

# Renal cell carcinoma with metachronous metastasis to the contralateral adrenal gland and urinary bladder: A case report

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**Abstract.** The adrenal gland and urinary bladder are rare localizations of metastases of renal cell carcinoma (RCC). In the present study, a case of metastasis to the contralateral adrenal gland and urinary bladder of clear cell-type RCC (ccRCC) in the left kidney is reported in a male who had undergone left radical nephrectomy at 55 years of age. Computed tomography (CT) revealed a mass in the right adrenal gland 5 years following surgery, and type-B ultrasound demonstrated a 1.0-cm solid space-occupying lesion in the right wall of the bladder. Consequently, laparoscopic right adrenalectomy and transurethral resection of the bladder tumor were performed. Furthermore, based on histopathological examination and immunohistochemical staining, the patient was pathologically diagnosed with contralateral adrenal gland and urinary bladder metastasis of ccRCC. CT performed at the 1-year follow-up detected multiple solid space-occupying lesions in the right kidney. Therefore, the patient was treated with sunitinib targeted therapy. To date, the patient is generally in good condition, without evident drug side effects or complaints of discomfort.

## Introduction

Renal cell carcinoma (RCC) accounts for 3% of all adult malignancies and 85% of all primary renal tumors; RCC is the third most common type of urological cancer, after prostate and bladder cancer (1). Currently, the incidence of RCC is rising, due to the increased number of incidental findings by imaging tests. In 2013, it was estimated that there will be 65,150 new cases of kidney and renal pelvis cancers and 13,680 cancer-related mortalities in the United States (2). It has been reported that the five-year cancer-related survival

rate was 90.4% for patients with localized disease, 62.3% for patients with regional lymph nodes metastasis, 10.4% for patients with distal metastasis (3). Of the newly diagnosed cases of RCC, ~25-50% will develop metastatic disease subsequent to surgical resection of the primary renal mass (4). RCC frequently metastasizes to distal organs, such as lungs, abdomen, bones and brain. Contralateral adrenal gland and urinary bladder metastasis are rare, and have been previously described case reports (5,6). To the best of our knowledge, RCC with metachronous metastasis to the contralateral adrenal and bladder has not been reported. For treatment of metastatic renal cell carcinoma, complete resection of metastases or not remains controversial (7). Cancer-specific survival rates between metastases resected and non-resected populations have previously been reported and prolonged survival was observed with metastases resection (8,9). In the present study, an unusual case of clear cell-type RCC (ccRCC) with metachronous metastasis to the contralateral adrenal gland and urinary bladder 5 years following nephrectomy is reported.

## Case report

A 55-year-old male was referred to the Department of Urology of the Zhejiang Xiaoshan Hospital (Hangzhou, China) in October 2005, exhibiting a case of left-kidney RCC. Radical nephrectomy was performed (Fig. 1), and the postoperative pathology findings confirmed cc-type and pT<sub>1a</sub>N<sub>0</sub>M<sub>0</sub>, according to the American Joint Committee on Cancer 2009 cancer staging (Fig. 2) (10). No recurrence was observed during the follow-up period until November 2010, when upper abdominal computed tomography (CT) revealed a 40x45-mm enhanced mass in the right adrenal gland (Fig. 3). Subsequent laboratory tests demonstrated the tumor to be hormonally inactive. In addition, type-B ultrasound revealed a 1.0-cm solid space-occupying lesion in the right wall of the bladder. Thoracic CT and bone scan did not identify any other metastases.

Following hospitalization, laparoscopic right adrenalectomy and transurethral resection of the bladder tumor were performed. Histopathological examination of the resected tissues confirmed cc carcinoma, which was identical to that of the left renal tumor previously experienced by the patient (Figs. 4-7). CT and intravesical instillation chemotherapy were

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Figure 1. Preoperative magnetic resonance imaging demonstrated the left renal lesion to be located in the lower pole.

