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CASE REPORT

Parotid matastasis of clear-cell renal cell carcinoma (ccRCC): a case report

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Abstract

Introduction: Malignant neoplasm of the mouth is a very common disease, being the sixth most common cancer location worldwide. **Objective**: This study was conducted with the aim of evaluating the applicability and the relationship between cell damage intensity and Oral cavity squamous cell carcinoma (OCSCC) clinical stages. **Methods**: A total of 44 individuals, 24 oral cancer patients and 20 healthy volunteers participated in this study. The exfoliated cells from the oral cavity were collected using a wooden spatula. All samples were analyzed by comet assay, micronucleus assay and cell death assay. **Results**: Our results indicate that the diagnosis of OCSCC increases the frequency of genotoxic damage (comet assay – 3.21x; micronucleus assay – 3.93x). However, it was not possible to establish a correlation between frequency of DNA damage and disease staging. The cell death assay was not effective for the proposed biomonitoring. Given these findings, we consider the comet and micronucleus assays to be adequate for biomonitoring DNA damage. **Conclusion**: With the current design, we could not demonstrate the applicability of these assays to correlate the intensity of DNA/cell damage and the clinical stages of OCSCC. Nevertheless, further studies need to be performed to enhance sample size and increase the statistical power of our findings

Keywords: cancer; parotid; metastasis; otorhinolaryngology; kidney.

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Introduction

Malignant neoplasms of the parotid gland are relatively uncommon, accounting for 3-6% of all head and neck (H&N) cancers and only 0.3% of all cancers[1]. Metastatic spread to the parotid is also uncommon, and is usually associated with primary malignancies of the skin (melanoma or squamous cell carcinoma)[2,3]. Metastasis occurs in only 1-4% of all salivary gland tumors, and the parotid is the most affected[4]. Approximately 0.1% of all salivary gland metastatic neoplasms originate from renal malignancies[5]. Parotid neoplasm is diagnosed from a thorough clinical history and physical examination of the patient. Imaging tests, particularly ultrasound (US) and computed tomography (CT) scans, are not essential and can be performed in selected cases to plan treatment. Fine-needle aspiration biopsy (FNAB) is

another diagnostic modality that can be utilized to determine whether the tumor is benign or malignant[6].

Metastatic tumors to the H&N region seldom present primary malignancies located below the clavicle. The most common primary neoplasms associated with parotid metastasis are melanoma and squamous cell carcinoma of the head and neck[3], and less than 3% of them spread from the kidneys[4]. Although rarely presented, renal cell carcinoma (RCC) is a primary tumor that can harbor potential metastatic spread to the parotid gland[1,3].

RCC is the seventh most common histological type of cancer in the Western world, with male predominance and peak incidence after the 5th decade of life. The classic triad of clinical presentation includes hematuria, pain, and abdominal mass. Several histological subtypes of RCC have been described, including the clear cell type (ccRCC), which comprises 70-75% of all RCCs[7].

Metastasis to the parotid probably occurs via the hematogenous route, since the tumor is highly vascular and associated with multiple arteriovenous shunts, as well as considering that the kidneys together receive roughly 25% of the cardiac output per minute[3].

In order of frequency, the most common sites for RCC metastasis are the lung, bone, liver, brain and skin, whereas spread to the H&N region is rare (8-14%), and when it occurs, the thyroid is the most affected organ[2]. RCC metastasis to the H&N region has already been identified in the thyroid and salivary glands, base of skull, paranasal sinuses, pharynx, tonsils, tongue and skin, but very rarely in the parotid[8].

Case report

A 69-year-old man, retired, from the municipality of Lucélia, state of Sao Paulo, Brazil, was assisted at a private clinic on 19 August 2016 with a history of a nodule in the right parotid region for the past three months. The patient also complained of cacosmia and denied pain, paresis, otalgia, chronic diseases, and drug allergy. On 3 November 2008, the patient underwent a left nephrectomy for ccRCC. The patient had been a smoker for 15 years and had stopped smoking two years before then (2006). His alcoholic consumption included a glass of wine a day. On physical examination, there were a parotid nodule and an axillary nodule, both on the right side.

