

# Cardiac Metastases of Renal Cell Carcinoma Revealed by Syncope: Diagnosis and Treatment

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## Key Words

Renal cell carcinoma · Cardiac metastases · Target therapy

## Abstract

**Introduction:** Cardiac metastases from renal cell carcinoma are very rare. In this report, we describe a case of ventricular metastases in the absence of vena cava or right atrial involvement. **Case Report:** We report the case of a 60-year-old man who had a past history of heavy tobacco intake and well-controlled arterial hypertension. He experienced sudden-onset palpitations, lost consciousness and, as a result, was involved in an accident on the public highway. Cardiac arrhythmia was suspected and, therefore, transthoracic echocardiography was suggested, which revealed a large right ventricular mass. Chest and abdominal computed tomography demonstrated a mass in the right ventricle, but without contiguous vena cava involvement, and a right renal mass related to the probable neoplasm. An ultrasound-guided renal biopsy showed a clear-cell renal cell carcinoma. A bone scan revealed a metastatic bone disease. The patient was started on sunitinib treatment, which was well tolerated. However, approximately 8 months later, reevaluation showed pulmonary metastases. The patient was subsequently started on treatment with everolimus, which, however, was poorly tolerated. Two months later, the patient died due to terminal respiratory insufficiency. **Discussion:** Based on the literature and our observations in this case, targeted antiangiogenic therapy should be considered as a viable therapeutic alternative to metastasectomy for patients with inoperable cardiac metastatic disease as long as there is no baseline systolic or diastolic dysfunction. The case also emphasizes the importance of a thorough history review and physical examination in the workup of patients with syncope.

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## Introduction

Renal cell carcinoma (RCC) accounts for 2–3% of all adult malignancies and is the third most frequent urological malignancy after prostate and bladder cancer. Approximately one third of patients present metastatic disease at diagnosis. Additionally, 30% of all other patients develop metastases at a later stage of their disease [1]. The most common sites of RCC metastases are the bone, liver, brain, lymphatic and lung. Cardiac metastases are rarer and were the object of only a few publications [2]. The most common mechanism of cardiac metastases is that of the extension of a tumor column to the vena cava as a luminal mass, with growth along the caval wall into the right heart chambers. Other possible mechanisms are that tumor cells from the kidney may disseminate to the heart by retrograde lymphatic or lymphohematogenous spread through the thoracic duct into the superior vena cava, or by the hematogenous spread of embolic cells [3]. In this report, we describe a case of ventricular metastases from RCC in the absence of vena cava or right atrial involvement, explain our novel management, and review the current approaches to treating such cases.

## Case Report

We present the case of a 60-year-old man who had a past history of heavy tobacco intake (33 pack-years) but did not drink alcohol. In addition, he suffered from arterial hypertension, which was well controlled by an angiotensin-converting enzyme inhibitor (captopril).

He experienced sudden-onset palpitations, lost consciousness and, as a result, was involved in an accident on the public highway. On arrival to the emergency room, clinical and radiographic examination showed some bruises of the face and the right shoulder. The patient had no history of antecedent chest pain, shortness of breath or dizziness. On physical examination, his blood pressure was 135/82 mm Hg and his heart rate was 77 beats/min. The patient's lungs were clear on auscultation with no abnormalities during the cardiac examination. The patient's abdomen was soft and nontender. An electrocardiogram showed normal sinus rhythm, with a prolonged QT interval. A cardiology consultation was requested to assess the cause of the underlying syncope and determine the significance of the abnormal electrocardiogram. Cardiac arrhythmia was suspected and, therefore, transthoracic echocardiography was suggested, which revealed an ejection fraction of 60% and a large right ventricular mass measuring 5.4 × 5.2 cm (fig. 1). There was no mass within the inferior vena cava or in the right atrium. Ultrasound of the abdomen showed a 10 × 11 cm right renal mass without renal obstruction. Contrast-enhanced chest and abdominal computed tomography (CT) demonstrated a mass in the right ventricle, but without contiguous vena cava involvement (fig. 2), and a right renal mass of 11.9 cm in size related to the probable neoplasm (fig. 3). The mass was adjacent to the renal fascia. There was no involvement of the renal vessels and no retroperitoneal nodes. An ultrasound-guided renal biopsy showed a clear-cell RCC. A bone scintigraphy showed hot spots in the cranium and the ribs in favor of metastatic bone disease.

