

# Metastasis of Renal Cell Carcinoma to the Mandible: A Case Report

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## ABSTRACT

Tumors metastasizing to the oral cavity are uncommon and comprise only approximately 1% of the neoplasms in the oral cavity. A 76-year-old man was referred from a local dental clinic with a 3-month history of swelling and pain in the right side of the mandible. He reported a history of clear-cell renal cell carcinoma in the left kidney treated by nephrectomy 18 years ago. Additionally, he had undergone right-upper lobectomy of the lungs for clear-cell renal cell carcinoma metastasis 13 years previously. Orthopantomogram showed multilocular radiolucent lesion in the right posterior region of the mandible. Computed tomography revealed a 3.5 × 4.0-cm sized lobulated contour mass with bone destruction in the right mandibular angle. Moreover, he underwent segmental mandibulectomy with excision of the lesion under general anesthesia, followed by reconstruction using a reconstruction plate. The postoperative histological diagnosis was clear-cell renal cell carcinoma. The kidneys did not show any evidence of recurrence.

**Key words :** Renal cell carcinoma, Mandible, Metastasis

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## INTRODUCTION

Tumors metastasizing to the oral cavity are uncommon and comprise only approximately 1% of all oral neoplasms<sup>1-3</sup>. The third most-common neoplasm metastasizing to the oral cavity is renal carcinoma<sup>3</sup>. Renal cell carcinoma (RCC) is the most common renal tumor type and accounts for 80~85% of all renal tumors<sup>4,5</sup>. There are four major subtypes: clear-cell, papillary, chromophobe RCC, and collecting-duct carcinoma<sup>5,6</sup>. Men are generally more affected, with a male : female ratio of 1.5 : 1, and most incidences are observed in the age of 60 and 70 years<sup>7,8</sup>. They are very rarely observed in Blacks and Asians<sup>7</sup>. RCCs generally grow slowly and metastasize late<sup>1,9</sup>.

The prognosis for RCC could vary and depends on the anatomic, histologic, clinical, and molecular features of the disease, with an overall survival rate of 74% at 5 years<sup>8</sup>. Patients with clear-cell RCC (ccRCC) had a worse prognosis compared with those with papillary and chromophobe RCC<sup>6</sup>. The cancer-specific survival rates at 5 years for patients with clear cell, papillary, chromophobe RCC were 68.9%, 87.4%, and 86.7%, respectively<sup>6</sup>. More than 20% of patients undergoing nephrectomy developed metastases during the follow-up period<sup>5</sup>. Metastases of RCC generally involve the lungs, regional lymph nodes, liver, bones, and brain<sup>8,10</sup>.

