Primary Clear Cell Carcinoma of Minor Salivary Gland of the Soft Palate: A case report

K A Saleh, MRCS (ENT)(Glasg), Nurishmah Md. Isa MS, Firouzeh, MD, B S Goh, MS (ORL-HNS)

Department of Otorhinolaryngology, Head and Neck Surgery, Medical Faculty, University Kebangsaan Malaysia Medical Center, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur

SUMMARY

Clear cells can be found in numerous salivary and non-salivary tumors in the head and neck region, including metastatic lesions. They are rare low-grade tumors accounting for less than 1 % of all salivary gland tumors and occur almost exclusively in the intra-oral minor salivary glands. Hyalinizing clear cell carcinoma (HCCC) is an extremely rare and recently described neoplasm predominantly affecting the oral cavity. Histologically, it is characterized by nests of glycogen-rich monomorphic clear cells within a hyaline stroma. HCCC often follows an indolent course with a limited metastatic potential. It is therefore important to differentiate this entity from other more aggressive clear cell tumors including metastatic tumors such as renal cell carcinoma. We hereby report a case of HCCC localized in minor salivary glands specifically in soft palate for its rarity, as well as to discuss the role of immunohistochemical stains, essential for its definitive diagnosis.

KEY WORDS:
Hyalinizing clear cell carcinoma, soft palate, salivary gland, immunohistochemistry

CASE REPORT

A 31-year-old male presented with intermittent foreign body sensation over the palatal region with a slow growing painless mass on the left side of the soft palate of 4 years duration. There was no history of bleeding or tumors elsewhere in the body. The patient denied history of alcohol consumption or tobacco/betel net-chewing. However, he admitted regular cigarette smoking. His dental and medical history were not remarkable. Intra-oral examination revealed an erythematous, ulcerated mass measuring 4 by 3 cm over the left side of the soft palate which crossed the midline and extended laterally to involve the left anterior pillar (Fig. 1). On palpation, the mass was non-tender and firm in consistency. The hard palate was spared and there was no clinical evidence of cervical lymphadeopathy.

Microscopic examination of the incisional biopsy showed infiltrating nests, cords and sheets of malignant cells separated by a prominent hyalinised stroma. The malignant cells were round to polygonal in shape with clear cytoplasm and centrally placed, mildly pleomorphic nuclei. Occasional mitotic figures were seen. Immunohistochemically staining the malignant cells showed they were positive for cytokeratin and negative for CD10, excluding metastatic renal cell carcinoma. Special stain with Periodic Acid-Schiff showed the cytoplasm was positive and sensitive to diastase treatment indicating glycogen. A pathological diagnosis of primary clear cell carcinoma was made. (Fig. 2) Computed tomography scanning of the head and neck demonstrated a heterogeneously enhancing mass measuring 3.5 by 3 cm in size which occupied the left side of the soft palate and encroached the lingual and left palatine tonsil inferiorly. Subsequent imaging studies (chest X-ray and renal ultrasonography) established a primary salivary origin based on the absence of detectable renal pathology. Wide surgical excision with adjuvant radiotherapy was planned, unfortunately the patient declined any treatment and defaulted subsequent follow up.

DISCUSSION

Clear cell tumors in the oral cavity constitute a heterogeneous group of lesions which may be odontogenic, metastatic or salivary gland in origin, the latter are usually malignant, including acinic cell carcinoma, mucoepidermoid carcinoma and epithelial myoepithelial carcinoma. HCCC is a new and rare low-grade salivary gland neoplasm which occurs in the

Table I: Differential diagnosis and staining patterns of clear cell tumors of the head and neck

Tumor type	PAS	PAS-D	Mucin	CK	EMA	p63	SMA	S100	CD10
• Hyalinizing clear cell carcinoma	+	-	-	+	+	+	-	-	-
• Mucoepidermoid carcinoma	+/-	-	+	+	n/a	n/a	-	-	-
• Epithelial myoepithelial carcinoma	-	-	-	+	+/-	n/a	+	+	-
• Acinic cell carcinoma	+	+	-	+	+	+	+	-	-
• Clear cell odontogenic carcinoma	n/a	n/a	n/a	+	+	n/a	n/a	+	-
• Renal cell carcinoma	+	-	-	+	+	n/a	-	+	+

PAS periodic acid- Schiff, PAS-D periodic acid- Schiff diastase resistance, CK cytokeratin, EMA epithelial membrane antigen, SMA smooth muscle actin, n/a not applicable, + positive, - negative.

