

## A rare case of oral metastasis of renal clear cell carcinoma: case report and review of literature

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### Abstract:

This is a case report of metastasis of renal clear cell carcinoma, a very rare malignant neoplasia, in the oral cavity. The patient went to the oral medicine clinic complaining of a nodule in the left upper gingival region that had started a month previously. Clinical evaluation revealed a large, red and bleeding nodule in the superior gingiva of the left side of the maxilla. A panoramic radiographic revealed alveolar bone destruction. Incisional biopsy was performed, and microscopic evaluation revealed an unspecified malignant neoplasia. The patient was referred to a local hospital for investigation. A systemic evaluation showed a large nodule in the right kidney, another nodule in the liver, small nodules in both lungs and two nodules in the brain. A biopsy of the right kidney was performed, showing a renal clear cell carcinoma. After that, new immunohistochemical analysis of the oral lesion was performed demonstrating it to be one more implant of renal neoplasia. The final diagnosis was renal clear cell carcinoma, with metastases in the liver, lung, mouth and nervous system. Unfortunately, the patient died six months after the diagnosis. The primary tumour was only discovered due to the oral manifestation of the disease, emphasising the importance of oral medicine in the diagnosis of metastatic lesions.

**Keywords:** Oral Manifestations; Carcinoma, Renal Cell; Gingiva

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## INTRODUCTION

Kidney cancer accounts for about 2.2% of malignant neoplasms in adults, and mouth metastases account for 1% of malignant tumours<sup>1,2</sup>. The primary tumours that metastasise to the oral cavity are: lung (21.1%), liver (12.3%), breast (10.5%), kidney (10.5%) and colorectal (8.8%)<sup>3</sup>. Oral metastases are more prevalent in the jaw bone and gingiva<sup>2</sup>. Head and neck metastases of kidney cancer are most commonly found in the skin and subcutaneous lymph nodes, parotid gland, tongue, oral mucosa, tonsils, nasal cavity, orbit, mandible and maxilla<sup>4</sup>. Metastases of renal carcinomas to the head and neck region are relatively rare<sup>2,4</sup>. Among the most affected areas of renal metastases are the lungs, bones, abdominal lymph nodes, adrenal gland, liver and brain<sup>5</sup>. The present case showed metastases in three of these sites.

The clinical aspects of kidney metastasis in the mouth vary according to the anatomical site involved, and in many times one should remember the aspect of the non-neoplastic proliferative process<sup>6</sup>. In general, metastases are characterised by painful or asymptomatic nodules of rapid growth that bleed easily, and that are covered by a fibrin-purulent membrane. Paraesthesia is observed in some cases<sup>4,7-10</sup>. Radiographically, most renal metastases are presented as radiolucent images of indefinite limits, followed by mixed images; bone destruction is also found, and the characteristics are common with metastases from other sites<sup>2,3,10,11</sup>.

The treatment of metastases consists of radiotherapy and chemotherapy with antiangiogenic drugs<sup>12,13</sup>. Surgical excision is very limited. These lesions present intense vascularisation that can limit surgical procedures and, when performed, surgery is solely for palliative care. It is performed in some cases for pain relief, improvement of function and psychological well-being<sup>9,11,12</sup>. Unfortunately, the prognosis of kidney metastatic lesions is quite poor<sup>12</sup>.

## CASE REPORT

A 63-year-old male patient attended the oral medicine clinic of the Federal University of Rio Grande do Sul with a complaint of gingival overgrowth. The patient reported having type II diabetes mellitus and arterial hypertension. The intra-oral exam revealed a double lobe nodule covering the gingiva and alveolar ridge on the left side of the maxilla. The lesion measured 5 x 3 cm, had a reddish colouration, was covered by a purulent membrane, bled easily when touched and

had a foul odour. The lesion had appeared 2 months earlier and showed a rapid growth (Figure 1A). No alterations were observed extra orally. The panoramic radiograph revealed a radiolucent lesion with diffuse borders indicating osteolysis between teeth 23 and 27 (Figure 1B). Provisional clinical diagnosis of malignant neoplasia or, eventually, a non-neoplastic proliferative process (pyogenic granuloma) were established. Based on that, an incisional biopsy was performed under local anaesthesia. During the procedure, the intense bleeding was controlled locally with collagen sponges and suture.

