

Hyalinizing Clear Cell Carcinoma of Minor Salivary Gland: Case Report

Madhavan MANOHARAN¹
Nor Hayati OTHMAN¹
Abdul Rani SAMSUDIN²

Departments of ¹Pathology and ²Surgery, Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan, Malaysia

Hyalinizing clear cell carcinoma is a low-grade neoplasm of the minor salivary gland composed exclusively of epithelial cells and not myoepithelial cells. It predominantly affects the oral cavity of adult females. It is microscopically characterized by hyalinizing stroma and clear cells, which are typically positive for cytokeratin markers and negative for S 100 and smooth muscle actin (SMA). Cystic degeneration can also be present. Pathologists should be aware of this new entity so as not to misdiagnose otherwise. To our knowledge, this is the first case report of its kind from Malaysia.

Key Words: clear cell, carcinoma, minor salivary gland, hyalinization.

INTRODUCTION

Hyalinizing clear cell carcinoma (HCCC) is a recently described neoplasm predominantly affecting the oral cavity in adult females (1). The tumor cells are characteristically clear and the stroma have areas of hyalinization. These cells are positive for cytokeratin and negative for S100 protein and smooth muscle actin. This immunohistochemical staining differentiates it from other salivary gland tumors having a predominantly clear cell component and also indicates that HCCC is composed only of epithelial cells (1,2). It is considered to be a low-grade indolent neoplasm, because of rare recurrence and metastasis (3,4). Because of the lack of awareness, HCCC is often misdiagnosed as poorly differentiated carcinoma, squamous cell carcinoma, acinic cell carcinoma, mucoepidermoid carcinoma and epithelial-myoepithelial carcinoma.

We report a case of HCCC in a 40-year-old Malay woman with swelling in the floor of the mouth of 2-year duration. In addition to typical features of HCCC, this case also showed cystic degeneration, which was not described, in earlier reports.

CASE REPORT

A 40-year-old Malay housewife was referred from a state hospital for a swelling in the floor of the left

side of the mouth. It began as a pea-sized, painless swelling 2 years earlier and gradually increased to the present size of 5 x 3 cm. It was hard in consistency and had ulcerated the floor of the mouth causing pain for the past 2 weeks. The left submandibular lymph node was palpable and measured 1 cm in size. Her oral hygiene was good. No other mass was palpable. She was hypertensive, but other systemic examination was normal. An oral incision biopsy of the mass was reported as moderately differentiated squamous cell carcinoma. A second opinion sought from another referral institution agreed with that report.

At the Hospital Universiti Sains Malaysia, a left hemimandibulectomy along with inferior alveolar nerve, left submandibular and left jugular lymph node dissection was performed. Grossly (Figure 1), the tumor was solid, gray white and 4.5 x 2 cm in size. It had ulcerated the floor of the mouth. Microscopically, the tumor was composed of large, polygonal cells with abundant clear cytoplasm and distinct cell borders and few cells containing eosinophilic cytoplasm (Figure 2). However, these clear cells were negative for mucin and glycogen. The cells were arranged in islands and trabeculae with stroma showing areas of hyalinization (Figure 3). There was small cystic degeneration (Figure 4) and perineural infiltration (Figure 5). Mitosis was less than 1 per 10 HPF (high power field). Immunohistochemically, these cells were positive for cytokeratin while negative for SMA, S 100 protein, epi-



Figure 1. Bisected hemimandibulectomy specimen shows an infiltrative grey-white tumor in the floor of the mouth.

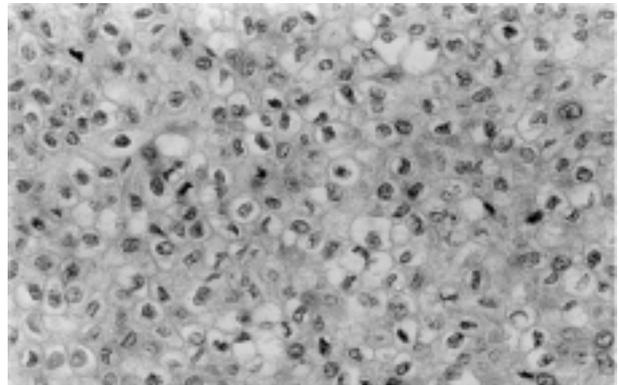


Figure 2. Tumor cells are predominantly polygonal with distinct cell border containing clear cytoplasm and round to oval nuclei (H&E; 400X).

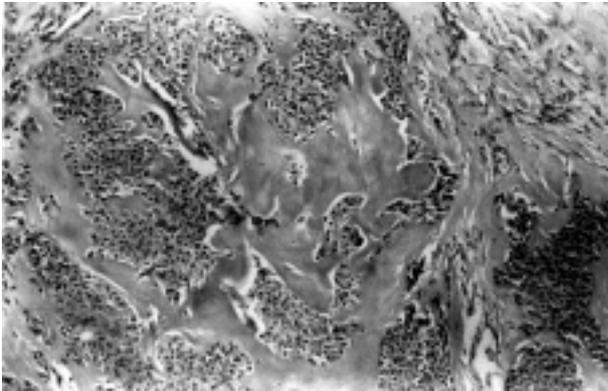


Figure 3. Tumor cells are arranged in irregular lobules with hyalinized stroma in between (H&E; 100X).