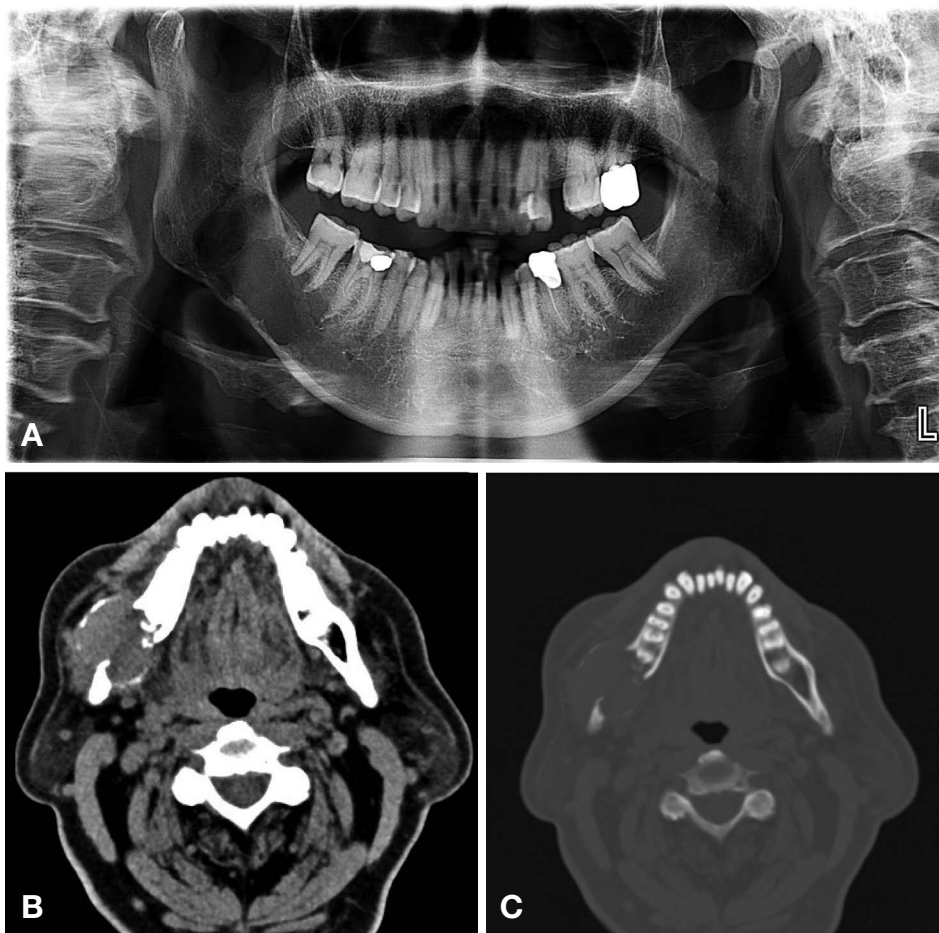
In this study, we report a rare case of a patient with metastatic ccRCC on the mandible.

## CASE REPORT

A 76-year-old man was referred from a local dental clinic (LDC) with a 3-month history of swelling and pain in the right

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**Figure 1.** Radiographic presentation. A. Orthopantomogram showing a radiolucent lesion in the right posterior region of the mandible. B. Computed tomography scan of the same lesion. C. Computed tomography scan: bone window.



**Figure 2.** Orthopantomogram findings showing a radiolucent lesion in the right ramus of the mandible.

side of the mandible. Although he had undergone endodontic treatment of the mandibular right first molar in LDC, his symptoms of persistent swelling, pain, and numbness did not

improve. He reported a history of ccRCC in the left kidney treated by nephrectomy 18 years previously. Additionally, he had undergone right-upper lobectomy of the lungs for meta-

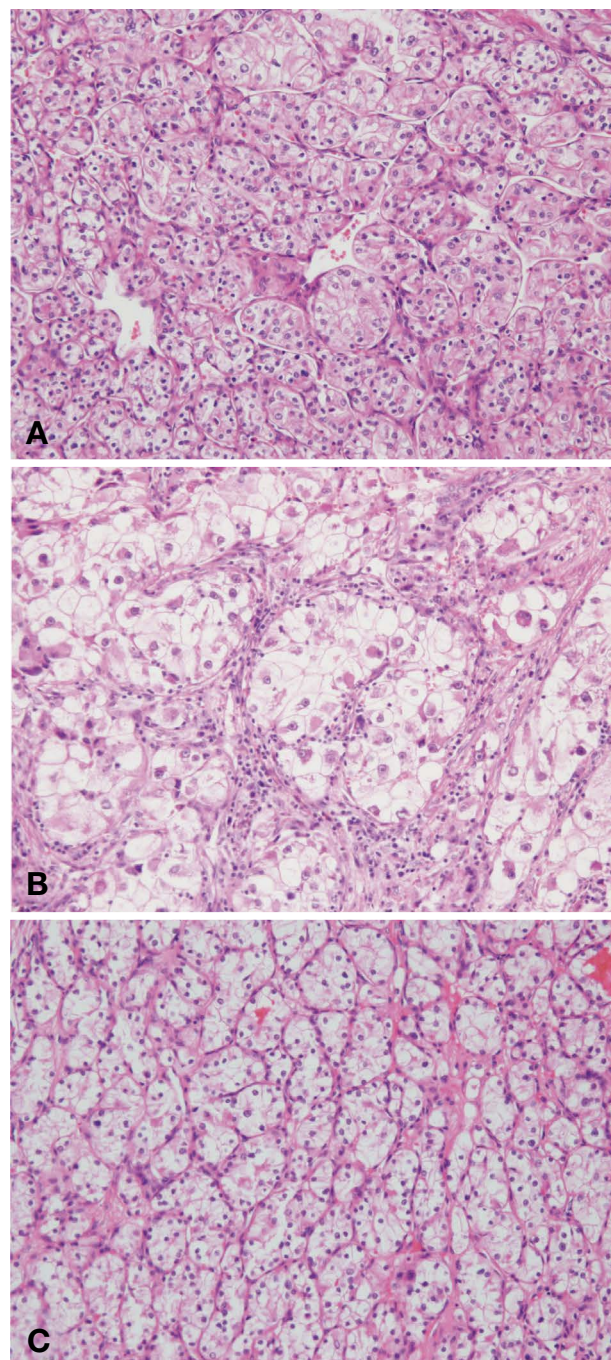
stasis of the ccRCC 13 years previously. After the lobectomy, he was administered interferon-alpha for 1 year. On clinical examination, painful swelling was noted on the right side of his lower face. Through intraoral examination, we noted gingival swelling in the right posterior region and mobility of the mandibular right second molar. Orthopantomogram findings revealed that a multilocular radiolucent lesion, involving the inferior alveolar nerve, was extended from the lower right first molar to the ramus in the right mandible (Fig 1A). Computed tomography (CT) (non-enhanced) revealed a  $3.5 \times 4.0$ -cm-sized lobulated contour mass with destruction in the right mandibular angle (Fig 1B, C).

