

# Chromophobe renal cell carcinoma with ipsilateral ureteral urothelial carcinoma: A case report

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**Abstract.** It is very rare for different types of urological tumours to occur together, and it is even rarer for chromophobe renal cell carcinoma (CRCC) to be combined with ipsilateral ureteral urothelial carcinoma (UUC), and the symptoms are relatively homogeneous, mostly presenting as symptoms that can be observed in malignant tumours alone, and therefore are often easily missed. In the present study, a case of a patient who was admitted to the hospital for more than 3 months with no obvious cause of terminal carnivorous hematuria was reported, and ureteral carcinoma was considered in the preoperative diagnosis but not renal carcinoma. After completion of preoperative tests, laparoscopic right nephrectomy and right ureterectomy was performed. The postoperative pathological diagnosis was CRCC of the right side and low-grade UUC of the right side, and the patient did not show any significant abnormality at the postoperative follow-up. By discussing this case and reviewing the relevant literature, the present study provides clinicians with more insight.

## Introduction

Chromophobe renal cell carcinoma (CRCC) originates from the distal convoluted tubule and collecting tubule and is a distinct subtype of RCC (1), accounting for ~5-10% of RCC (2) and is the third most common type of renal cancer (3). Upper tract urothelial carcinoma (UTUC) is a relatively rare type of uroepithelial malignancy, including renal pelvic carcinoma and ureteral carcinoma, and the incidence of UTUC has been reported to account for 5-10% of all uroepithelial carcinomas in Europe and the United States (4). Multiple primary cancers of the urinary tract are very rare (5), and it has been recently

reported that renal cancer accounts for 2% of all multiple primary cancers in the first and 2.4% in the second (6). The combination of ureteral urothelial carcinoma (UUC) with CRCC is extremely rare and has hardly been reported. The treatment of multiple primary cancers of the urinary tract remains controversial, but surgery remains the best option. In the present study, a case of CRCC combined with ipsilateral UUC and full-length resection of the affected kidney and ureter was presented. It is combined with the relevant literature to provide relevant reference material for this type of disease.

## Case report

A 59-year-old male patient was admitted to the Department of Urology of the Affiliated Hospital of Zunyi Medical University (Guizhou, China) in November 2021 with no apparent cause of terminal carnal hematuria for >3 months. The patient had no urinary frequency, urgency, or painful urination and no significant lumbar pain. He had undergone laparoscopic cholecystectomy 20 years ago and denied family history of hereditary disease. Renal function tests showed blood creatinine 101  $\mu\text{mol/l}$ , uric acid 402  $\mu\text{mol/l}$ , GFR: right kidney, non-functional; and left kidney 62.03 ml/min. Computed tomography (CT) suggested fluid in the right kidney and upper right ureter, multiple cysts in the right kidney with partial marginal calcification (Fig. 1A), dilatation and fluid in the middle and lower right ureter, slight thickening of part of the ureteral wall, and occupying lesions observed in the ureter (Fig. 1B). Cystoscopy suggested that a persistent hematuric ejection was observed at the opening of the right ureter. The initial diagnosis was: i) Right ureteral space-occupying lesion: tumour; ii) right hydronephrosis with no function and iii) right renal cyst. Preoperatively, the possibility of renal malignancy was not considered. After perfect preoperative preparation, laparoscopic right nephrectomy and right ureteral resection was performed under general anesthesia, and the resected tissue was sent for pathological examination.

Pathological findings in general: Right post-renal and ureterectomy specimen with a dilated, cystic nephrectomy with smooth walls and a greyish-yellow, multi-housed mass at the upper pole of the kidney, ~3.5x3x2.5 cm in size, with poorly defined corticomedullary demarcation. A cauliflower-like neoplasm measuring ~5x0.8x0.7 cm was identified 1.8 cm from the ureteral section, occupying the entire ureteral lumen

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Table I. Different pathological types of renal cell carcinoma combined with UUC.

	Duration of medical history	Average maximum diameter of renal tumours	Average maximum diameter of ureteral tumours
Papillary renal cell carcinoma combined with UCC	Shorter (~1 month)	~2 cm	~2 cm
Clear cell renal cell carcinoma combined with UUC	Medium (~2 months)	~3 cm	~4 cm
CRCC combined with UCC	Longer (>3 months)	~4 cm	~5 cm

UUC, ureteral urothelial carcinoma; CRCC, chromophobe renal cell carcinoma.