Figure 4. Tumor exhibits areas of cystic degeneration (H&E; 40X).

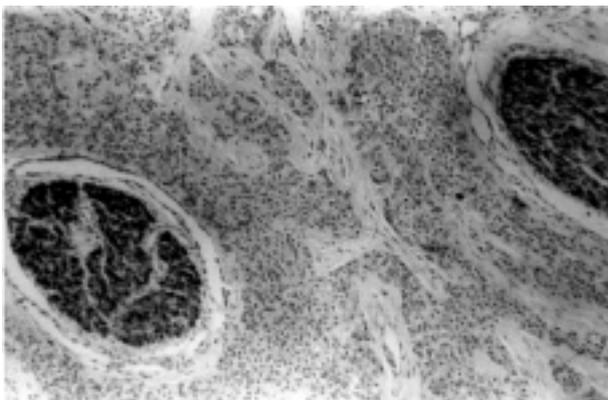


Figure 5. Nerve twigs (dark due to positive S 100 staining) are surrounded by tumor cells which are S 100 negative (S 100; 100X).

thelial membrane antigen (EMA) and carcinoembryonic antigen (CEA). A definite diagnosis of HCCC was made. The inferior alveolar nerve, submandibular and jugular lymph nodes were free of tumor. Review of the previous biopsy slides showed islands of polygonal tumor cells with distinct cell borders, containing clear cytoplasm. However, the stroma was scanty and did not show hyalinization.

No recurrence or metastasis developed during the 22 months of follow-up.

DISCUSSION

Clear cell occurs in several different tumors of the salivary gland, including benign tumors such as

oncocytoma, myoepithelioma and malignant tumors such as acinic cell carcinoma, mucoepidermoid carcinoma and myoepithelial-epithelial carcinoma. Another type of clear cell carcinoma of the minor salivary gland has been reported under various names (5). Almost all of those cases had about 2-cm swelling in the oral cavity and behaved as a low-grade neoplasm. The tumor cells were positive for cytokeratin markers and negative for S 100 and SMA. In 1994, Milchgrub et al. (1) studied eleven cases of similar type and proposed the term "hyalinizing clear cell carcinoma". This neoplasm was thought to be low-grade in nature and was proposed to arise from epithelial cells. Initially, Batsakis et al. (6) refuted its low-grade behavior and its epithelial origin. However, others (3,7) disagreed with him and HCCC has been accepted as a low-grade malignancy that arises purely from epithelial cells.

As in the present case, HCCC occurs commonly in the minor salivary gland of the oral cavity of older females and rarely in the parotid gland, larynx (1,8) and also in jaw bones (4). Microscopically, HCCC is characterized by trabeculae and islands of clear cells with hyalinized stroma. However, smaller cells with eosinophilic cytoplasm as well as areas of squamous metaplasia have also been reported (2,4). As clear cells are known to occur in many salivary gland tumors, demonstration of CK positivity and S 100 and SMA negativity would be mandatory to diagnose HCCC (1,2). Rarely were the tumor cells positive for carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA). This case was positive only for CK and negative for SMA, S 100, EMA and CEA. The clear cells are usually due to accumulation of glycogen and not mucin (1). Rarely, it may also be due to fixation artifacts (9), as in our case, which revealed neither glycogen nor mucin. Perineural invasion and no vascular invasion by tumor cells is frequently observed (1). Perineural invasion was also seen in our case. Unlike previous HCCC reports, we also observed cystic degeneration, but the significance of its presence was not yet clear.

Initial biopsy of the present case was reported as moderately differentiated squamous cell carcinoma by two independent pathologists. This is a regrettable but somewhat acceptable error, as HCCC is a recently described entity and the biopsy tissue might not have all the typical features. HCCC could also be misdiagnosed as poorly differentiated carcinoma, acinic cell carcinoma,

myoepithelial-epithelial carcinoma, squamous cell carcinoma and mucoepidermoid carcinoma (1). Though recurrence appears common due to the infiltrative margin, HCCC behaves as a low-grade neoplasm (3,4). Only occasional cases have presented metastasis (1). Our case did not recur or develop metastasis during the 22 months of follow-up. This low-grade neoplasm could be treated by a wide excision, though further case studies and long-term follow-up would be necessary to document it.

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RESUMO

Manoharan M, Othman NH, Samsudin AR. Carcinoma de células claras hialinizantes de glândula salivar menor. Relato de caso. *Braz Dent J* 2002;13(1):66-69.

O carcinoma de células claras hialinizantes é uma neoplasia de baixo grau que acomete glândulas salivares menores sendo composto exclusivamente de células epiteliais não envolvendo células mioepiteliais. Afeta predominantemente a cavidade oral de mulheres adultas. Microscopicamente caracteriza-se por proliferação de células claras epiteliais espessas positivamente (expressão positiva) para marcadores de citoqueratina sendo não espessas (negativas) para actina músculo liso (SMA) em um estroma "evolutivo" à hialinização. Degenerações císticas também podem estar presentes. Patologistas devem estar a par desta "nova" atualidade para não chegar ao diagnóstico incorreto. A nosso ver, esse é o primeiro relato de caso deste tipo de carcinoma na Malásia.

Unitermos: células claras, carcinoma, glândula salivar menor, hialinização.

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