The patient was started on sunitinib treatment (50 mg/day – 4 weeks on, 2 weeks off) with intravenous zoledronic acid (4 mg/6 weeks), which was well tolerated. However, approximately 8 months later, the patient presented dyspnea at rest. A reevaluation CT scan showed a pulmonary metastases with several mediastinal nodes and left pleural effusion. It was decided that a change in systemic therapy was needed given the progression of lung metastatic disease. The patient was subsequently started on a treatment with everolimus

(10 mg once daily), which was poorly tolerated with persistent transaminitis despite a decrease in dose (5 mg daily). Two months later, the patient was admitted to our department due to terminal respiratory insufficiency for comfort measures and terminal illness care. He died 2 days later.

## Discussion

Although primary cardiac tumors are rare, cardiac metastases are not infrequent, with autopsy series having reported a 5- to 20-percent incidence of metastatic carcinomas to the heart and pericardium in patients dying of malignancies [3]. The most common secondary tumors of the heart originate from leukemia, melanoma, lung cancer, breast cancer, and lymphoma. Cardiac metastases from RCC, which are extremely rare, usually occur in either of 2 circumstances. First, advanced RCC characteristically extends into the renal vein and the inferior vena cava in 5–15% of patients, and into the right atrium in about 1% of patients, thereby obstructing venous return to the heart. Second, there can be a primary tumor that metastasizes to the heart, which occurs in 10–20% of patients who are dying of widespread, systemic RCC [3, 4].

Clinically, secondary heart tumors usually remain silent, particularly as the vast majority of cardiac metastases are small. Frequently, cardiac involvement is not noticed until after death. However, ultrasound examination of the heart should be performed as soon as symptoms of heart failure, angina pectoris, embolism or rhythm disturbances develop, or a new heart murmur becomes audible, or as soon as heart size increases radiologically. Additional information may be obtained by CT or nuclear magnetic resonance imaging [5, 6].

Cardiac involvement in metastatic RCC poses a unique therapeutic challenge. Surgical resection is only indicated in exceptional cases of solitary intracavitary heart metastases, leading to obliteration of cardiac chambers or valve obstruction if the tumor of origin was surgically resected in toto, and the patient appears to have a good prognosis [7]. However, in the majority of cases, when the metastases are diffuse, the treatment is palliative. Metastatic RCC is highly resistant to cytotoxic agents, hormones, and radiotherapy. In order to improve the outcome in advanced RCC, different treatments have been investigated, including immunotherapy (interleukin 2, interferon) and targeted therapeutic agents (sunitinib, sorafenib, pazopanib, axitinib, bevacizumab, temsirolimus and everolimus), which are now standard treatment for metastatic RCC [1, 4, 7].

Although these treatments have transformed the prognosis of metastatic RCC in recent years, their efficacy and safety in treating patients with metastatic disease in highly vascular organs such as the heart are not currently well known, with only a few reports on this topic [1, 7]. After a careful review of the risks and benefits associated with sunitinib, we decided to pursue this novel therapeutic approach, which has been shown to be effective in stabilizing the size of cardiac and bone metastases, and no significant cardiotoxicity has occurred.

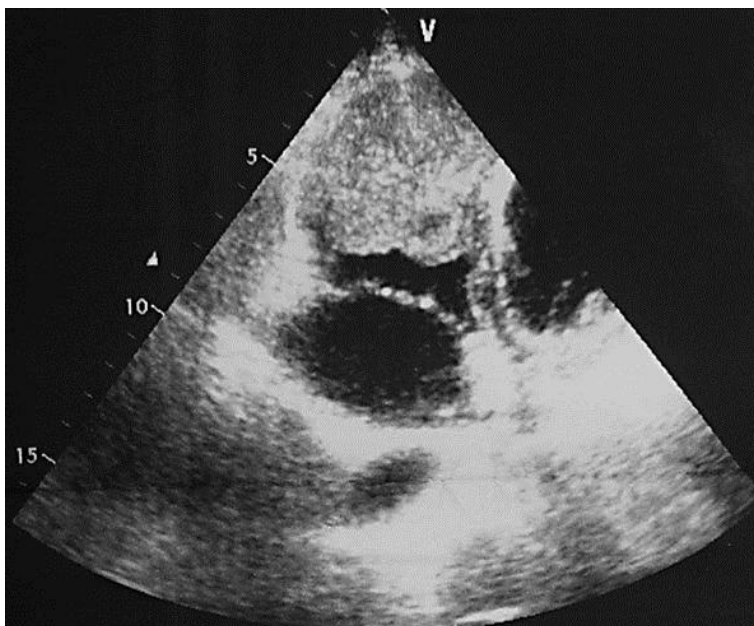
On reviewing the literature, the present case report is one of the few cases that describe a right ventricular metastatic tumor arising from RCC in the absence of vena cava or right atrial involvement. We suggest that despite potential vascular toxicities, targeted antiangiogenic therapy should be considered as a viable therapeutic alternative to metastasectomy for patients with inoperable cardiac metastatic disease as long as there is no baseline systolic or diastolic dysfunction. The case also emphasizes the importance of a thorough history review and physical examination in the workup of patients with syncope.