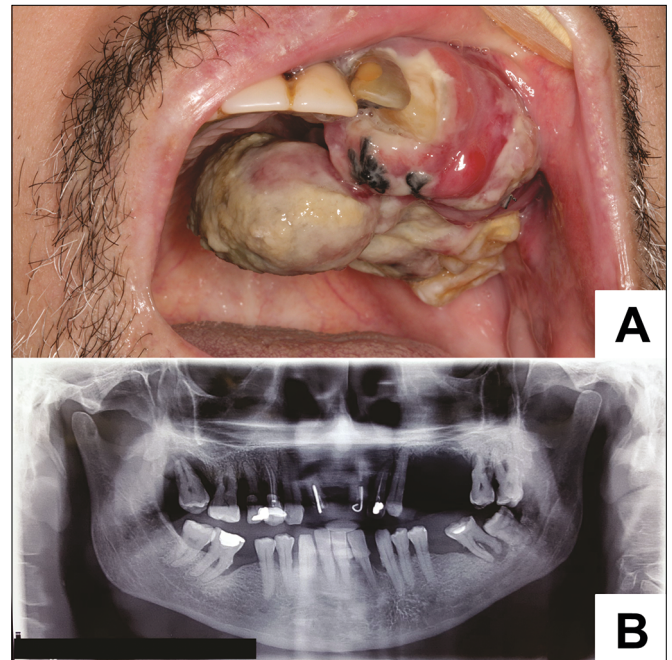
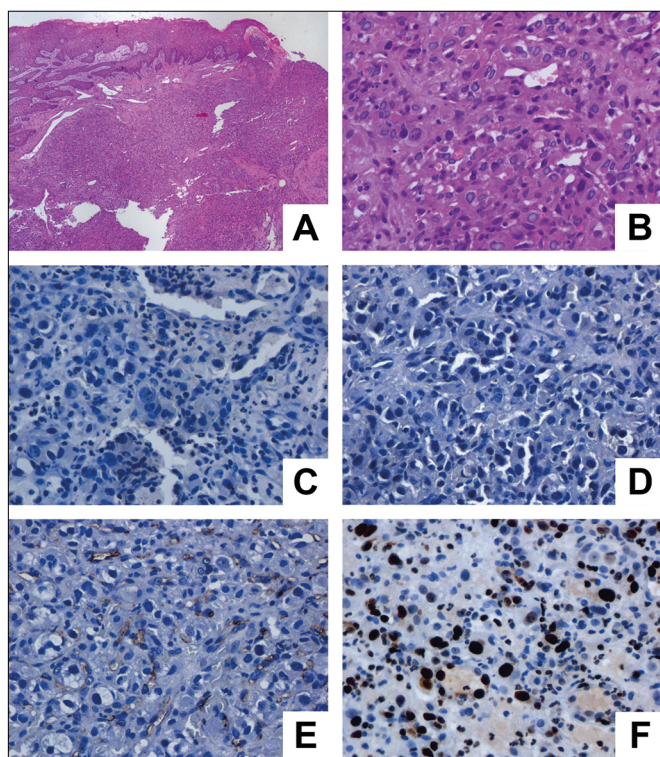


Figure 1. Clinical presentation. A, Intraoral view. B, Panoramic radiography.

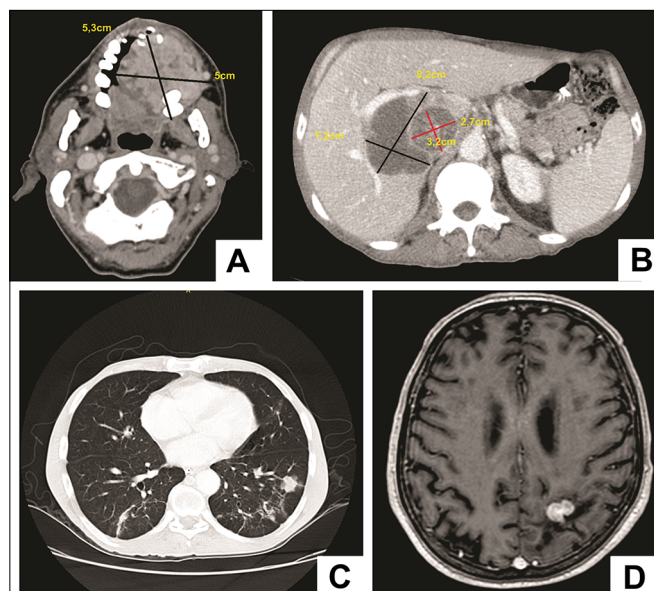
Histopathological analyses revealed a hypercellularised solid tumour invading adjacent tissues and extending near the surface epithelium. The connective tissue surrounding the lesion showed intense vascularisation (Figure 2A). At higher magnification, the cells displayed pleomorphism, hyperchromatism, an epithelioid aspect, clear cytoplasm and ruptured nuclei, interspersed by delicate vascular spaces. The tissue arrangement was diffuse, and few mitoses were observed (Figure 2B). In the initial immunohistochemical evaluation, the tumour cells were negative for AE1/AE3, discarding a tumour of epithelial origin (Figure 2C). The cells were also negative for S100 and CD34, ruling out the hypotheses of amelanotic melanoma and angiosarcoma, respectively (Figure 2D and 2E); CD34-negative cells excluded the initially-raised possibility of angiosarcoma (Figure

