

## RENAL CELL CARCINOMA METASTASIS TO THE SINONASAL CAVITY: CASE REPORT\*

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**SUMMARY** – Renal cell carcinoma accounts for 3% of all adult malignant tumors. Common sites of metastases are lungs, bone, liver, brain and adrenal glands. Metastatic disease to the head and neck ranges from 15% to 30%. The 5-year survival rate after nephrectomy is 60%-75%, but with multiorgan metastases the 5-year survival rate is significantly lower, 0-7%. A case is presented of a female patient diagnosed with renal cell carcinoma metastases to the paranasal sinuses, diagnosed and treated at the Department of ENT and Head and Neck Surgery, Zadar General Hospital, Zadar, Croatia. The tumor was surgically removed. Unfortunately, the patient died one year after the procedure due to multiorgan failure. Although metastases of renal cell carcinoma to the head and neck are very rare, it should be first suspected when investigating a metastatic tumor in this region. Surgical excision offers the best hope for long term survival. In case of unresectable tumor, other treatment options should be considered such as radiotherapy, immunotherapy and chemotherapy.

**Key words:** *Carcinoma, renal cell; Neoplasm metastasis; Paranasal sinus neoplasms; Case reports*

### Introduction

Renal cell carcinoma (RCC) accounts for 3% of all adult malignant tumors<sup>1,2</sup>. About 20%-50% of RCC patients will eventually develop metastasis after nephrectomy<sup>2</sup>. Common sites of metastases are lungs (76%), bone (42%), liver (41%), brain and adrenal glands<sup>1,3</sup>. Metastatic disease to the head and neck ranges from 15% to 30%<sup>3,4</sup>. Metastases to the sinonasal cavity are very rare. Most malignant tumors occurring in the nasal and paranasal sinuses are primary ones, while metastatic tumors in this region are very rare<sup>5,6</sup>. Metastatic RCC to the sinonasal cavity presents as an intranasal mass causing recurrent epistaxis, nasal obstruction, facial pain and orbital mass<sup>1,4,5,7</sup>. The overall prognosis of a renal metastatic disease to the nose and paranasal sinuses is very poor. Nevertheless,

recent studies have shown that these lesions can have a very good response to higher doses of radiotherapy<sup>1</sup>. Metastases of RCC to the head and neck skin are also very rare (9%) and up to now only 80 cases have been reported in the literature<sup>6</sup>.

We report on a female patient with metastatic RCC to the nasal cavity. We discuss its clinical presentation, treatment and final outcome.

### Case Report

A 61-year-old female patient presented to the ENT Department due to episodes of recurrent epistaxis and continuous nasal obstruction. Previously, she was treated at the Department of Urology due to RCC. She was operated on (nephrectomy) and received radiotherapy treatment. Follow up multisystem com-

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Fig. 1. Tumor mass protrusion from the nasal cavity.

puted tomography (CT) scan showed multiple RCC metastases to the liver, pancreas and vertebrae. She received palliative chemotherapy at the Department of Oncology. Upon admission to the ENT Department, local finding showed a tumor mass filling and protruding from the nasal cavity (Fig. 1). Paranasal sinus CT scan showed a soft-tissue mass in the nasal cavity with no erosion of the surrounding bone (Fig. 2). Under local anesthesia, the patient underwent tumor removal, transnasal endoscopic approach. After intranasal topical decongestion, we injected lidocaine with epinephrine (1:100,000) along the inferior and medial meatal wall. Initial horizontal incision was performed at the site of the anesthetic application. Attachment of the inferior turbinate to the lateral nasal wall was severed with endoscopic scissors straight osteotome following bipolar cautery. Pathologic findings were consistent with metastatic RCC. The tumor measured 3 cm in longest diameter, dark-red colored,



Fig. 3. Dark-red colored excised tumor measuring 3 cm in longest diameter.

mainly thrombotic, with broad areas of hemorrhage and inflammation (Fig. 3). Microscopically, the tumor showed alveolar pattern of cells with abundant, clear cytoplasm and large, oval, hyperchromatic nuclei, conspicuous nucleoli, and brisk mitotic activity. To confirm the diagnosis of metastatic clear cell carcinoma, immunohistochemical staining for Cytokeratin-7 (DAKO, Denmark; dilution 1:50), Cytokeratin-18 (DAKO, Denmark; dilution 1:25), epithelial membrane antigen (EMA, DAKO, Denmark; dilution 1:50) and Vimentin (DAKO, Denmark; dilution 1:3000) was performed. Immunohistochemical examination showed diffusely positive reaction with EMA and vimentin mononuclear antibodies, but Cytokeratin-18 and Cytokeratin-7 were negative (Figs. 4 and 5). The patient was referred to the Oncology

