

# Atypical Location of Oral Metastasis as the First Manifestation of Renal Carcinoma. Case Report

## Localización Atípica de Metastasis Oral como Primera Manifestación de Carcinoma Renal. Reporte de Caso

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**ABSTRACT:** Oral cavity metastatic tumors derived from primary tumors from other corporal regions are rare, representing barely 1 % of all malignant tumors. Differential diagnosis of these lesions is challenging due to the wide spectrum of lesions with similar clinical presentation and especially when the presence of a primary tumor goes undetected. We present the case of a 55-year-old male with a painless tumor in the anterior maxillary region, vestibular gingiva and palate, with a 2-month evolution. Anatomopathological diagnosis was malignant clear cell tumor, highly suggestive of clear cell renal carcinoma metastasis, and the oral lesion constituted the first sign of illness.

**KEY WORDS:** oral metastasis, renal cell carcinoma, oral mucosa, maxilla.

## INTRODUCTION

Metastatic lesions derived from primary tumors in other parts of the body are rare in the oral cavity, representing only 1 % of all malignant intraoral neoplasias, where they can localize both in soft and hard tissue (van der Waal *et al.*, 2003; Will *et al.*, 2008; Praderio *et al.*, 2017). The most frequent primary tumor location that metastasizes to the oral cavity is lung (21.1 %), followed by liver (12.3 %), kidney and breast (10.5 %) and colorectal (8.8 %) (Liu *et al.*, 2018). However, this location varies according to sex, with the highest frequencies in males corresponding to lung, followed by kidney and liver, and metastatic sites are mostly located in soft tissue (Oliver-Puigdomènech *et al.*, 2021). In general, the first signs of concern for underlying malignant neoplasias are pain, rapid volume increase, dental mobility or displacement of anatomical

structures, paresthesia and pathological fractures (Hirshberg *et al.*, 2014).

In this report, we present a case of metastasis in the oral cavity derived from a clear cell renal carcinoma, which constituted the first and only manifestation of an underlying malignant process.

## CASE REPORT

On November 2nd, 2017, a 55-year-old male patient, without morbid or surgical background, allergies, nor alcohol or tobacco use, was referred from the Emergency Service of the Barros Luco Trudeau

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Hospital (HBLT), Santiago, Chile, to the Maxillofacial Surgery Service of the same hospital. The reason for consult was the presence of a volume increase detected in the vestibular gingiva and anterior maxillar palate. The patient declared 2 months of evolution, with no pain but with a burning sensation when ingesting citrus and spicy foods. The patient also reported a month-and-a-half prior excision of the lesion, which relapsed shortly after. The excised tissue was not submitted for histopathological studies.

Physical segmentary head and neck examination revealed no palpable lymphadenopathies and the intraoral examination detected a gingival tumor associated to the superior central incisors from tooth 1.3 to tooth 2.1. This lesion was asymptomatic, with firm and fibrous consistency, well-defined margins, about 3 cm in length, reddish-colored, protruding from the upper lip and extending to the palate with similar characteristics (Fig. 1). The adjacent teeth presented plural fixed prosthetic restauration. The retroalveolar X-ray showed dental rhizolysis of teeth 1.1 and 1.2, in addition to periradicular bone loss between teeth 1.3 and 2.1 (Fig. 2).



Fig. 1. A mass associated to the upper central incisors from teeth 1.3 to 2.1, approximately 3 cm in diameter, reddish and protruding from the upper lip.

On November 7th, 2017, an excision biopsy was performed under the diagnostic hypothesis of giant cell peripheral granuloma. A sample of approximately 3 x 4 cm was obtained from vestibular gingival mucosa and another sample of about 1 x 0.5 cm was excised

from palate gingival mucosa. It is important to note that during the procedure, there was profuse bleeding of the area, which had to be contained using local haemostatic measures.

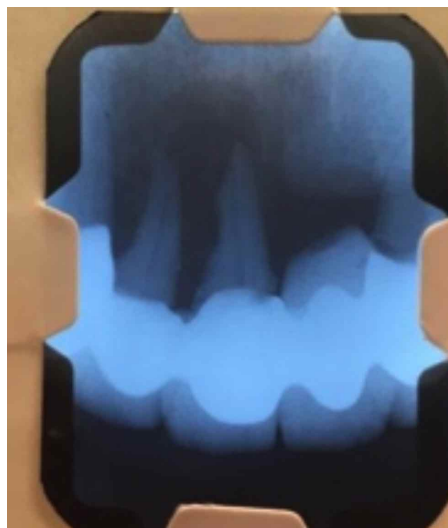


Fig. 2. Retroalveolar radiography showing rhizolysis in teeth 1.1 and 1.2, in addition to periradicular bone loss between teeth 1.3 and 2.1.