2E). Immunostaining for Ki67 was high, confirming the highly proliferative behaviour of the lesion (Figure 2F). Thus, the preliminary diagnosis was of undifferentiated malignant neoplasia and the possibility a metastatic lesion was considered by the team. The patient was referred to a hospital to perform complementary tests and stabilise the systemic condition, since his haemoglobin was 6.5 g/dL.



**Figure 2.** Histologic findings. A, a solid, highly cellularized and non-encapsulated neoplasia is shown (HE, 400x). B, Higher magnification revealed undifferentiated and pleomorphic cells and ruptured nuclei (HE, 400x). C to F, Immunohistochemical features. C, cells negative for AE1/AE2 and D, S100. E, cells positive for CD34 in the on the lumen of blood vessels. F, cells were highly positive for Ki67, indicating the aggressive behavior of the lesion (400x).

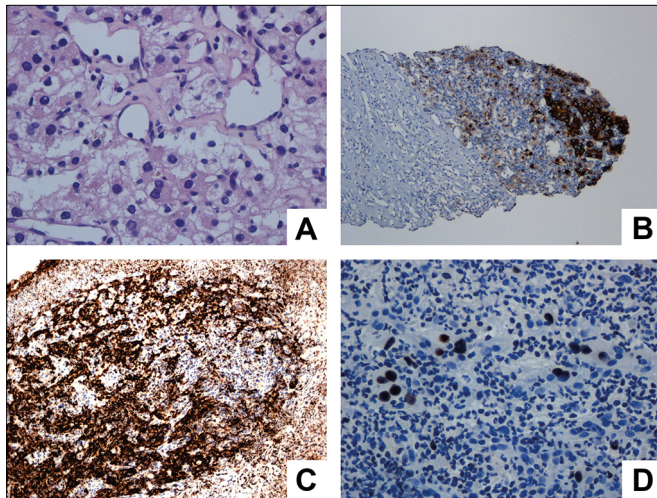
After admission, a computed tomography scan of the face was performed, which revealed destruction of the alveolar ridge from tooth 23 to 28, associated with a large tumour mass invading the left maxillary sinus. In the same tomography axis, in the soft tissue window, an extensive lesion was observed in the left maxilla across the midline of the palate measuring 5.3 x 5 cm in its largest diameters (Figure 3A). MRI of the skull revealed two intra-axial nodular lesions in the left parietal lobe, measuring about 1.5 x 1.2 cm and 1.3 x 1.2 cm (Figure 3D), indicating metastatic implants in the central nervous system.



**Figure 3.** A - Computed tomography findings of the head in the axial section of the soft tissue window. B - Computed tomography of the abdomen, axial section showing the kidney tumor and the metastases in the liver. C - Computed tomography of the chest, axial section showing the metastatic implants in the lungs. D - Magnetic resonance showing the metastatic implants in the brain, in parietal lobe.

The axial sections of the chest CT showed several hyperdense nodules in both lungs (Figure 3C). In the axial section of the abdomen scans, an expansive lesion of 8.2 x 7.2 cm in the right kidney (Figure 3B) was observed, revealing the primary tumour site. Another metastatic implant, characterised by a nodular lesion with a more calcified interior, that measured 3.2 x 2.7 cm, was also observed in the central portion of the liver (Figure 3B).