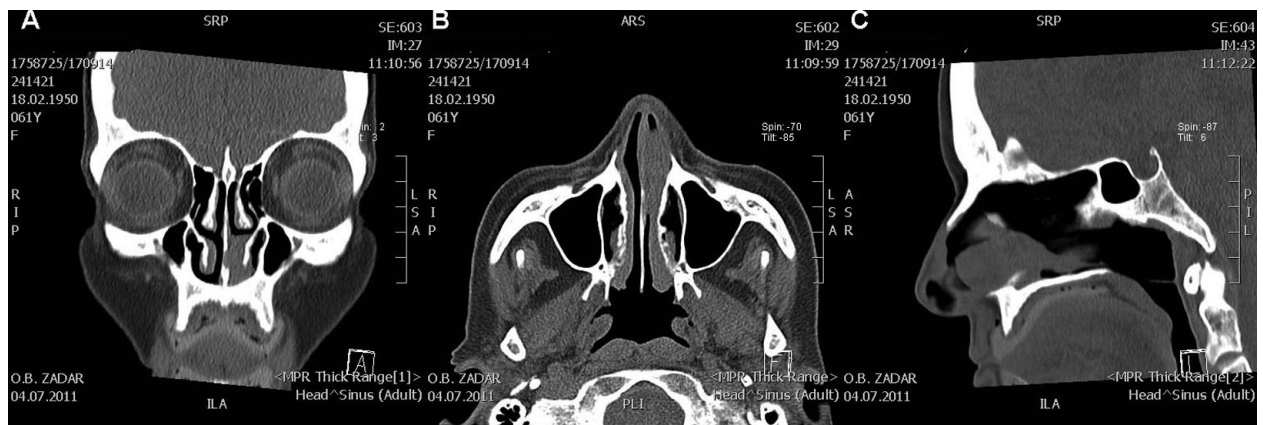
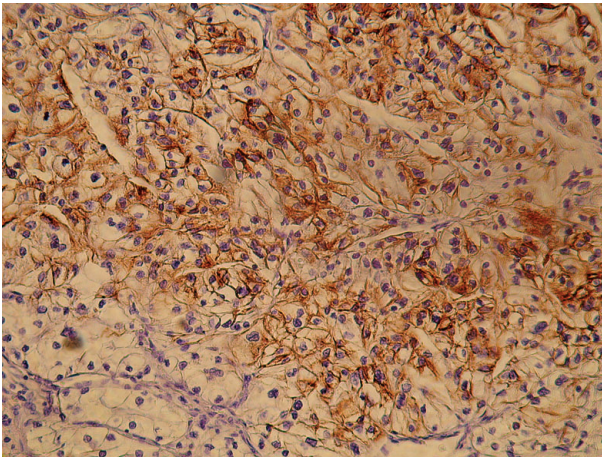


Fig. 2. Computed tomography scan showing soft tumor mass in the nasal cavity with no calcification or erosion of the surrounding bone: frontal (A), horizontal (B) and sagittal (C) projection.



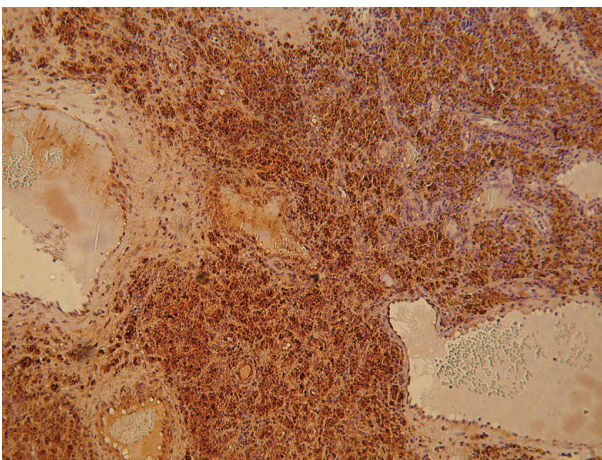


*Fig. 4. Strongly positive cytoplasmic immunostaining with epithelial membrane antigen (EMA, X100).*

Department for further treatment. Unfortunately, six months after the surgery, the patient died due to complications of multiorgan failure.

## Discussion

About 14%-16% of RCC patients have metastases above the clavicle, which makes this tumor the third most frequent infraclavicular primary tumor to metastasize to the head and neck and the first to metastasize to the sinonasal region<sup>1,3,4,7</sup>. Sinonasal metastasis can be the presenting feature of RCC in almost 8% of patients<sup>1</sup>. Nevertheless, only 1% of patients with the hypernephroid type of RCC have no other obvi-