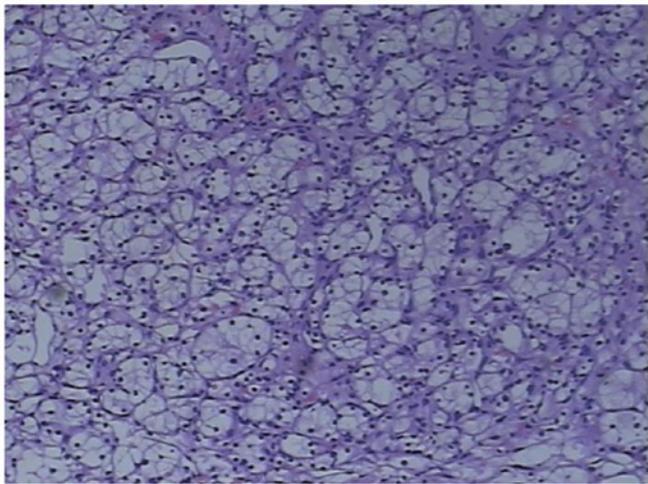


Figure 2. Hematoxylin-eosin staining of the right renal specimen revealed clear renal cell carcinoma. Formalin-fixed paraffin-embedded renal specimen were cut into 4- $\mu$ m sections and stained with hematoxylin-eosin to evaluate the cell pattern. The sections were scanned under a light microscope and images were captured at a magnification of  $\times 200$ . The lesional cells exhibited a nested growth pattern, in a background of delicate, arborizing vasculature.

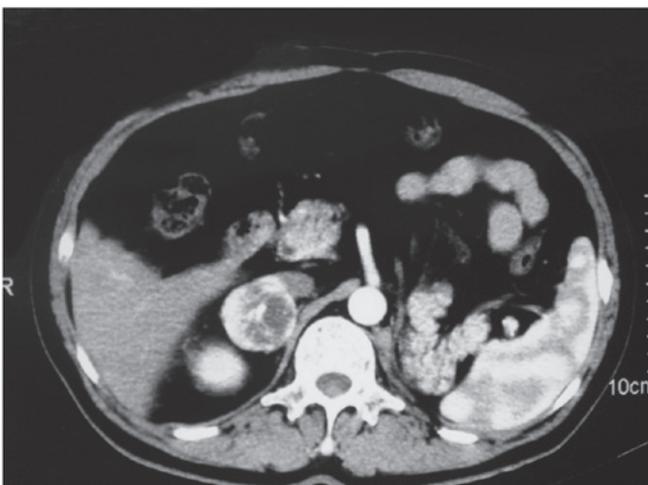


Figure 3. Computed tomography identified a 40x45-mm enhanced mass in the right adrenal gland.

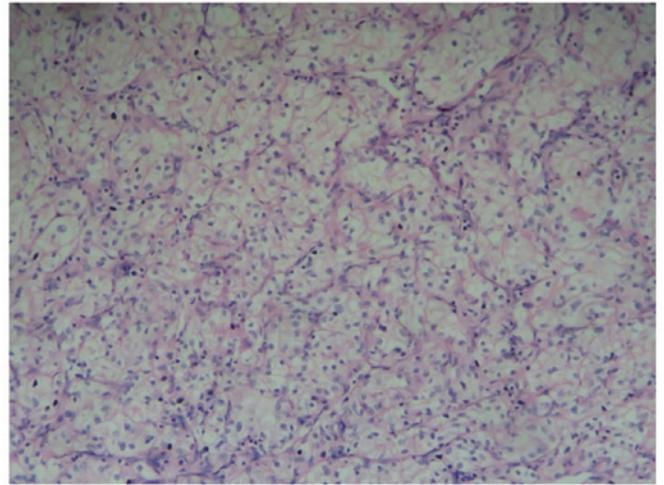


Figure 4. Hematoxylin-eosin stain of the right adrenal gland specimen revealed metastatic clear cell renal cell carcinoma replacing normal adrenal tissue ( $\times 200$ ).