An incisional biopsy guided by ultrasonography was performed in the right kidney; the histological analysis showed a renal neoplasm with clear cytoplasm cells (Figure 4A). In the immunohistochemical evaluation, cells were positive for CD10 (Figure 4B), confirming a clear cell renal carcinoma. Supported by these findings, a complementary immunohistochemical evaluation of the initial mouth biopsy was performed, showing positivity for CD10 (Figure 4C) and PAX8 (Figure 4D). Based on these findings, the final diagnosis was clear cell renal cell carcinoma, with metastasis in the mouth, brain, lung and liver. The treatment of choice was radiosurgery for the brain metastases, 10 sessions of radiotherapy for the mouth metastasis and palliative chemotherapy with pazopanib. However, the patient died six months after diagnosis.



**Figure 4.** A - Histologic findings of kidney biopsy showing malignant renal neoplasm with clear cytoplasm cells (HE, 400x). B - Immunohistochemical analysis of kidney cells showing immunopositivity for CD10 (100x). C - Immunohistochemical analysis of oral tissue for renal markers CD10 and PAX8 (D) (400x).

## DISCUSSION AND REVIEW OF LITERATURE

Metastases in oral tissues are very rare<sup>2,3</sup>. Table 1 summarises the cases published in the literature of renal cell carcinoma in the last 10 years. Most cases present as nodular lesions, display a predilection for males and for people in their fifth decade. Table 1 still points a higher occurrence in the tongue and parotid gland. In general, metastases to tissues of the oral cavity mostly affect the posterior region of the mandible, a well-vascularised region which facilitates the spread of neoplastic cells<sup>2,3,14</sup>. The other particularity of this condition is its variety of clinical presentations, with many cases mimicking a non-neoplastic proliferative process<sup>6,15</sup>.

The present case showed an atypical site for kidney metastases, in the gingiva and alveolar ridge on the maxilla, since only 2 of the 39 cases from the English literature had a similar location<sup>7,16</sup>. A very important characteristic of metastatic kidney neoplasms is the intense vascularisation that can lead to the patient suffering from large blood losses; this was also present in our case and had already been reported by other authors<sup>9,17</sup>.

The radiographic aspect resembles other malignant metastatic neoplasms in the oral cavity<sup>2,3</sup>. In panoramic or periapical radiographs, radiolucent images of ill-defined limits can be seen with destruction of the involved cortical bone, as observed in our case<sup>11,18</sup>. At early diagnosis, although atypical, no radiographic changes are found<sup>10</sup>. The CT shows osteolytic images when the cortical bone is involved, and soft tissue lesions present

isodense images. Similar aspects were observed in our case, as the bone of the inferior wall and lateral portion of the maxillary sinus was destroyed by the condition (Figure 3A). In the present case, contrast was not used in CT, but when it is used a high contrast enhancement is observed<sup>11,17,19</sup>.

Ultrasound exams are most frequently used when the lesions are located in the parotid or submandibular gland. When changes in salivary glands are detected, this change is rarely considered to be a metastasis, but benign or malignant tumours of the salivary gland are considered, with the exception of patients who already have a history of the neoplasm of origin<sup>20</sup>.

Histological evaluations for clear cell renal cell carcinoma show intense vascularisation, cells with pleomorphic and hyperchromatic nuclei and may present cells with a clear cytoplasm<sup>21,22</sup>. If the patient does not have a history of primary neoplasia, the correct diagnosis is not possible without immunohistochemical analysis. The main markers used are PAX8, presenting positivity in approximately 90% of cases, and CD10 with positivity in 98%. Another classic marker is AE1/AE2, positive in 88% of the cases. The reported case was negative for this marker, which can be explained by its poorly differentiated cells<sup>23</sup>. In addition to these markers, another that can be used is CK7, an important marker for epithelial tumours and with high expression in renal tumours<sup>9,23</sup>.

The patient of the present case report had an advanced clinical stage disease, with metastases in the liver, lungs and brain. All these conditions were discovered as a result of detection of the lesion in the oral cavity. In advanced cases like this, with manifestation in oral cavity, is not uncommon the primary tumour be discovered by the oral manifestation<sup>6,15,24</sup>. The most common sites for metastasis of renal carcinoma are the lungs, intra-abdominal lymph nodes, bone and liver<sup>6</sup>.

As for treatment, pazopanib was the drug elected for this patient. Other drugs frequently employed are the sunitinib and sorafenib. These drugs are an angiogenic inhibitor acting on VEGF receptors, which results in decreased tumour volume<sup>25,26</sup>. For brain metastases, as in this case, stereotactic surgery or radiosurgery is a technique for treating surgically inaccessible intracranial lesions, delivering narrow radiation beams to a precisely-targeted area<sup>27</sup>.

