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Recurrent papillary renal cell carcinoma with concomitant ipsilateral upper urinary tract urothelial carcinoma and metachronous urothelial carcinoma of the bladder

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Introduction

Concomitant renal cell carcinoma (RCC) and ipsilateral upper urinary tract urothelial carcinoma (UTUC) is very uncommon, with only about 50 reported cases in the literature.[1] Patients who developed synchronous, ipsilateral RCC and UTUC are on average 64.5-years-old, are 3-fold more likely to have disease in the left kidney and are more often men.[2] Of these, 24% have a significant smoking history and 34% ultimately develop bladder malignancy. To our knowledge, there have been no reported cases of simultaneous UTUC with recurrent RCC in the same kidney. Here, we present a novel case of recurrent RCC in a 59-year-old male with synchronous, ipsilateral UTUC and metachronous urothelial carcinoma of the bladder and prostate. We illustrate an unusual clinical phenomenon and highlight novel predictive markers and prognosticators to aid in monitoring and managing similar disease presentations.

Case presentation

This is a 59-year-old male with a 25-pack year smoking history who presented with gross hematuria and was found to have a 5.6 × 4.4 cm left renal mass suspicious for RCC and no evidence of metastases (Fig. 1). He underwent a robotic-assisted left laparoscopic partial nephrectomy without complication. His final pathology demonstrated a T3aNxM0 papillary renal cell carcinoma, clear cell subtype, Fuhrman Grade 2–3, with negative margins. He was monitored with surveillance computed tomography imaging. At two-years follow-up, a soft tissue mass occupying the left renal pelvis was visualized suspicious for UTUC (Fig. 2). Ureteroscopic biopsy identified high-grade papillary urothelial carcinoma of the renal pelvis. He subsequently underwent left robotic-assisted laparoscopic nephroureterectomy. Histopathological examination of the kidney and ureter not only revealed a 4.2 cm invasive high-grade papillary urothelial carcinoma of the renal pelvis (Fig. 3), but also a synchronous, incidental 0.8 cm recurrent papillary RCC. The RCC had a Fuhrman nuclear grade of 3 due to the presence of obvious irregular nuclei measuring greater than 20 μm and prominent large nucleoli at low power magnification. It did not have sarcomatoid features or exhibit lymphovascular invasion. At 6-month follow-up, the patient developed recurrent, intermittent gross hematuria. Cystourethroscopic evaluation demonstrated multiple papillary-appearing bladder tumors lateral to the left ureteral orifice. He then underwent transurethral resection of bladder tumors as well as transurethral prostate biopsy, which demonstrated non-invasive high-grade papillary urothelial carcinoma in both the bladder and prostate. His hematuria has since resolved and he is being monitored with computed tomographic imaging of the abdomen/pelvis for surveillance of his contralateral kidney/ureter and maintenance cystoscopy. He has also been referred to medical oncology for consideration of adjuvant immunotherapy in the setting of multiple primary malignant tumors.

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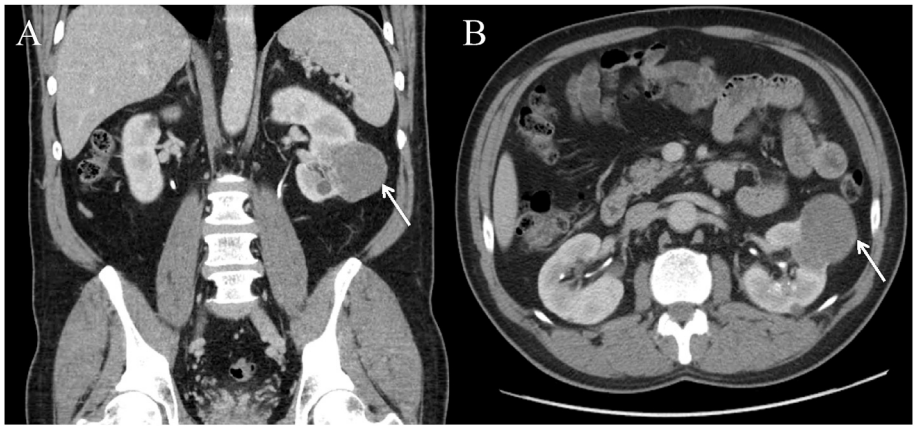

Fig. 1. Preoperative computed tomography (A) coronal (B) axial demonstrating a 5.6 × 4.4 cm exophytic mass in the left renal midpole anterior cortex suspicious for renal cell carcinoma.

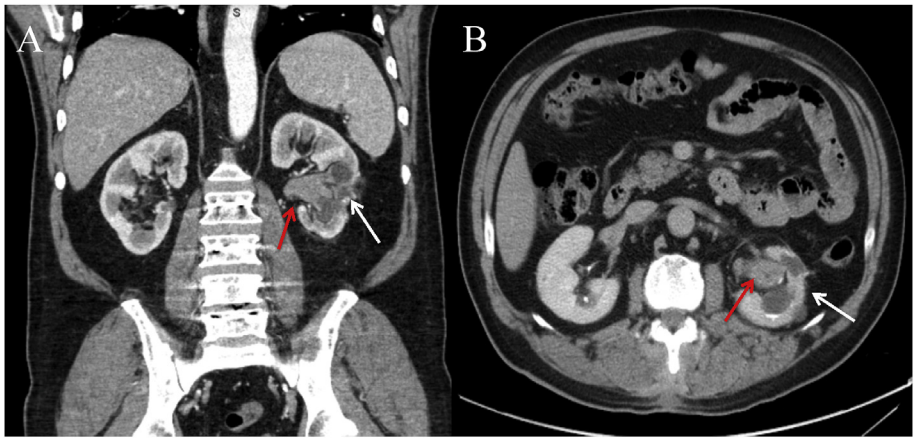

Fig. 2. Postoperative computed tomography (A) coronal and (B) axial demonstrating a 2.1 × 1.7 cm soft tissue mass occupying the left renal collecting system (red arrow) as well as postsurgical changes of the previously visualized left renal mass (white arrow).