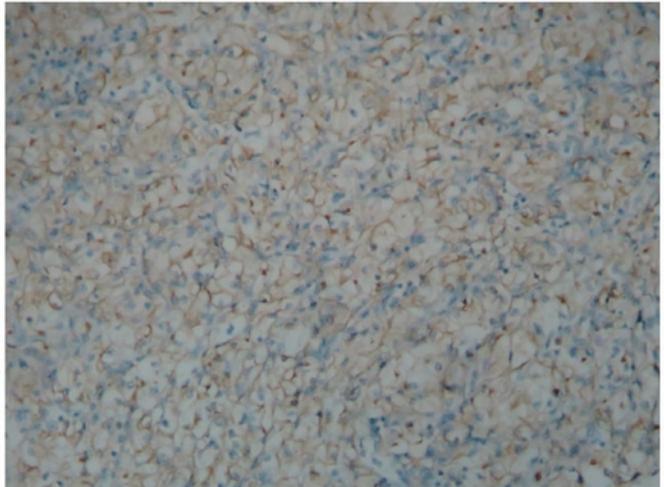


Figure 5. The slides were examined under light microscope at a magnification of  $\times 200$ . The infiltrated tumor cells in the right adrenal gland were positive for CD10.

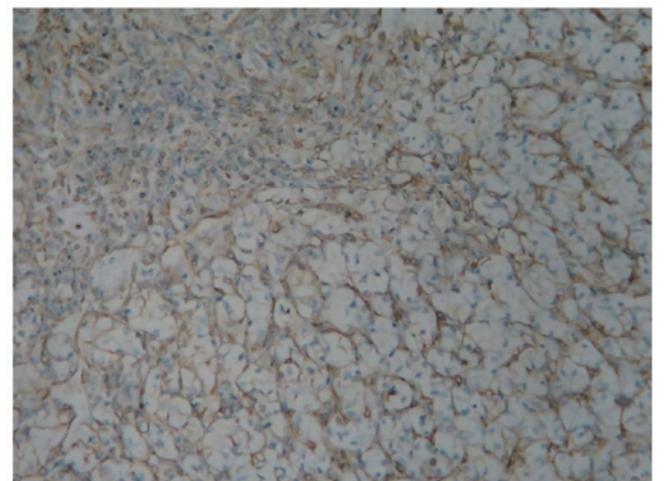


Figure 6. The slides were examined under light microscope at a magnification of  $\times 200$ . The infiltrated tumor cells in the right adrenal gland were positive for vimentin.

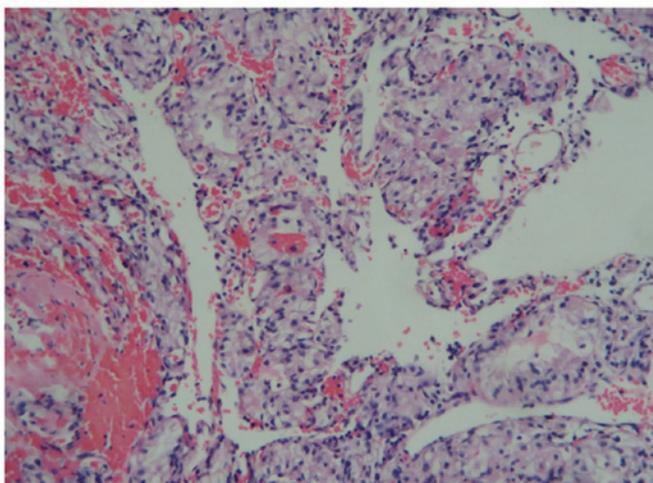


Figure 7. Hematoxylin-eosin staining of the urinary bladder revealed metastatic renal cell carcinoma. The tumor shows a clear cell pattern that is identical, histologically, to the previous renal cell carcinoma. Original magnification,  $\times 200$ .