As for the control of the metastatic lesion in the oral cavity, the team opted to perform ten radiotherapy sessions; any surgical procedure was discarded due to

**Table 1.** List of cases publish in the last 10 years.

Author, year	Site	Age, gender	Site	Clinical presentation	Radiographic aspects	Other metastasis sites	Treatment	Follow-up time	Outcome
Yoshitomi <i>et al.</i> 2010 <sup>15</sup>	Tongue	47 yo, male	Tongue	Reddish nodule	N/I	Adrenal gland, pleura and bilateral lesion in the lungs	Nephrectomy and local excision of the tongue, followed by chemotherapy with sunitinib and sorafenib	2 years	Alive
Morvan <i>et al.</i> 2011 <sup>19</sup>	Tongue	48 yo, female	Tongue	Nodule	Computed tomography: isodense image in the tongue	Left suprarenal and L5 vertebra	Local resection and radiotherapy	5 years	Alive
Novak <i>et al.</i> 2012 <sup>29</sup>	Tongue	63 yo, male	Tongue	Nodule	Absence	Absence	Nephrectomy and local excision of the lesion followed by cryotherapy	3 years	Alive
Ganini <i>et al.</i> 2012 <sup>17</sup>	Tongue	70 yo, male	Tongue	Nodule	Computed tomography: oval lesion with high contrast enhancement	Adrenals, abdominal lymph nodes and lungs	Embolisation of the lingual artery	8 months	Dead
Schwab <i>et al.</i> 2012 <sup>7</sup>	Upper gingiva bilaterally	63 yo, male	Upper gingiva bilaterally	Nodule	N/I	Brain, bones, lungs lymph nodes and adrenals	Local resection, whole brain radiation therapy, sunitinib and sorafenib.	N/I	N/I
Serouya <i>et al.</i> 2012 <sup>30</sup>	Submandibular gland	60 yo, male	Submandibular gland	Submandibular mass	Ultrasound: 1 cm mass in the submandibular gland	Absence	Nephrectomy and Local resection	3 years	Alive
Ghazali <i>et al.</i> 2013 <sup>31</sup>	Tongue	64 yo, female	Tongue	Nodule	N/I	Absence	Local resection and immunotherapy	5 months	Dead
Suojanen <i>et al.</i> 2013 <sup>4</sup>	Lower lip	71 yo, male	Lower lip	Nodule	Absence	Mediastinum and pleura	Palliative local resection	N/I	N/I
Mazeron <i>et al.</i> 2013 <sup>32</sup>	Tongue	66 yo, male	Tongue	Nodule	N/I	Absence	Brachytherapy, chemotherapy with sunitinib, partial glossectomy	5 months	Dead
Jallu <i>et al.</i> 2013 <sup>18</sup>	Mandibular ramus	68 yo, male	Mandibular ramus	Increased facial volume	Panoramic radiography: osteolytic lesion	Absence	Palliative chemotherapy and radiotherapy	N/I	N/I
Sikka <i>et al.</i> 2013 <sup>33</sup>	Bilateral inferior posterior alveolar gingiva	73 yo, male	Bilateral inferior posterior alveolar gingiva	Nodule	Absence	Absence	N/I	N/I	N/I

