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Clear cell-rich salivary duct carcinoma involving the palate

Carcinoma do ducto salivar rico em células claras envolvendo o palato

Fernanda A. Felix[1]; Carla Francielly Lima[1]; Lucas A. M. Santana[1]; Sílvia F. Sousa[2]; Cleverson Luciano Trento[1]; Wilton M. Takeshita[1]

1. Universidade Federal de Sergipe, Sergipe, Aracaju, Brazil. 2. Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais Brazil.

ABSTRACT

Salivary duct carcinoma (SDC) is a rare and aggressive neoplasm arising from salivary glands. SDC occurs most frequently in major salivary glands, with isolated cases arising from the minor salivary glands. The occurrence of clear cells in salivary gland tumors is uncommon and is rarer in SDC cases. We report the case of a 51-year-old male diagnosed with a clear cell variant of SDC in the minor salivary gland, involving the left hard palate. Immunohistochemical analysis revealed positivity for HER2/neu and GATA-3. The patient was submitted to radical surgical excision, neck dissection, and radiotherapy. Unfortunately, he died 14 months after the cancer diagnosis.

Key words: salivary duct carcinoma; minor salivary gland; immunohistochemistry.

RESUMO

O carcinoma do ducto salivar (CDS) é um tumor raro e agressivo que se origina nas glândulas salivares. O CDS ocorre mais frequentemente nas glândulas salivares maiores, porém, há casos isolados de acometimento nas glândulas salivares menores. A ocorrência de células claras em tumores de glândulas salivares é incomum, sendo ainda mais rara nos casos de CDS. Relatamos o caso de um homem de 51 anos de idade que foi diagnosticado com a variante de células claras de CDS em glândula salivar menor, envolvendo o palato duro do lado esquerdo. A análise imuno-histoquímica revelou positividade para HER2/neu, GATA-3. O paciente foi submetido a excisão cirúrgica radical, esvaziamento cervical e radioterapia. Entretanto, ele faleceu 14 meses após o diagnóstico do câncer.

Unitermos: *carcinoma do ducto salivar; glândula salivar menor; imuno-histoquímica.*

RESUMEN

El carcinoma ductal de las glándulas salivales (CDS) es un tumor raro y agresivo que surge de las glándulas salivales. El CDS ocurre con mayor frecuencia en las glándulas salivales mayores, sin embargo, existen casos aislados de afectación en las glándulas salivales menores. La aparición de células claras en los tumores de las glándulas salivales es infrecuente y más rara en los casos de CDS. Presentamos el caso de un varón de 51 años al que se le diagnosticó la variante de células claras del CDS en la glándula salival menor, que afecta al paladar duro izquierdo. El análisis inmunohistoquímica reveló positividad para HER2/neu y GATA-3. El paciente fue sometido a escisión local quirúrgica radical, disección del cuello y la radioterapia. Desafortunadamente, murió 14 meses después del diagnóstico de cáncer.

Palabras clave: *carcinoma ductal de las glándulas salivales; glándula salival menor; inmunohistoquímica.*

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INTRODUCTION

Salivary duct carcinoma (SDC) is a rare and aggressive neoplasm of the salivary glands, whose group of lesions exhibit a wide variety of morphological forms[1]. It was first recognized by Kleinsasser *et al*.[2] in 1968, as a group of ductal lesions, presenting an invasive component and central necrosis, similar to ductal breast carcinoma. Some authors believe that SDC originates from the excretory duct reserve cells of the salivary glands or may be the result of a malignant transformation of the ductal cells in pleomorphic adenoma[3, 4]. Genetic alterations in SDC show mutations in ERBB2 (also known as HER2/neu), TP53, HRAS, PIK3CA, and androgen receptor (AR)[5].

It is more common in men aged between 50 and 70 years. SDC is responsible for 2% of salivary gland cancers, and is observed mainly in the parotid glands (71.8%), followed by the submandibular glands (14.5%), and minor salivary glands (8.3%)[6]. SDC presents aggressive behavior with rapid progression and invasion of adjacent tissues[7]. In general, SDC appears as tumors smaller than 4 cm and involve regional lymph nodes, which are additional risk factors for poor prognosis[6, 7].