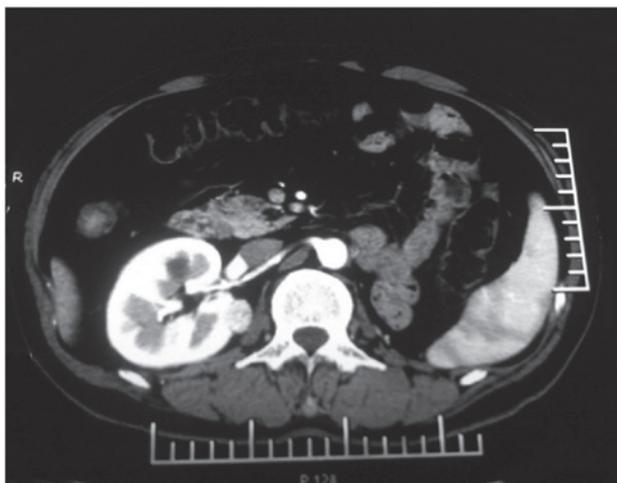


Figure 8. Computed tomography scan detected multiple solid space-occupying lesions in the right kidney.

regularly reviewed following surgery. However, 1 year later, CT scanning detected multiple solid space-occupying lesions in the right kidney (Fig. 8). Consequently, the patient was treated with first-line sunitinib targeted therapy.

At present, the patient is generally in good condition, without obvious drug side effects and discomfort complaint.

## Discussion

RCC possesses a propensity for distal metastasis, which may occur in all organs, including the lung, lymph node, liver and bone. However, RCC rarely metastasizes to the adrenal gland and urinary bladder (4,11). In a previous study of  $>400$  patients who had undergone radical nephrectomy for RCC, isolated contralateral adrenal gland metastases accounted for 2.5% of the total cases (6,12). Additionally, Saitoh *et al* (13) reported 1.6% of clinically detectable bladder metastases in 1,451 autopsy cases of patients with RCC (5,6,12,14).

Nonetheless, cRCC with metachronous metastasis to the contralateral adrenal gland and urinary bladder has not been reported thus far.

Contralateral adrenal gland metastasis is hypothesized to develop through the hematogenous route. Dieckmann *et al* (15) suggested that the adrenal gland may act as 'fertile soil' and 'raise' the seeding tumor cells from the contralateral primary RCC, since the adrenal gland exhibits high affinity for metastases of RCC (15,16). The mechanism by which RCC metastasizes to the urinary bladder remains unclear, although it has been suggested to occur via the hematogenous route, lymphatic system or urinary stream (5). The hematogenous metastasis pathway may occur through the systemic circulation or through retrograde venous dissemination, such as via the gonadal and ureteral vein, when the renal vein is obstructed by cancer emboli (14). When a tumor invades the kidney pelvis, or following diagnostic biopsy using an ureteroscope, it may metastasize via the urinary stream (5). Additionally, direct extension and seeding implantation have been proposed as potential mechanisms for metastasis of RCC, since cancer cells have been detected in the urine of patients with RCC (17).

Patients with distal metastases present a worse prognosis than those without metastatic tumors, with a 5-year survival rate of  $<10\%$  (11), although radical nephrectomy and resection of a single or limited metastases may prolong the survival rate by 30% (6). Patients with metastatic RCC may benefit from minimal invasive surgeries, such as laparoscopic and endoscopic resection of metastatic neoplasms from RCC (6). However, depending on the tumor size and the strength of the adhesion to the peripheral organs, minimal invasive surgeries may not always be possible to perform. Surgical treatments rarely present complications, and should be recommended in all cases of RCC for a curative outcome (18). Despite the fact that the majority of patients with RCC that had undergone surgery succumbed as a result of RCC, their survival time was longer than those who had not undergone surgical treatment (6).

In a randomized phase III trial, Motzer *et al* (19) reported that the median progression-free survival of patients treated with sunitinib was 11 months. In the present case, the patient experienced metastasis of RCC to the contralateral kidney following resection of the adrenal gland and urinary bladder tumor. Therefore, the patient was advised to receive first-line sunitinib targeted therapy, which is known to be an effective treatment for metastatic RCC (20). To date, the patient is generally in good condition, without any evidence of drug side effects or complaints of discomfort.

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