Continued **table 1.**

Ray <i>et al.</i> 2013 <sup>34</sup>	Tongue	65 yo, male	Tongue	Nodule	Absence	Lungs	Nephrectomy, excision of the tongue lesion followed by palliative chemotherapy with Sunitinib and radiotherapy	N/I	N/I
Hosn-Centenero <i>et al.</i> 2013 <sup>35</sup>	Parotid Gland	63 yo, male	Parotid Gland	Increased facial volume	Magnetic resonance: nodule in parotid gland	Absence	Parotidectomy and radiotherapy	N/I	N/I
Ahmadnia <i>et al.</i> 2013 <sup>36</sup>	Lower Gingiva	57 yo, male	Lower Gingiva	Nodule	Panoramic radiography: ill-defined radiolucent lesion	Absence	Nephrectomy	N/I	N/I
Zhang <i>et al.</i> 2014 <sup>11</sup>	Posterior region of mandible	47 yo, male	Posterior region of mandible	Nodule	Panoramic radiography: Ill-defined radiolucent lesion	N/I	Palliative local mandible resection	N/I	N/I
Zhang <i>et al.</i> 2014 <sup>11</sup>	Anterior Region of Maxilla	60 yo, male	Anterior region of maxilla	Nodule	Computed Tomography: osteolytic damage in maxilla	N/I	Resection of alveolar process	N/I	N/I
Kotak <i>et al.</i> 2014 <sup>37</sup>	Lower lip	64 yo, Male	Lower lip	Nodule	N/I	Lung	Local resection	N/I	N/I
Bidokhty <i>et al.</i> 2014 <sup>38</sup>	Tongue	80 yo, male	Tongue	Nodule	N/I	Absence	Local resection, chemotherapy with sunitinib and Sorafenib.	6 months	Alive
Altuntas <i>et al.</i> 2015 <sup>9</sup>	Tongue	70 yo, male	Tongue	Nodule	N/I	Lungs, mediastinal lymph nodes, second lumbar vertebra and right kidney	Partial palliative glossectomy, Interferon and Sunitinib	7 months	N/I
Rusha <i>et al.</i> 2016 <sup>6</sup>	Inferior alveolar gingiva	60 yo, male	Inferior alveolar gingiva	Nodule	N/I	Lungs	Radiotherapy, tyrosine kinase inhibitor and Sorafenib	3 months	Alive
Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	66 yo, female	Parotid Gland	Immobile nodule in the face	N/I	Absence	Total parotidectomy, radiotherapy	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	76 yo, female	Parotid Gland	Immobile nodule in the face	N/I	Absence	Total parotidectomy	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Submandibular gland	97 yo, female	Submandibular gland	Immobile nodule in the face	N/I	Absence	N/I	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	69 yo, male	Parotid Gland	Immobile nodule in the face	N/I	Absence	Resection of the tumour	N/I	N/I

Continued table 1.

Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	69 yo, male	Parotid Gland	Nodule in the face	N/I	Absence	Superficial parotidectomy	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	NI, male	Parotid Gland	Nodule in the face	N/I	Lungs	Total parotidectomy	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Small salivary gland of left retromolar region	NI, female	Small salivary gland of left retromolar region	Nodule	N/I	Absence	Resection of the tumour	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	NI, female	Parotid Gland	Nodule	N/I	Absence	Total parotidectomy	N/I	N/I
Majewska <i>et al.</i> 2016 <sup>20</sup>	Parotid Gland	60 yo, female	Parotid Gland	Multiple nodules	N/I	Absence	Resection of the tumour	N/I	N/I
Shirazian <i>et al.</i> 2016 <sup>39</sup>	Anterior superior gingiva	45 yo, male	Anterior superior gingiva	Nodule	Periapical radiography: a saucer shape bone resorption	Absence	N/I	N/I	N/I
Raiss <i>et al.</i> 2017 <sup>40</sup>	Tongue	55 yo, male	Tongue	Multiple nodules	Computed tomography: expansive lesion with hyperdense foci	Bilateral pulmonary metastases and muscle metastases	Chemotherapy with Sunitinib, Doxorubicin and Gemcitabine	10 days	Dead
Danić <i>et al.</i> 2017 <sup>41</sup>	Tongue	51 yo, male	Tongue	Mucosal thickening	Computed tomography: Isodense image in the tongue	Liver and lungs	Nephrectomy and chemotherapy	6 months	Dead
Derakhshan <i>et al.</i> 2018 <sup>16</sup>	Anterior Region of Maxilla	54 yo, male	Anterior Region of Maxilla	Nodule	Cone beam computed tomography: intraosseous ill defined hypodense image with ragged borders	N/I	Chemotherapy and radiotherapy	11 months	Dead
Derakhshan <i>et al.</i> 2018 <sup>16</sup>	Maxillary posterior alveolar region	51 yo, male	Maxillary posterior alveolar region	Nodule	N/I	Lungs	Chemotherapy	6 months	Alive
Morita <i>et al.</i> 2018 <sup>5</sup>	Mucosa of the Cheek	75 yo, male	Mucosa of the Cheek	Submucosal nodule in the face	Computed tomography: ill- defined, soft tissue mass lesion in the left side buccal submucosa	N/I	Resection of the tumour	22 months	Alive
Vasilyeva <i>et al.</i> 2018 <sup>10</sup>	Anterior superior gingiva	78 yo, female	Anterior superior gingiva	Nodule	Periapical radiograph: no alterations	Right femoral head and greater trochanter.	N/I	N/I	N/I
Boulanger <i>et al.</i> 2019 <sup>42</sup>	Inferior posterior alveolar gingiva	82 yo, male	Inferior posterior alveolar gingiva	Nodule	N/I	Femur and the 10th rib	Palliative radiotherapy	N/I	Dead

Continued table 1.