This article was accepted: 1 February 2012
Corresponding Author: Saleh Khaled Aboud, UKMMC, ORL-HNS, Jalan Yaacob Latif, Bander Tun Razak, Cheras, Cheras, Selangor 56000, Malaysia
Email: talibaliraqi2002@yahoo.com

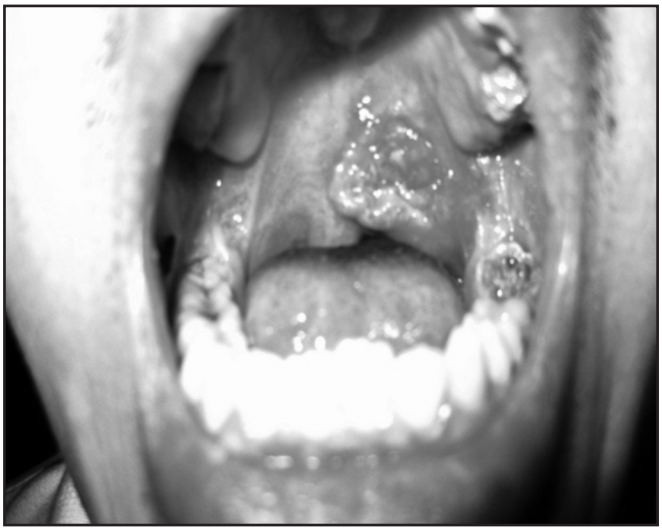

Fig. 1: Palatal mass at the time of presentation over the left soft palate which extending laterally to involve the left anterior pillar.

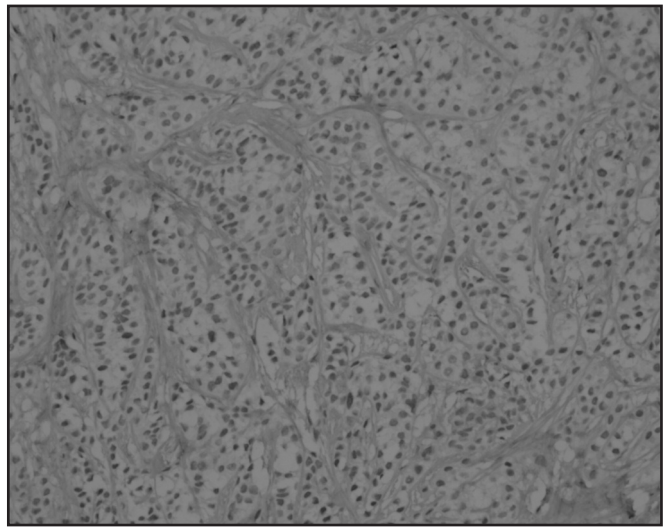

Fig. 2: Immunohistochemical study with CD10 shows the malignant cells are negative for CD10, excluding metastatic renal carcinoma. CD10, X 20.

intraoral minor salivary gland. It was first described as a distinct entity in 1994 by Milchgrub *et al.* in their series of 11 patients. Since then, the recognition and consequent reporting of this neoplasm has increased in the English literature. It occurs more commonly in the sixth and the seventh decades with a female predilection affected twice as often as male[1]. The common intraoral site includes the palate, followed by the lips and the buccal mucosa. The natural course is an indolent, painless, submucosal mass with limited metastatic potential. By definition, clear cell carcinoma contains a significant proportion of clear cells, but it does not fit to any recognized neoplastic entities. Microscopically, the tumor has infiltrative borders and the individual tumor cells are principally characterized by optically clear cytoplasm with well –defined borders and a centrally placed nucleus with minimal nuclear pleomorphism and a very low mitotic index with infiltrative borders. HCCC should be considered in the differential diagnosis of tumors with the histology marked by monomorphic glycogen rich clear cells arranged in cords, trabeculae, or clusters surrounded by a typically hyalinized stroma. Because of the characteristic hyaline stroma of the clear cell carcinoma, it is often termed HCCC, but this is not a constant feature[2]. As HCCC is an uncommon tumor and only occasionally reported in the literature, the diagnosis can be challenging. Immunohistochemical studies and special stains can be extremely helpful in distinguishing HCCC from other tumors with clear cell features. The tumor cells express epithelial markers such as cytokeratins and epithelial membrane antigen. The clear cells showed a positive PAS reaction. Myoepithelial antigens (S 100 Protein and smooth muscle actins) are not expressed in HCCC as the mucin stain. These findings are useful to rule out any other possible neoplasms that present with clear cell morphology.

Table I summarizes the immunohistochemical staining pattern of clear cell tumors in the HCCC differential diagnosis. Adverse biologic behavior of HCCC ranges from multiple recurrences to local nodal or distant metastasis. Perineural, perivascular invasion and metastases to local lymph nodes and distant metastases to the lung were reported in literatures. A high degree of vascularity and pronounced atypia in addition to the lack of prominent hyaline stroma is generally regarded as the hallmark of renal cell carcinoma. Furthermore, the lack of residual salivary gland structures and close approximation of lesional tissue with the overlying epithelium in the incisional biopsy warranted the consideration of renal cell carcinoma as one of the prime diagnosis. Being a tumor of low malignant potential, wide surgical excision is the treatment of choice with, or without pre/postoperative radiotherapy. The decision to include node dissection or radiotherapy is generally based on the presence of positive margins, high grade histology, invasion (vascular/neural), positive neck node and mitotic activity[3]. Options for reconstruction of the soft palate can be achieved by either basic hard palate prosthesis with extension into the oropharynx or microvascular radial forearm fasciocutaneous free-flap. Close follow up is important as the recurrences are known to occur even after several years following the primary treatment.

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