### Disclosure Statement

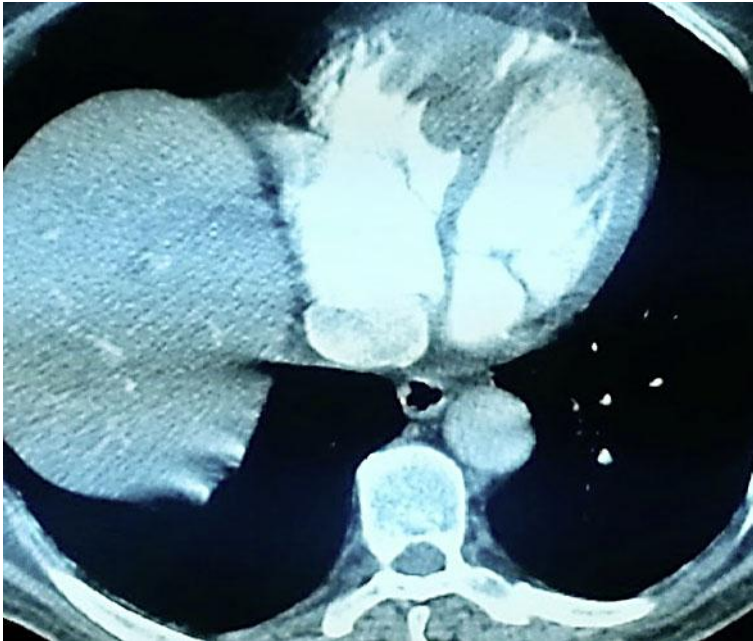
The authors have no conflicts of interest to declare.

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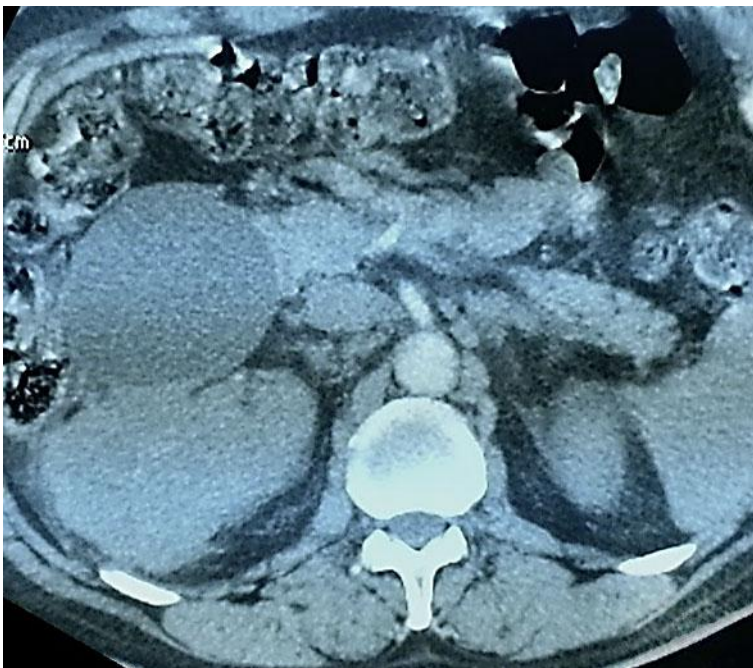
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**Fig. 1.** Large right ventricular mass in transthoracic echocardiography.



**Fig. 2.** Right ventricular metastases in the chest CT scan.



**Fig. 3.** Tumor of the right kidney in the abdomen CT scan.