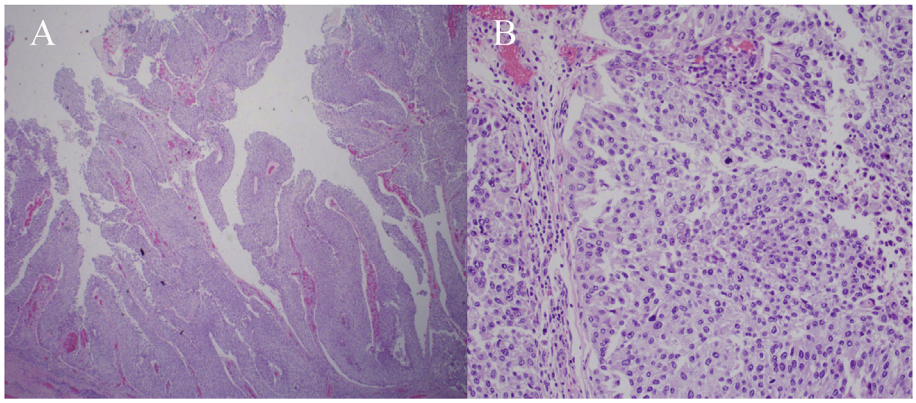

Fig. 3. Histopathological examination of soft tissue mass involving the left renal pelvis demonstrating high-grade invasive papillary urothelial carcinoma (A) H&E stain, ×100 (B) H&E stain, ×200.

Discussion

Concomitant development of RCC and UTUC in the ipsilateral kidney is an uncommon occurrence, of which recurrent RCC at the time of presentation is exceedingly rare. Conversely, metachronous urothelial carcinoma of the bladder in patients with UTUC has been well characterized, with an estimated incidence of 45%.[3] This case presentation of a unique clinical scenario demonstrating recurrent, synchronous, ipsilateral RCC and UTUC in the kidney with metachronous urothelial carcinoma of the bladder and prostate raises several key topics.

Firstly, risk factors for development of synchronous RCC and UTUC are similar to those of RCC and UTUC alone, with the most prevalent risk factor being cigarette smoking. This patient had a

prominent history of smoking, with smokers being two to three times more likely to develop RCC or UTUC than compared to non-smokers[8]. Carcinogenic compounds in tobacco smoke induce mutations in tumor suppressor genes (e.g. p53) and cellular markers of proliferation (e.g. Ki67), both of which are common genetic aberrancies in urothelial cancer.[4] For patients with multiple primary malignant tumors where concurrent smoking illustrates a direct impact on tumor suppressor gene down-regulation, it is imperative to mitigate such recognizable risk factors.

Disease recurrence following partial nephrectomy for localized disease in the setting of simultaneous urothelial carcinoma of the renal pelvis is unknown. Although cross-sectional imaging commonly detects incidental renal tumors, in this case there was no enhancing lesion appreciable in the surgical bed of the original partial nephrectomy on surveillance imaging. This may be attributed to the soft-tissue pelvicalyceal mass possibly impeding adequate enhancement along the anterior cortex. Nonetheless, in cases of solitary and localized RCC, approximately 20% will experience disease recurrence. Larger tumors (median 4.1 cm) and higher clinical stage at presentation (cT3 or greater) are associated with local tumor bed recurrence, both of which were present in this patient.[5] It is fitting that a similar risk stratification profile would predict disease recurrence in cases of concomitant UTUC.

Thirdly, predictive disease markers for recurrence of UTUC and development of metachronous bladder tumors may help elucidate closer surveillance management strategies for these patients. Metachronous bladder cancer in patients with UTUC has been largely attributed to be secondary to downward seeding of tumor cells.[4] Our patient developed multiple non-muscle invasive bladder cancers about 6-months post-operatively from his radical nephroureterectomy. Significant risk factors for metachronous bladder cancer include high-grade tumors and history of a non-functioning kidney, of which only the former was present in this case. When predicting prognosis of patients with UTUC and metachronous bladder cancer, a novel study recently analyzed cancer-specific survival of 88 patients treated with radical nephroureterectomy for UTUC and demonstrated that higher p53 tumor expression levels were an independent risk factor for poorer survival.[4] Expression level of p53, high-grade disease, and non-functioning ipsilateral kidney may, at the very least, be combined to prognosticate and individualize closer follow-up for patients at risk for recurrent disease in the setting of UTUC and metachronous bladder cancer.

Conclusions

We present the first case of recurrent RCC and concomitant, ipsilateral UTUC with metachronous urothelial carcinoma of the bladder and prostate. This case report highlights the need for closer surveillance for disease recurrence following partial nephrectomy in the setting of simultaneous renal pelvis urothelial carcinoma. The aggressiveness of this rare clinical presentation advocates the development of novel clinical-pathological markers such as p53 expression levels to improve disease surveillance.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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