Histopathological analysis with common Hematoxylin/Eosin stain showed distended and partially ulcerated oral mucosa, with extensive proliferation of cells displaying a clear cytoplasm, round hyperchromatic nuclei and some signs of atypia in the connective tissue. These cells were found distributed along cords and solid nests with a tendency to form alveolar patterns separated by thin partitions of connective tissue with marked vascular proliferation. Neoplastic cells were observed up to the surgical margin (Figs. 3 A and B). The sample was positive for PAS (Periodic Acid-Schiff) stain and sensitive to PAS diastase. Immunohistochemical analysis was positive for anti-keratin (monoclonal antibody clone AE1/AE3), CD10 antigen and PAX-8 protein (Figs. 3C-E) but negative for cytokeratins CK7 and CK20, while Ki67 marker was positive in 30-40 % of cells (Fig. 3F). The results of these immunohistochemical analyses correlate with a renal clear cell malignant neoplasia pattern and discard other types of malignant clear cell neoplasias which could derive from maxillofacial tissues.

The anatomopathological diagnosis was malignant tumor of clear cells highly suggestive of renal clear cell carcinoma metastasis. Staging was performed by computerized tomography of head, neck, thorax, abdomen and pelvis, with contrast, in addition

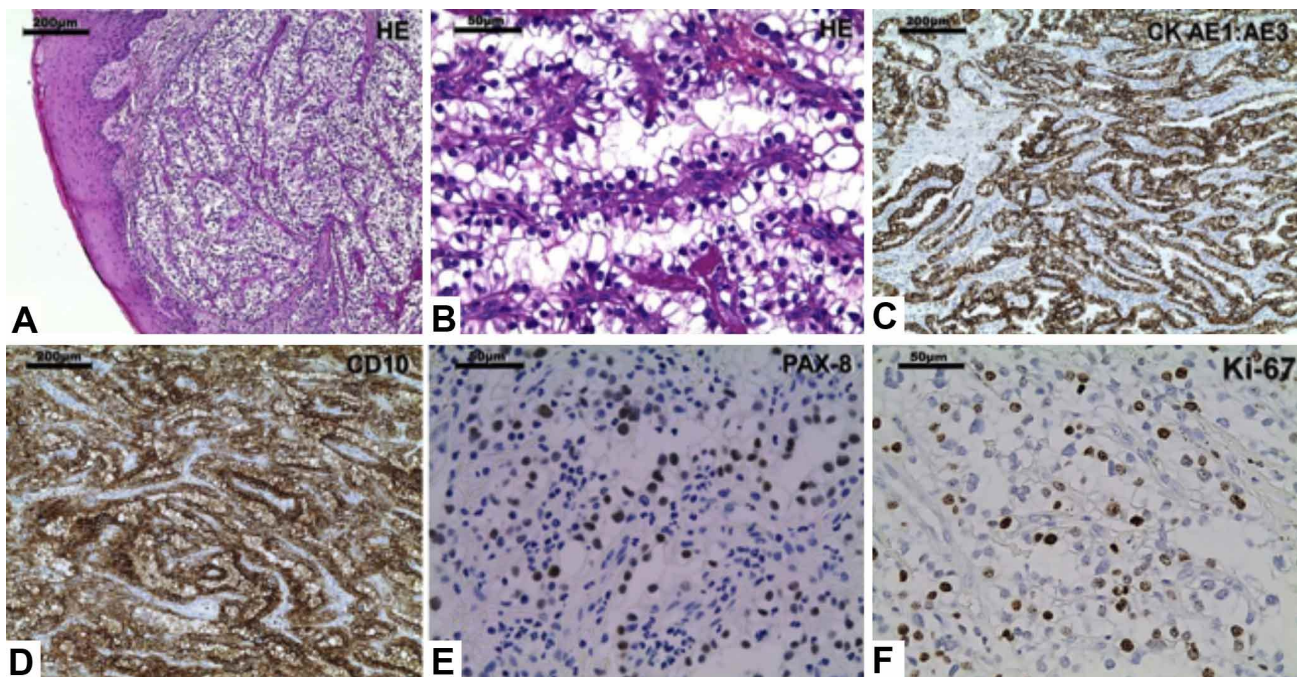


Fig. 3. Representative images from metastatic clear cell renal carcinoma. (A-B) Hematoxylin and eosin staining (HE). (C) IHC labeling with monoclonal anti-cytokeratin antibody (clone AE1/AE3). (D) Low magnification showing CD10. High magnification of PAX-8 (E) and KI-67 labeling (F).

to blood analyses. The results of these analysis identified a tumor on the right kidney associated with lung and oral cavity metastasis. According to the results, the patient was classified as poor risk IMDC (International Metastatic RCC Database Consortium) and thus cytoreductive nephrectomy was contraindicated. The patient rejected treatment.

From the date of diagnosis to the dental examination, the patient had been derived to ophthalmology due to diagnostic suspicion of melanoma in the right eye and the patient's wife reported a 13-kg weight loss. During 2021, this condition progressed with ocular metastasis in addition to multiple bone metastases in hips, femurs and pelvis. The oncological committee rejected systemic treatment and derived the patient to palliative care, since the patient was ranking 4 on the ECOG (Eastern Cooperative Oncology Group) scale.