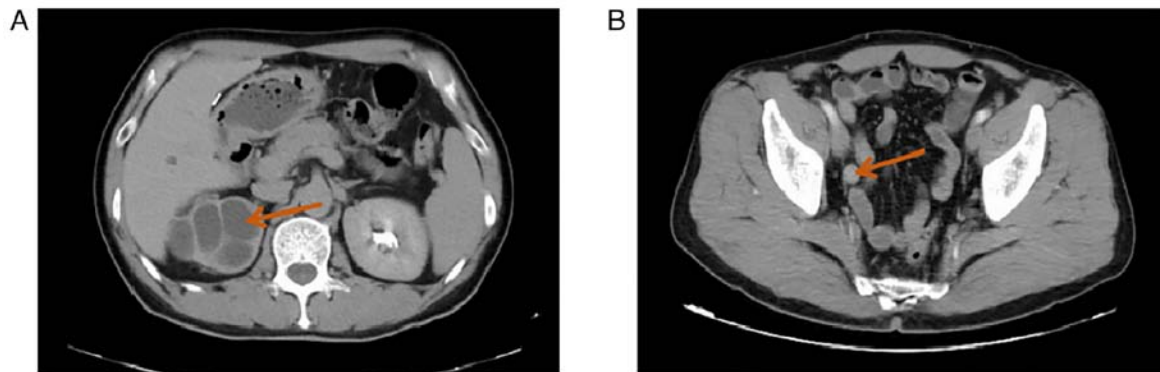


Figure 1. Computed tomography of the whole abdomen. (A) Hydronephrosis of the right kidney with multiple cysts in the right kidney and partial marginal calcification. (B) Occupational lesion in the right lower and middle ureter.



Figure 2. Removal of kidney and ureter.

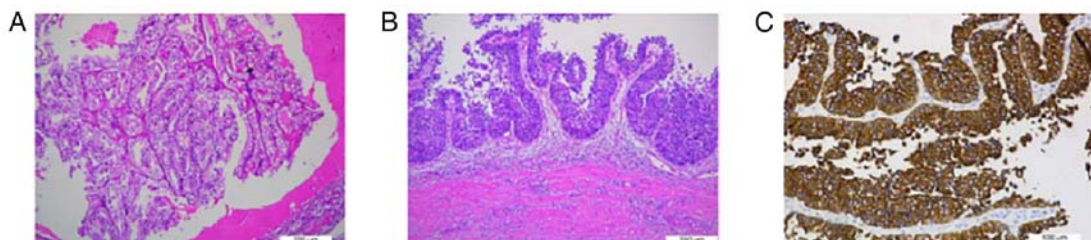


Figure 3. Pathological examination. (A) Excised kidney (H&E; magnification, x100). (B) Removed ureter (H&E; magnification, x100). (C) Ureteral tumour cells positive for creatinine kinase.

(Fig. 2). Microscopic examination: i) Low grade RCC of the right kidney. The tumour cells were tightly arranged, with abundant cytoplasm, pale and transparent, slightly reticulated, with clear envelope, moderate or mildly eccentric nuclei, inconspicuous heterogeneity and rare nuclear division (H&E staining at room temperature, light microscope, slicing thickness of 5  $\mu$ m). The nuclei were moderately or mildly eccentric, with no obvious heterogeneity. Immunohistochemistry suggested cancerous tissue: Positive for PAX-8, CA9, creatinine kinase (CK) 7, weakly positive for P504s, partially positive for CD10 and TFE3, negative for RCC and CD117. Combined with the morphological and immunohistochemical findings, CRCC was considered with WHO/ISUP classification of grade 2 (Fig. 3A). 2. Low grade UUC of the right side. The uroepithelium of the bladder was seen to be papillary with increased cellular hierarchy and loss of polar disorder, with large deep stained nuclei and visible nuclear division (H&E staining at room temperature, light microscope, slicing thickness of 5  $\mu$ m). There was local superficial infiltration and the cancer did not invade the muscular layer of the ureteral wall. No cancerous tissue was involved in the ureteral section and immunohistochemistry (CK staining at 37°C for 30 min, light microscope, slicing thickness of 5  $\mu$ m) showed positive CK of cancerous tissue (Fig. 3B and C).

After surgery, the patient was treated with anti-infection, hemostasis, fluid replacement and maintenance of water-electrolyte balance. The abdominal drainage tube was open and well positioned, with light red drainage, and was removed in the afternoon of the third postoperative day; the catheter drained light yellow urine daily; bladder irrigation chemotherapy was administered on the fourth postoperative day. The patient was discharged one week after the operation and was instructed to have bladder irrigation once a week for eight consecutive times and then changed to once a month for ten consecutive times. The patient was asked to repeat cystoscopy and CT of the whole abdomen every three months, and the results of the follow-up examinations showed no recurrence and the patient had no particular discomfort.

## Discussion

RCC accounts for 3% of adult tumours (7) and UTUC accounts for 5-10% of all urothelial carcinomas. However, it is very rare for different types of urological tumours to occur together. Graves and Templeton (8) reported the first case of renal cancer combined with UTUC in 1921. The majority of subsequent studies could be found to be kidney cancer combined with bladder or pelvis cancer, with the lowest proportion of kidney cancer combined with ureteral cancer (9). Oka *et al* (10) counted 1,352 cases of genitourinary tumours and only one case was RCC combined with urothelial metastatic cell carcinoma. There are few studies of CRCC combined with UUC and a small number of studies related to multiple primary cancers of the urinary tract, whether renal carcinoma combined with UUC or renal carcinoma combined with metastatic ureteral cancer, the type of renal carcinoma was almost always clear cell RCC, the reason for which is not clear. In terms of the location of tumour presentation, those located on the same side are slightly more frequently reported than those on different sides, but remain rare.