We suspected the lesion to be ameloblastoma of the mandible or metastatic ccRCC. Histological examination of the frozen intraoperative biopsy specimen indicated ccRCC. He underwent segmental mandibulectomy with excision of the lesion under general anesthesia, followed by reconstruction using a reconstruction plate. The kidneys did not show any evidence of recurrence. As the patient refused further surgical reconstruction of the mandible, only regular follow-up examinations were performed for 6 months. Following this period, the patient complained of pain on the right mandible again, and we suspected the recurrence of ccRCC after performing an orthopantomogram (Fig 2). The patient underwent mandibulectomy again, including coronoidectomy. ccRCC was confirmed by biopsy. After the second surgery, his pain disappeared, and he was monitored for 20 months.

All three histological examinations performed following nephrectomy, lobectomy, and mandibulectomy showed characteristics of clear cells (Fig 3A~C). Microscopic analysis of the metastatic ccRCC in the mandible showed prominent vasculature and well-defined epithelial cells with clear cytoplasm. Immunohistochemical staining showed positive immunoreactivity for epithelial membrane antigen and CD10.

## DISCUSSION

Tumors metastasizing to the oral cavity are uncommon and comprise only approximately 1% of all oral neoplasms<sup>1-3</sup>. In men, malignant neoplasms that metastasize to the oral cavity commonly originate from the lungs. In women, the primary site is most frequently the breast tissue<sup>2</sup>. The third most common neoplasm metastasizing to the oral cavity is renal carcinoma<sup>3</sup>. Renal cancer comprises approximately 3% of all malignancies worldwide. The most common type of renal tumor is RCC, which accounts for 80~85% of all renal tumors<sup>4,5</sup>.



**Figure 3.** Histological analysis showing clear-cell characteristics (hematoxylin and eosin stain;  $\times 200$ ). A. Histological presentation of the primary RCC in 2000. B. Histological presentation of the metastatic RCC in the lungs in 2003. C. Histological presentation of the metastatic RCC in the mandible in 2018. RCC, renal cell carcinoma.

ccRCC is the most common histological type of RCC<sup>5,6</sup>. RCCs generally grow slowly and metastasize late<sup>1,9</sup>. Approximately

30% of patients are diagnosed with metastatic disease, and 20~40% of those that had undergone nephrectomy develop metastases during the follow-up period<sup>5,8,9</sup>. Metastatic lesions are more frequently observed in the mandible than in the maxilla<sup>3,11</sup>. The molar region is most frequently involved (>50%), followed by the premolar (38%)<sup>3</sup>. The metastatic lesion is situated in the angle and the ramus of the mandible (29%); the condyle is involved (3.5%) and the coronoid process (1.6%)<sup>12</sup>. Good blood supply to the mandibular molar region is believed to contribute to hematogenous metastasis<sup>3,7,11</sup>.