The patient underwent a FNAB of the right parotid on 16 September 2016, with suspected malignancy. At FNAB, there were no cytological elements that allowed a definitive conclusion; however, the main differential diagnosis was between adenoma and carcinoma. On 9 December 2016, an excisional biopsy of the right axillary lymph node was performed, and sebaceous adenoma was diagnosed. On 13 January 2017, the patient underwent total parotidectomy and the results revealed a clear-cell tumor and parotid tissue with preserved histological appearance, as shown in Figures 1 and 2. On 31 January 2017, immunohistochemical staining evidenced a clear-cell carcinoma of a very likely renal primary site, as shown in Figures 3 and 4. Immunohistochemistry (IHC) revealed positive staining for epithelial membrane antigen and focal positive staining for low molecular weight vimentin and cytokeratin (35 BH 11), and

negative staining for CK-7, CK-20, smooth muscle actin and high molecular weight cytokeratin (34 BE 12), as shown in Chart 1.

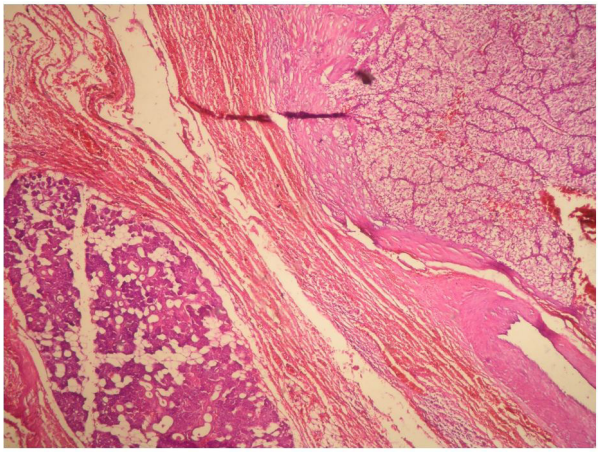

Figure 1. Histological section (40x) containing clear-cell carcinoma and parotid tissue.

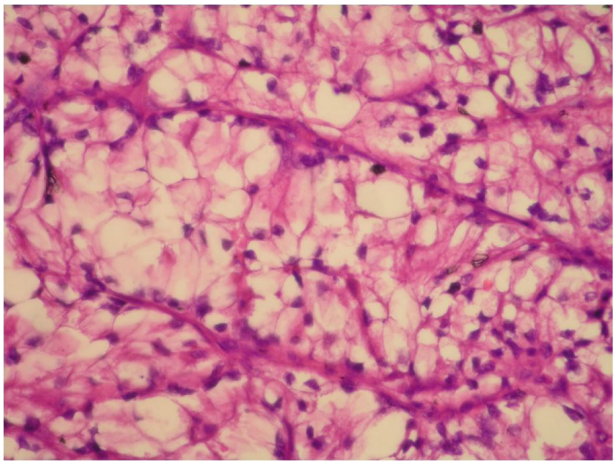

Figure 2. Histological section (400x) showing clear-cell carcinoma obtained from the parotid gland.

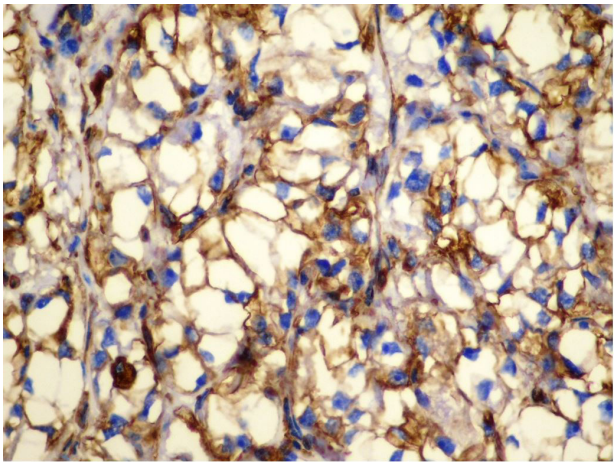

Figure 3. Immunohistochemical staining for vimentin on histological section (400x) obtained from the parotid gland.