Clear cells may be found in several salivary and non-salivary neoplasms of the head and neck, including metastatic tumors. In addition, the occurrence of clear cells in salivary gland tumors is uncommon, representing less than 1% of cases, and even rarer in SDC[8, 9]. SDC treatment involves radical surgical excision, neck dissection, radiotherapy and, sometimes, adjuvant chemotherapy[7, 10, 11]. This type of tumor exhibits a high recurrence rate and risk for distant metastasis, especially, when diagnosed in late-stage[6]. Nevertheless, the 5-year survival rate of treated SDC patients ranges between 43%-64%[6, 12]. Here, we present an uncommon variant case of clear cell SDC arising from the minor salivary gland of the palate, and we address its clinical and pathological features.

CASE REPORT

A 51-year-old male patient sought our oral diagnosis service to evaluate a tumor mass on the left hard palate. Extraoral examination revealed facial asymmetry, enlarged and fixed regional lymph nodes. During the intraoral examination, a lesion was observed in the hard palate region, extending to the buccal space and vestibular fundus of upper left premolar and molar. Clinically, the lesion was a tumor mass with irregular surface and shape, exophytic and diffuse borders, erythematous color, flaccid consistency, painless on palpation, measuring in its largest diameter 2.4 cm. Around the lesion, we noticed poor positioning and mobility of adjacent teeth (**Figure 1**). Previous medical history revealed no abnormalities.

Panoramic radiograph showed an ill-defined radiolucent lesion, with a "ground glass" aspect covering the left maxillary sinus region. In addition, root resorption in the adjacent teeth was also observed. Computed tomography (CT) revealed an infiltrative heterogeneous solid mass involving the palate and the left maxillary sinus, extending to the piriform cavity and the left orbital floor (**Figure 2**). In fact, we also observed a low-attenuation area, suggestive of cribriform necrosis. As consequence, the provisional diagnosis of malignant neoplasm was raised, and an incisional biopsy was performed on the vestibular fundus region of the left premolars.

Histopathological analysis of the fragment revealed multiple ductal structures of tumor cells with lumens containing several degrees of necrotic tissue (comedonecrosis) (**Figure 3A/B**). This component was arranged in a cribriform pattern exhibiting fenestrations that resemble a Roman bridge. Cytological features exhibited cells with polygonal or elongated morphology, well-defined borders, nuclei of different sizes and shapes, broad and clear cytoplasm, sometimes with fine granular appearance, which is compatible with the moderate subtype of clear cells (**Figure 3C**). Also, it was possible to observe prominent nucleoli, dispersed chromatin, binucleated cells, and mitosis figures (**Figure 3D**). Immunohistochemical staining revealed tumor cells positive for HER2/neu and GATA-3 (**Figure 4**). Based on histopathological and immunohistochemical findings, the diagnosis was SDC.

The patient underwent radical surgical excision, neck dissection, and adjuvant radiotherapy. Unfortunately, he died after 14 months of follow-up from underlying condition complications.

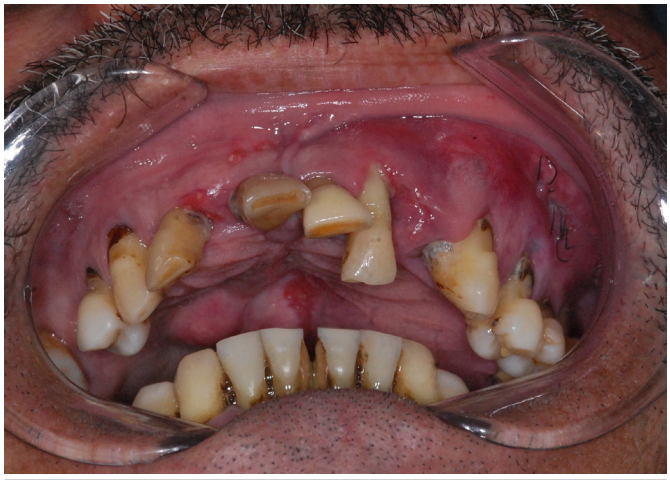

FIGURE 1 – *Intraoral evaluation showing swelling on the hard palate, left side, erythematous mucosa, and poorly positioned teeth*