Nesbitt <i>et al.</i> 2019 <sup>43</sup>	Buccal mucosa	59 yo, male	Buccal mucosa	Ulcerative Nodule	N/I	Lungs	Whole brain radiotherapy and local palliative radiation.	N/I	N/I
Netto <i>et al.</i> 2019 <sup>24</sup>	Mucosa of the cheek	68 yo, male	Mucosa of the cheek	Facial Asymmetry	Computed tomography: expansive lesion with hyperdense foci	Right kidney cortex and parenchyma	Chemotherapy and radiotherapy for orofacial metastatic tumour	4 months	Dead

the high vascularisation of the lesion and also due to the patient's systemic condition, rendering it impossible to perform any surgical procedure. Due to the intense vascularisation of the lesion, surgical procedures are quite limited. Total or partial resection of the lesion is indicated palliatively; it is performed to preserve the organ or to provide more comfort to the patient<sup>9,11</sup>. Local radiotherapy can be an interesting option. In this regard, Morvan *et al.* and Rusha *et al.*, have been successful in controlling metastatic lesions using radiotherapy<sup>6,19</sup>.

In cases of advanced stages of the disease, as for our patient, the prognosis is quite poor. In our literature review of similar cases, the longest survival time was 11 months; however, other authors report a smaller survival time, such as 6 months<sup>16,28</sup>.

## CONCLUSION

Metastatic lesions in the oral cavity are a very rare entity. Diagnosis is extremely difficult, especially when the patient has no history of neoplasms. The treatment of these conditions is very aggressive for the patient, and for this reason the treatment requires a multidisciplinary team.

## CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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## CONFLICT OF INTEREST

All authors declare no conflict of interest.

## REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018 Nov;68(6):394-424.
2. Hirshberg A, Shnaiderman-Shapiro A, Kaplan I, Berger R. Metastatic tumours to the oral cavity - pathogenesis and analysis of 673 cases. *Oral Oncol.* 2008 Aug;44(8):743-52.
3. Liu Y, Vargo RJ, Bilodeau EA. Analytic survey of 57 cases of oral metastases. *J Oral Pathol Med.* 2018;47(3):275-80.
4. Suojanen J, Färkkilä E, Helkamaa T, Loimu V, Törnwall J, Lindqvist C, *et al.* Rapidly growing and ulcerating metastatic renal cell carcinoma of the lower lip: a case report and review of the literature. *Oncol Lett.* 2014 Nov;8(5):2175-8.
5. Morita Y, Iwagami T, Kawakita C, Kusuyama Y, Niki-Yonekawa A, Morita N. Oral metastasis of renal cell carcinoma mimicking recurrence of excised malignant myoepithelioma: a case report. *Mol Clin Oncol.* 2018 Jul;9(1):66-9.
6. Ali RAE, Mohamed KEH. Metastatic clear cell renal cell carcinoma presenting with a gingival metastasis. *Clin Pract.* 2016 Jun;6(2):847.
7. Schwab B, Lee WT. Bilateral renal cell carcinoma metastasis in the oral cavity. *Am J Otolaryngol.* 2012;33(1):154-5.
8. Matamala GN, Ángeles MDL, Toro F. Oral metastasis of renal cell carcinoma, presentation of a case. *Med Oral Patol Oral Cir Bucal.* 2008 Nov;13(11):E742-4.
9. Altuntaş O, Petekkaya İ, Süslü N, Güllü İ. Renal cell carcinoma metastatic to the tongue: a case report and review of the literature. *J Oral Maxillofac Surg.* 2015 Jan;73(6):1227-30.
10. Vasilyeva D, Peters SM, Philipone EM, Yoon AJ. Renal cell carcinoma metastatic to the maxillary gingiva: a case report and review of the literature. *J Oral Maxillofac Pathol [Internet].* 2018 Feb; 22(4):102-7. Available from: <http://www.jomfp.in/text.asp?2018/22/4/102/224631>
11. Zhang L, Yang H, Zhang X. Metastatic renal cell carcinoma to the jaws: report of cases. *World J Surg Oncol.* 2014;12(1):204.
12. Umer M, Mohib Y, Atif M, Nazim M. Skeletal metastasis in renal cell carcinoma: a review. *Ann Med Surg.* 2018 Jan;27:9-16.
13. Guevremont C, Jeldres C, Perrotte P, Karakiewicz PI. Sorafenib in the management of metastatic renal cell carcinoma. *Curr Oncol.* 2009;16(Suppl 1):S27-32.
14. Kaplan I, Raiser V, Shuster A, Shlomi B, Rosenfeld E, Greenberg A, *et al.* Metastatic tumors in oral mucosa and jawbones: unusual primary origins and unusual oral locations. *Acta Histochem.* 2019 Nov;121(8):151448.