*Fig. 5. Strongly positive cytoplasmic immunostaining (vimentin, X100).*

ous metastasis except for the head and neck<sup>1</sup>. Thyroid gland is the most common site of metastasis for this tumor, but it can also occur in the cervical lymphatic vessels, the mandible, the sinonasal cavity, and the skin of the face and scalp<sup>1,3</sup>. We report on a case of RCC metastases to the head and neck region (nasal cavity). The clinical course of these tumors is very particular; while some hypernephromas regress spontaneously, others demonstrate metastases several years after initial treatment. Indeed, a case of a recurrent disease 17 years after initial nephrectomy has been reported<sup>3</sup>. In our case, the recurrent disease to the head and neck appeared two years after initial treatment. The metastatic spread to the head and neck is either *via* hematogenous route (invasion of the local vascular network; through the atrial septal defect; bypassing the pulmonary capillary filtration mechanisms; tumor emboli travelling past the inferior vena cava; associated multiple arteriovenous shunts) or an alternative lymphatic route (*via* regional lymphatic vessels into the thoracic duct). Once the tumor reaches the head and neck, it can anastomose with the great veins of the head and spread to the nose and sinuses, face and scalp skin and thyroid gland<sup>1,4,5</sup>. Due to a very vascular tumor stroma, epistaxis is the most common symptom of the sinonasal tumor metastasis.

High vascularity of the tumor is caused by Hippel-Lindau gene mutation responsible for up-regulation of hypoxia induced factor 1a that causes angiogenesis through vascular endothelial growth factor up-regulation. Other possible symptoms of the sinonasal tumor metastases are nasal obstruction, facial pain and swelling, orbital pain and protrusion<sup>5,8,9</sup>. In the present case, recurrent epistaxis and nasal obstruction were the leading symptoms of the disease. Differential diagnosis of a sinonasal lesion with epistaxis includes hemangioma, angioendothelioma, Wegener's granulomatosis and midline granuloma. However, a bleeding necrotic mass in the sinonasal cavity should always be suspected of primary RCC that need to be either diagnosed or ruled out.

Radiological examination (CT scan) is valuable in the diagnosis of the disease extent. RCC metastases to the sinonasal tract have similar radiological appearances to the primary malignant lesions in this region. The enhancement, destruction, and lack of tumor calcification should suggest metastatic hypernephroma<sup>1</sup>.

In the present case, CT scan showed a soft tissue mass, with no destruction of the surrounding bone structures and no calcification.

Renal cell carcinoma metastases are mainly multiple, but metastases in the sinonasal cavity are usually single. Patients with single lesions should be treated surgically very aggressively because it offers the best possible treatment outcome. In cases of multiple tumors, surgery is mainly limited to tumor debulking and diagnostic purposes.

Another possible treatment option for these tumors is radiotherapy<sup>1,10</sup>. While these tumors are primarily described as radio-resistant, recent studies showed good radiotherapy responses (palliative response in 86% of treated patients)<sup>1,3,4</sup>. Furthermore, immunotherapy has also been proposed as a possible optional treatment for metastatic RCC<sup>5,10</sup>. In general, the 5-year survival rate after nephrectomy is 60%-75%; however, with multiorgan metastases, the 5-year survival rate is significantly lower, 0-7%<sup>3</sup>. Unfortunately, our patient died within the first year of metastasis treatment due to the extensive tumor involvement of multiple internal organs.

## Conclusion

Although RCC metastasis to the head and neck is very rare, it should be first suspected when investigating a metastatic tumor in this region. Surgical excision offers the best hope for long term survival and reduces pain, epistaxis, and disfigurement from the expanding

tumor. In case of unresectable tumor, other treatment options should be considered such as radiotherapy, immunotherapy and chemotherapy.

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## Sažetak

### METASTAZA KARCINOMA BUBREGA U NOSNO-SINUSNOJ ŠUPLJINI

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Od svih malignih tumora ljudskog organizma tumor bubrega je zastupljen u oko 3% slučajeva. Česta mjesta metastaziranja su pluća, kosti, jetra, mozak i nadbubrežna žlijezda. Pojava metastaza ovoga karcinoma u području glave i vrata kreće se oko 15%-30%. Postotak petogodišnjeg preživljenja nakon nefrektomije je 60%-75%, dok je istovjetno preživljenje s prisutnim metastazama znatno kraće, 0-7%. U ovom radu prikazuje se bolesnica kojoj je dijagnosticiran karcinom bubrega s metastazom u nosnoj šupljini i paranasalnim sinusima. Dijagnostički postupak i kirurško liječenje obavljeno je u Općoj bolnici Zadar, Odjel otorinolaringologije i kirurgije glave i vrata. Tumor je uspješno kirurški odstranjen, ali je bolesnica preminula nakon godinu dana zbog višeorganskih metastaza. Metastaza bubrežnog karcinoma u području glave i vrata je vrlo rijetka. Kirurška ekscizija je metoda izbora, a u slučaju neresektabilnog tumora moguće je primijeniti radioterapiju, imunoterapiju i kemoterapiju.

Ključne riječi: *Karcinom bubrežnih stanica; Tumorske metastaze; Paranasalni sinus, tumori; Prikazi slučaja*