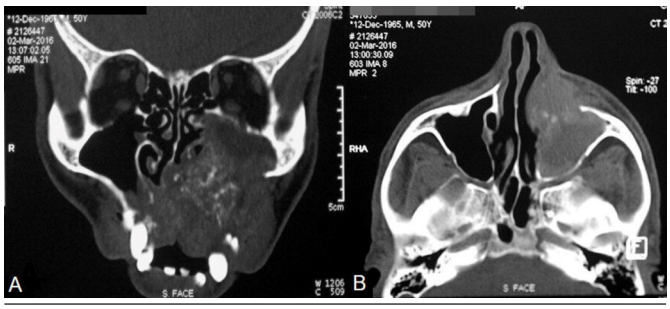

FIGURE 2 – *CT showing the extent of the lesion*

A) coronal section showing lesion invasion to the left maxillary sinus, nasal cavity, and orbital floor region; B) axial section showing the extension of the lesion to the left maxillary sinus floor and nasal septum deviation.

CT: computed tomography.

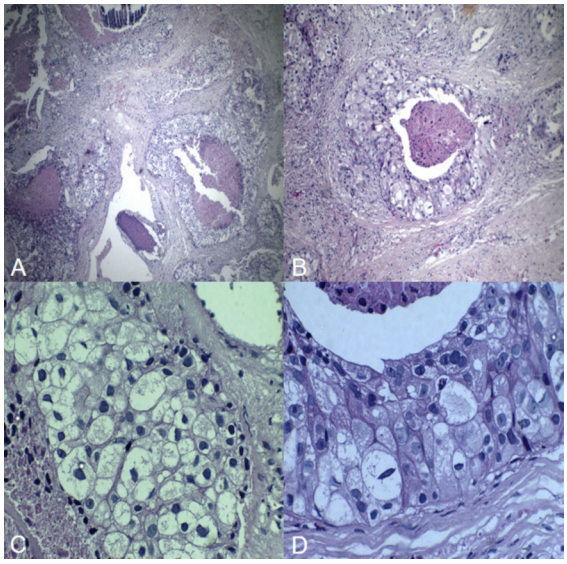

FIGURE 3 – *Histopathological features*

A and B) intraductal component of SDC with comedonecrosis (HE), scale 40× and 100×; C and D) ductal cells with granular and clear cytoplasm, nuclei of different sizes and shapes, prominent nucleoli, and dispersed chromatin (HE, scale 400×).

SDC: salivary duct carcinoma; HE: hematoxylin and eosin.

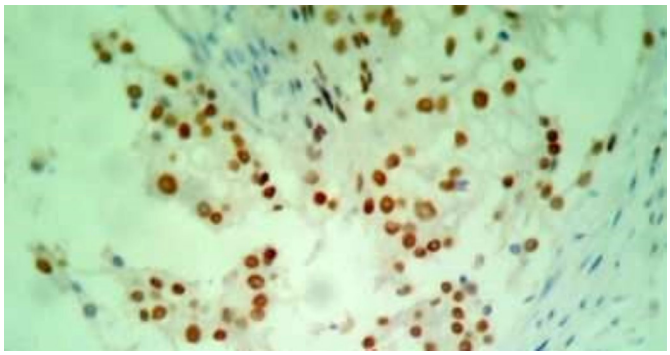

FIGURE 4 – *Result of immunohistochemistry*

GATA-3 immunohistochemistry was positive for salivary duct carcinoma, showing strong staining.