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15. Yoshitomi I, Kawasaki G, Mizuno A, Nishikido M, Hayashi T, Fujita S, et al. Lingual metastasis as an initial presentation of renal cell carcinoma. *Med Oncol*. 2011;28(4):1389-94.
  16. Derakhshan S, Rahrotaban S, Mahdavi N, Mirjalili F. Metastatic renal cell carcinoma presenting as maxillary lesion: report of two rare cases. *J Oral Maxillofac Pathol*. 2018 Jan;22(Suppl 1):S39-43.
  17. Ganini C, Lasagna A, Ferraris E, Gatti P, Paglino C, Imarisio I, et al. Lingual metastasis from renal cell carcinoma: a case report and literature review. *Rare Tumors*. 2012 Aug;4(3):130-3.
  18. Jallu A, Latoo M, Pampori R. Rare case of renal cell carcinoma with mandibular swelling as primary presentation. *Case Rep Urol*. 2013 Jun;2013:806192.
  19. Morvan JB, Veyrières JB, Mimouni O, Cathelinaud O, Allali L, Verdalle P. Clear-cell renal carcinoma metastasis to the base of the tongue and sphenoid sinus: two very rare atypical ENT locations. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2011 Apr;128(2):91-4.
  20. Majewska H, Skálová A, Radecka K, Stodulski D, Hyrcza M, Stankiewicz C, et al. Renal clear cell carcinoma metastasis to salivary glands – a series of 9 cases: clinico-pathological study. *Pol J Pathol*. 2016 Mar;67(1):39-45.
  21. Jatti D, Puri G, Aravinda K, Dheer DS. An atypical metastasis of renal clear cell carcinoma to the upper lip: a case report. *J Oral Maxillofac Surg*. 2015 Feb;73(2):371.e1-e6. DOI: <http://dx.doi.org/10.1016/j.joms.2014.09.006>
  22. Lee C, Park JW, Suh J, Nam KH, Moon KC. Histologic variations and immunohistochemical features of metastatic clear cell renal cell carcinoma. *Korean J Pathol*. 2013 Oct;47(5):426-32.
  23. Ma F, Dai L, Wang Z, Zhou L, Niu Y, Jiang N. Correction: evaluating prognosis by CK7 differentiating renal cell carcinomas from oncocytomas can be used as a promising tool for optimizing diagnosis strategies. *Oncotarget*. 2018 Jun;9(49):29285.
  24. Netto R, Freitas Filho SAJ, Cortezzi W, Merly F, Andrade VM, Pires FR. Metastasis of renal cell carcinoma causing significant facial asymmetry. *Case Rep Surg*. 2019 Nov;2019:6840873.
  25. Costantino C, Thomas GV, Ryan C, Coakley FV, Troxell ML, Li X, et al. Metastatic renal cell carcinoma without evidence of a renal primary. *Int Urol Nephrol*. 2015 Nov;48(1):73-7.
  26. Rini BI, Plimack ER, Takagi T, Elson P, Wood LS, Dreicer R, et al. A phase II study of pazopanib in patients with localized renal cell carcinoma to optimize preservation of renal parenchyma. *J Urol*. 2015 Mar;194(2):297-303. DOI: <http://dx.doi.org/10.1016/j.juro.2015.03.096>
  27. Leksell L. Occasional review stereotactic radiosurgery. *J Neurol Neurosurg Psychiatry*. 1983 Sep;46(9):797-803.
  28. Costantino C, Thomas GV, Ryan C, Coakley FV, Troxell ML. Metastatic renal cell carcinoma without evidence of a renal primary. *Int Urol Nephrol*. 2015;48(1):73-7.