## DISCUSSION

Renal cell carcinoma is the third most frequent infraclavicular neoplasia that metastasizes to the head and neck area (Will *et al.*, 2008; Liu *et al.*, 2018; Oliver-

Puigdomènech *et al.*, 2021). Metastasis occurs when highly aggressive malignant neoplastic cells spread from the primary lesion through lymph or blood vessels to spawn the growth of secondary tumors at distant sites (Liu *et al.*, 2018). These dissemination patterns are complex and the distribution of metastatic nodules is not random. In this context, a study reported that different metastatic dissemination patterns are related to the clonal structure of the primary tumor; rapidly-progressing metastasis is seeded from primary tumors with monoclonal structure, while slow-progressing metastasis derives from highly heterogeneous primary tumors (Turajlic *et al.*, 2018).

In contrast to the case we report here, oral metastases derived from distant tumors most regularly occur in patients over the age of 60 and, only in about 20 % of the cases, are diagnosed before a primary tumor is detected (van der Waal *et al.*, 2003; Hirshberg *et al.*, 2014). The most frequent locations of oral cavity metastasis are, in descending order, the molar mandibular area, the premolar area and the mandibular branch-angle, followed by attached gingiva and tongue (Ríos *et al.*, 2010; Hirshberg *et al.*, 2014; Guimarães *et al.*, 2016; Liu *et al.*, 2018). Soft tissue lesions usually occur as fast-growing exophytic masses similar in appearance to telangiectatic granulomas with clinical

presentations ranging from asymptomatic lesions to haemorrhagic and/or purulent lesions, frequently eliciting functional impotence (Ríos *et al.*, 2010; Liu *et al.*, 2018).

Differential diagnosis of these lesions is challenging due to the wide range of lesions with similar clinical presentation and presumption of a clear cell renal carcinoma metastasis is highly unlikely without prior detection of a primary tumor. The clinical appearance in this case compelled us to consider, as main differential diagnoses, giant cell granuloma, haemangioma and pyogenic granuloma. Therefore, a biopsy was essential for reaching a definite diagnosis (Maestre-Rodríguez *et al.*, 2009; Ali & Mohamed, 2016). It is important to highlight the great angiogenic capacity of renal cancer, during both its development and progression. These tumors overexpress pro-angiogenic factors - such as the vascular endothelial growth factor - and anti-angiogenic factors that induce structural and functional alterations in blood vessels, resulting in abnormal blood flow which can hinder resection (Mennitto *et al.*, 2020). In this case, excisional biopsy of the lesion was hampered by profuse bleeding which could be explained by the angiogenic potential of this cancer.

Prognosis of metastatic renal carcinomas relies upon TNM (tumor, lymph node and metastasis staging system) stage, tumor size and the presence of regional foci. Five-year survival rate is 49 % for all renal cell cancer types. For single metastasis and oligometastasis cases, treatment consists of radical nephrectomy complemented with systemic adjuvant therapy or immunotherapy, while generalized metastasis is treated with immunotherapies associated to targeted systemic therapies (Ljungberg *et al.*, 2022). In the present case, bone and eye metastases were identified at stage IV, being the latter very rare when originating from a renal carcinoma (Parra-Rodríguez *et al.*, 2015). Due to the multiple metastases, the patient was not submitted to surgical resection, and was given only palliative care.

## CONCLUSION

In this case report we present a metastatic lesion of renal clear cells in the oral mucosa, corresponding to an extremely infrequent lesion, with an unspecific clinical manifestation that can mimic reactive benign lesions. Therefore, this type of lesion presents an

important diagnostic challenge and should thus be considered during differential diagnosis. It is imperative to perform extensive histological studies in order to obtain an accurate definite diagnosis and to design a suitable treatment, due to the fact that a lesion such as this could constitute the first manifestation of an undiagnosed cancer.

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**RIQUELME, M. V.; DE LA FUENTE, M. E.; VERGARA, G. V.; SABELLE, H. N.; ESPINOZA, S. I.; BORGNA, C. V.** Localización atípica de metástasis bucal como primera manifestación de carcinoma renal. Reporte de un caso. *Int. J. Odontostomat.*, 17(3):288-292, 2023.

**RESUMEN:** Los tumores metastásicos de cavidad oral derivados de tumores primarios de otras regiones corporales son raros, representando apenas el 1 % de todos los tumores malignos. El diagnóstico diferencial de estas lesiones es desafiante debido al amplio espectro de lesiones con presentación clínica similar y especialmente cuando la presencia de un tumor primario pasa desapercibida. Presentamos el caso de un varón de 55 años con una tumoración indolora en región maxilar anterior, encía vestibular y paladar, de 2 meses de evolución. El diagnóstico anatomopatológico fue de tumor maligno de células claras, altamente sugestivo de metástasis de carcinoma renal de células claras, y la lesión bucal constituyó el primer signo de enfermedad.

**PALABRAS CLAVE:** metástasis oral, carcinoma de células renales, mucosa oral, maxilar.

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