Because of its rarity, the diagnosis of a metastatic lesion in the oral cavity is challenging in recognizing that a lesion is metastatic and in finding the location of the primary lesion<sup>3</sup>. The clinical presentation of a metastatic lesion in the oral cavity can be misdiagnosed as a benign tumor<sup>3</sup>. In our case, we suspected ameloblastoma because radiographic findings showed that the mandibular right second molar root was involved in radiolucent lesion, and CT findings revealed a relatively demarcated, lobulated contour mass with bone destruction. Radiologically, most metastatic tumors cause bone destruction similar to the primary tumors. The differential diagnoses of destructive mandibular lesions include osteomyelitis, pyogenic granuloma, odontogenic cyst, benign neoplasm, primary malignant tumor, systemic disease with bone involvement, and metastatic malignancies<sup>1,9</sup>. Histologically, several mandibular tumors exhibit clear-cell features. Neoplasms are divided into primary and metastatic or secondary tumors. Odontogenic tumors with clear-cell characteristics include odontogenic cysts, calcifying epithelial odontogenic tumor (clear-cell variant), clear-cell ameloblastoma, and clear-cell carcinoma. Non-odontogenic tumors with clear-cell characteristics include acinic-cell, mucoepidermoid, and squamous-cell carcinoma, clear-cell oncocytoma, and salivary tumors<sup>1,10</sup>. The differential diagnosis can be difficult using conventional light microscopy. Taking a thorough medical history can facilitate the diagnosis, while immunohistochemical studies can assist in the diagnosis, as monoclonal antibody and vimentin reveal a strong reaction in ccRCC<sup>10,13</sup>. Therefore, biopsy should be performed for a definitive diagnosis when a metastatic lesion is suspected.

Patients with metastatic tumors are generally asymptomatic; however, some may complain of symptoms, such as swelling, pain, bleeding, tooth loss, trismus, and/or hypoesthesia<sup>3,9,11</sup>. Surgical resection can relieve pain and improve the prognosis<sup>3,10</sup>. In cases where the oral tumor is the only metastatic lesion, resection seems to result in improved prognosis, although the reported follow-up period is relatively short<sup>3</sup>. The

magnitude of bone resection is based on preoperative radiographic imaging and visual inspection. Smits et al.<sup>15</sup> reported that tumor-positive bone resection margins were present in 21.3% of segmental mandibulectomies and that these patients had a significantly worse survival rate. Furthermore, a false-positive rate of 16% for CT/magnetic resonance imaging in determining bone involvement preoperatively was found<sup>15</sup>. Ideally there should be an intraoperative feedback (cytology and frozen section) on the bone resection margin status to improve the surgical results. Inevitably, resection results in dysfunction of speech, deglutition, and salivary control, and is often accompanied by facial disfigurement. The mandibular defect, which is not reconstructed, resulted in severe deviation of the mandible with resulting abnormal maxillofacial relationship<sup>14,15</sup>. To limit these adverse effects, it is preferable to perform immediate bone reconstruction, often with a free flap<sup>15,16</sup>. In our case, the patient did not want further mandibular reconstruction because of his old age. The prognosis for RCC is variable and depends on anatomic, histologic, clinical, and molecular features of the disease, with an overall survival rate of 74% at 5 years<sup>8</sup>. However, the prognosis of patients with metastatic oral cavity neoplasms is generally poor<sup>7,11</sup>. Interestingly, the survival rate decreases to 8% in cases of metastatic RCC<sup>8</sup>.

In conclusion, the possibility of metastasis should not be overlooked in patients with a history of ccRCC, even when the ccRCC occurred a long time ago.

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