Most of the symptoms of different pathological types of kidney cancer combined with UCC are similar, with hematuria and back pain as the main symptoms (11). However, the duration of the patients' history and the maximum diameter of the tumors were found to be slightly different in the available studies. Patients with papillary RCC combined with UCC had a shorter history of ~1 month, with the average maximum diameter of the kidney tumor being ~2 cm and the average maximum diameter of the ureteral tumor being ~2 cm. Patients with clear cell RCC combined with UUC had the second longest history, ~2 months, with an average maximum diameter of ~3 cm for renal tumours and 4 cm for ureteral tumours; patients with CRCC combined with UCC had a longer history, >3 months on average, with an average maximum diameter of ~4 cm for renal tumours and 5 cm for ureteral tumours (Table I) (12-16). Although the early symptoms of simple kidney cancer are not obvious, and even ~50% of the patients have no discomfort (17). When the typical triad of kidney cancer is present, most patients are already in the advanced stage and have a poor prognosis. The most common symptom of ureteral cancer is carnal hematuria, and patients often complain of hematuria. When repeated carnal hematuria, unilateral lumbar pain and upper urinary tract fluid accumulation are present, and after examination to exclude the possibility of urinary stones, the possibility of ureteral occupational lesions needs to be considered (18).

At this point, the likelihood of an occupying lesion in the ipsilateral kidney is extremely low, and most clinicians interrupt their diagnostic thinking at this point, which can easily lead to a missed or misdiagnosed occupying lesion in the ipsilateral kidney. Therefore, although the chance of different types of urological tumours occurring at the same time is very low, the possibility of the same or different types of tumours in other parts of the urinary tract should still be noted when a patient is examined and a detailed preoperative examination and clinical analysis is essential.

Ureteral carcinoma has been widely reported and may be primary to the uroepithelium or may result from metastatic clear cell RCC, thus identification of the source of ureteral carcinoma is also critical. CK7 and CK20 negative in metastatic clear cell urothelial carcinoma, are often positive for RCC antigen, Vimentin and PAX-8, as opposed to pathological findings in primary uroepithelial carcinoma (19). In this case, the immunohistochemical staining was positive for CK and negative for the rest, suggesting that the patient had ureteral carcinoma of primary uroepithelial origin. The etiology of co-occurrence of renal and ureteral carcinoma is unclear.

For the treatment of renal cancer combined with ureteral cancer, total nephro-ureterectomy remains the best treatment option at present, but in a separate discussion of surgical options for renal cancer, partial nephrectomy has become the preferred approach for patients with stage T1 (20). The 2020 European Society of Urology guidelines recommend that for single, <1 cm diameter, urological enhanced CT urography on which there is no surgery with preservation of the renal unit can be considered for low-grade upper urinary tract uroepithelial carcinoma with infiltrative manifestations, which allows for maximum tumour control while avoiding the side effects associated with radical resection. For certain special ureteral cancer patients, such as those with low malignancy and who

must undergo surgery to preserve the renal unit, complete tumour resection with end-to-end ureteral anastomosis, ileal substitution ureterotomy or autologous kidney transplantation can be the main treatment (21-23). By contrast, when renal cancer is combined with ipsilateral ureteral cancer, total ureterectomy remains recommended.

The prognosis of patients with multiple primary urological malignancies has been reported (24) as not being worse than that of patients with multiple primary malignancies, while Dutta *et al* (25) suggested that the prognosis of patients with multiple primary malignancies is mainly influenced by the more malignant tumour. It has also been revealed that their prognosis, although improved than that of metastatic tumours, remains poor overall (9). As there are few studies in the literature, low sample sizes and no systematic statistical analysis, it is not sufficient to draw definitive prognostic conclusions. However, early diagnosis and treatment will result in more treatment options and less trauma, and will certainly help the prognosis of patients.

In conclusion, although CRCC with ipsilateral UUC is extremely rare but not difficult to diagnose pathologically, it remains challenging to diagnose and treat early as well as to maximize the protection of renal function and improve the quality of life of patients, and more cases still need to be accumulated to understand their prognosis.

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Authors' contributions

PW and JD were responsible for clinical patient management. PW was responsible for data collection and article writing and literature review. LW provided pathology information. GL was responsible for article review and revision. GL and JD acted as project leaders for the aforementioned grants and financial support provided. All authors confirm the authenticity of the raw data in the article. All authors read and approved the final manuscript.

#### Ethics approval and consent to participate

Not applicable.

#### Patient consent for publication

Written informed consent for the publication of the patient's clinical information and images was obtained from the patient.

#### Competing interests

The authors declare that they have no competing interests.

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