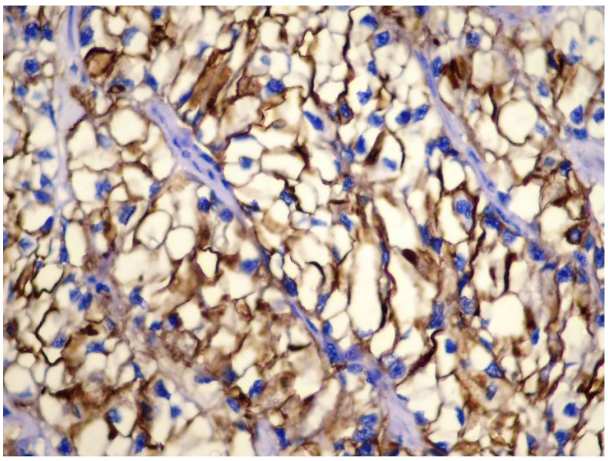

Figure 4. Immunohistochemical staining for 35 BH 11 on histological section (400x) obtained from the parotid gland.

Chart 1. Diagnostic immunohistochemical panel of histological section of the parotid gland obtained from the study patient showing probable clear-cell renal cell carcinoma (ccRCC).

Marker	Control	Result
Vimentin	Internal	Positive
35 BH 11	External	Focal positive
CK 7	External	Negative
CK 20	External	Negative
34 BE 12	External	Negative
EMA	External	Positive
LA4	External	Negative

At IHC, the neoplasm consisted predominantly of clear cells. Thus, combining the histological and immunohistochemical aspects, the most likely suggested diagnosis was ccRCC. On 17 October 2017, the patient presented satisfactory clinical evolution with no signs of neoplasm locoregional recurrence.

Discussion

Malignant neoplasms of the parotid gland have low prevalence and are mostly associated with primary malignancies. However, the likelihood of metastasis should be considered in cases of masses located in the parotid[1].

RCC has a 3:2 male predominance and a peak incidence in the 6th and 7th decades of life. Although risk factors such as smoking, hypertension, and obesity have been identified, most cases are sporadic. RCC has a classic triad, but over 50% of the cases are diagnosed incidentally during abdominal imaging tests[9].

RCC is not an important differential diagnosis in parotid masses, but it should be considered in cases of patients with previous history the disease. FNAB

is the method of choice for initial investigation, but attention should be paid to its high false negative rate.

When a clear-cell tumor is identified, the final diagnosis can only be obtained through IHC[8]. Positive immunohistochemical staining for cytokeratin is important to exclude melanoma as the primary malignancy, since most parotid metastases originate from this neoplasm. Negative immunohistochemical staining for CK-7 assists in excluding the thyroid origin of the carcinoma. Classically, RCC presents positive immunohistochemical staining for vimentin and cytokeratin, and negative staining for CK-7 and CK-20. All of these markers were present in this case report[5].

In an analysis of 26 cases of RCC metastatic to the parotid gland, the parotid lesion was the first sign of renal malignancy in 14 (54%) patients and was located in the other 12 (46%) patients only after primary treatment of the neoplasm, which can occur in periods ranging from months to years. The longest interval observed between nephrectomy and parotid metastasis was 10 years, with only one report in the literature[2]. In the present case, the patient had a history of nephrectomy resulting from RCC, which was relevant for considering renal metastasis. After investigation, FNAB and IHC were performed and showed the renal origin of the clear-cell carcinoma. No facial nerve palsy was observed, which is consistent with the literature[8].

The treatment of choice for primary RCC ranges from partial to radical nephrectomy, or even cytoreductive therapy, whereas parotid metastasis is ideally managed by local excision with disease-free margins with facial nerve preservation, when possible[8].

Conslusion

This is a rare case of RCC with unilateral metastasis to the right parotid gland, with very few reports in the literature to date. In addition, a long interval was observed between nephrectomy and parotid metastasis (eight years). In cases of parotid masses, the diagnostic hypothesis of RCC metastasis is remote due to its very low incidence. However, in patients with a clinical history of RCC, it is important to consider this diagnosis and conduct a systemic investigation, such as the one performed in this case report.

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