCC to be reached.

The patient has attended regular maxillofacial follow-up and remains disease free with no evidence of local or regional recurrence at 18 months.

**Discussion**

Clear cell tumours of the head and neck are rare. Histologically, these tumours are characterised by populations of cells with clear, glycogen-rich cytoplasm. It is important, however, to note that this cellular appearance may present in a wide range of
lesions, especially in variants of salivary gland tumours including myoepithelioma, acinic cell carcinoma and mucoepidermoid carcinoma. This variety may create a diagnostic dilemma for the histopathologist, making correct classification a challenge. HCCC must be distinguished from histologically similar lesions to allow for the correct surgical management to be implemented.

Figure 3 Histopathological examination of excisional specimen. A monomorphic population of clear cells was noted, interspersed by prominent hyalinised collagenous stroma (H&E staining X60) (a). The lesion at higher magnification showing populations of round and polygonal clear cells (H&E staining X200) (b).

Figure 4 Immunohistochemical staining for CK7 (a), CK14 (b) AE1/AE3 (c) was diffusely strongly positive, with focal weaker positivity for Cam5.2 (d).
HCCC has been described by the WHO as a diagnosis of exclusion\(^\text{12}\). In HCCC, immunohistochemical stains for myoepithelial origin, distinguishing it from clear cell myoepithelial tumours\(^\text{13}\). Similarly, markers for metastatic renal cell carcinoma will be negative.

HCCC has now been associated with a specific gene rearrangement, which may help to separate it from other mimics. Molecular markers have shown an \(E\text{WSR1-ATF1}\) translocation in 82% of cases\(^\text{10,11}\), as well as the absence of \(MAML2\), a common gene rearrangement found in mucoepidermoid carcinoma\(^\text{6}\). These changes appear to be specific to HCCC when considering salivary gland lesions and ultimately may require a revision of the description by WHO\(^\text{12}\).

It is important to note that \(E\text{WSR}\) translocations have been found in a range of clear cell lesions from other sites including clear cell odontogenic carcinoma\(^\text{11}\), and care needs to be taken during interpretation of this molecular finding.

Overall, HCCC is thought to have a good prognosis. Batsakis\(^\text{14}\) first used the term ‘clear cell carcinoma of the salivary gland’ to describe what was originally thought to be myoepithelial carcinoma. When Milchgrub \textit{et al.} analysed the clinical, epidemiological and histopathological features, the term ‘hyalinizing clear cell carcinoma’ was proposed\(^\text{2}\), and it was initially thought to be low grade and rarely metastasised. The indolent nature of the tumour has led to the primary treatment modality to be excision only with no adjuvant treatment. However, more recent articles have shown that the tumour can display aggressive local behaviour\(^\text{15}\) with 11.5% developing recurrent disease and 25% with evidence of metastatic disease. Wide local excision alone continues to be the treatment of choice, although radiotherapy may be provided should the margins not be cleared adequately, and close follow-up is recommended for all patients affected.

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**Conflict of interest**

The authors declare that there is no conflict of interest.

**Ethical Approval**

None required.

**References**