DISCUSSION

SDC is a high-grade adenocarcinoma of the ductal epithelium of salivary glands with high recurrence rate, distant metastasis, and poor clinical outcome[6]. The etiology of SDC remains unknown, although some studies have identified common genomic alterations in those tumors[5, 11]. The World Health Organization (WHO) has classified SDC into the salivary gland tumors, as high and low-grade SDC, showing a variety of growth patterns[1, 13].

Although the highest rates of SDC are recorded in major salivary glands, some cases have been reported in minor salivary glands. In the study by Gao *et al*. (2016)[14], from the 2536 cases of malignant salivary gland tumors evaluated, 43 were SDC, representing approximately 1.7% of all malignant neoplasms in this group. From these, only nine were registered in minor salivary gland. In contrast to the study by Otsuka *et al*. (2016)[7], this rate is even lower, out of 141 SDC cases, only three cases arose from minor salivary glands. When analyzing only the cases registered in minor salivary glands, about one-third of these cases affect the palate, corroborating the location of the present case[15].

Clinical features of SDC shown that men are more affected than women, with an incidence between the fifth and seventh decades of life, initially expressing as a painless, no-ulcerated, rapidly growing tumor mass[7, 12]. Tumor size is less than 4 cm in 60.3% of cases[7]. In imaging studies, SDC is shown as a heterogeneous, solid mass, with ill-defined border, invading adjacent tissue. Similarly, central low-attenuation is suggestive of cribriform necrosis, which may be useful in the differential diagnosis of other malignant salivary gland tumors[16]. For comparison, SDC diagnosed on the palate may extend to the maxillary sinus, as described in the present case[17].

Usually, SDC exhibits high-grade histology similar to invasive ductal carcinoma of the breast, frequently accompanied by pleomorphic cells that form aggregates resembling distended ducts and solid nests with a cribriform pattern, and comedonecrosis, a type of necrosis characterized by luminal inflammation with devitalized cells[18, 19]. Besides, these cells may contain cytological atypia, vesicular chromatin, prominent nucleoli, mitotic figures and, sometimes, clear cytoplasm[13]. Although rare (1%-2% of cases), the occurrence of clear cells has been reported in malignant and benign salivary gland tumors, such as mucoepidermoid carcinoma (MEC), acinic cell adenocarcinoma, and adenoid cystic carcinomas[8, 9, 20]. In fact, this cell variant is even rarer in SDC cases, whose significance is still under investigation. In this regard, it is believed that the clear cell subtype changes in a tumor may reflect clonal evolution, which is a consequence of hydropic degeneration

of organelles or due to the accumulation of substances in the cytoplasm[8, 9]. Due to the features mentioned above, differential diagnosis of SDC must be made with metastatic infiltrating ductal carcinoma of the breast and high-grade MEC[21].

Although SDC diagnosis is commonly established through hematoxilin and eosin (HE) staining, immunohistochemical evaluation has an important therapeutic function. Immunohistochemical analysis shows that positive expressions of ck-7, AR, and HER 2/neu are usually reported in SDC, with overexpression of HER2/neu associated with poor outcome[12, 22]. In addition, Schwartz *et al*. (2013)[23] highlight the importance of GATA-3 as a novel biomarker for the differential diagnosis between salivary gland tumor and metastatic breast cancer, in special for SDC diagnosis. In the presented case, the tumor cell immunopositivity pattern was compatible with SDC, confirming the presence of primary salivary gland neoplasm and ruling out the possibility of non-salivary neoplasms.

SDC treatment includes as options such as surgery combined with radiotherapy, radiotherapy alone, chemotherapy, and regional dissection, depending on the overall stage, lymph node involvement, and patient systemic condition[6, 7, 10-12]. In case of local lymph node metastasis, or local recurrence, adjuvant therapy should be considered. Survival rates are variable, and some features are associated with a negative prognosis, such as age, tumor size, anatomical location, and tumor grade[6, 7, 12]. In our case, the overall condition and therapeutic approach were insufficient to control the disease, and the patient died after 14 months due to disease complications.

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CORRESPONDING AUTHOR

Lucas Alves da Mota Santana ID 0000-0002-8261-1504
e-mail: lucassantana.pat@gmail.com