# *Synchronous metastatic renal cell carcinoma to the genitourinary tract: two rare case reports and a review of the literature*

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*Synchronous metastasis of renal cell carcinoma (RCC) to the ureter or the bladder represents an extremely rare event. We report one case of synchronous metastasis of RCC to the ipsilateral ureter and one case of solitary synchronous metastasis of RCC to the urinary bladder. We review the literature and discuss possible mechanisms of dissemination. We discuss the surgical management of metastases from RCC as well as the surgical options in the treatment of these rare occurrences.*

**Key Words:** metastasis, renal cell carcinoma, ureter, bladder, synchronous

## First case presentation

A 73-year-old woman presented with persistent left shoulder pain after sustaining a fall 6 months prior. Magnetic resonance imaging (MRI) of the shoulder incidentally demonstrated multiple lung nodules, believed to be most consistent with a metastatic process. Ultrasonography revealed a 7.1 cm left upper pole renal mass. Subsequent MRI of the abdomen confirmed the presence of a 7 cm left posterior interpolar renal mass, but also revealed marked left hydronephrosis and proximal hydroureternephrosis to the mid lumbar ureteral level, where a 1 cm obstructing lesion was noted, Figure 1. Voided urine cytology revealed no evidence of urothelial carcinoma.

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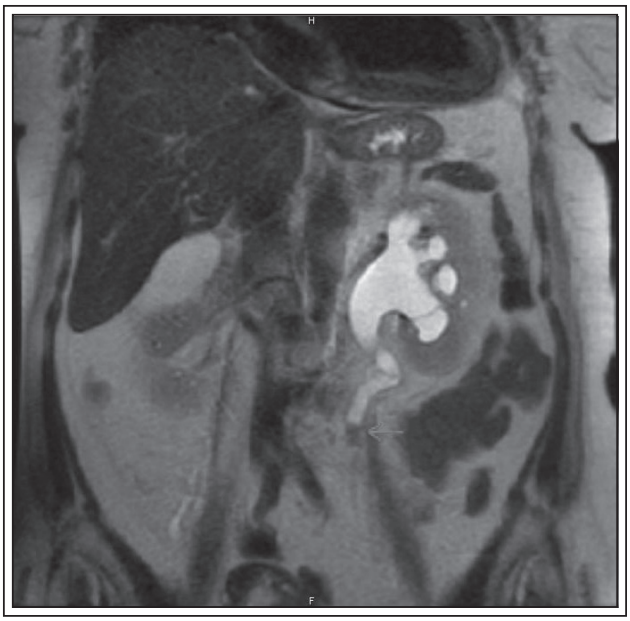

**Figure 1.** MRI T2 weighted coronal image demonstrates dilation of the left collecting system and ureter to the level of a 1 cm intraureteral mass (arrow).

A radical nephrectomy and proximal ureterectomy was performed through a flank incision without complication. A fixed, intraluminal ureteral mass could be palpated consistent with the preoperative imaging. The ureter was dissected caudally into the pelvis to ensure that the ureteral lesion would be removed along with the kidney. An intraoperative frozen section was negative for urothelial carcinoma and consistent with renal cell carcinoma (RCC). The patient's postoperative course was uneventful and she was discharged home on postoperative day 6. Final pathology revealed a 6.5 cm clear cell RCC, Fuhrman grade IV with focal sarcomatoid change. The 1 cm ureteral mass proved to be metastatic RCC with the same histologic characteristics as the renal primary tumor. The patient has been enrolled in an adjuvant trial involving antivascular endothelial growth factor (VEGF) therapy.

## Second case presentation

A 63-year-old female presented with total painless gross hematuria on two separate occasions. Physical exam was only remarkable for mild right sided costovertebral angle (CVA) tenderness. There was no palpable flank or abdominal mass. Urinalysis revealed 15-20 rbc/hpf and was otherwise unremarkable. The remainder of the patient's laboratory investigations, including liver function tests, were within normal limits. Computed

**Figure 2.** Axial contrast enhanced CT of the pelvis demonstrates an enhancing mass on the posterior aspect of the urinary bladder.

tomography (CT) urography was remarkable for a 7.7 cm x 6.2 cm heterogeneous enhancing mass in the lower pole of the right kidney abutting but not invading the right renal collecting system. A large, hyperattenuating mass was also seen in the dome of the bladder, measuring 3.8 cm x 3.7cm, Figure 2. There was no evidence of pelvic or retroperitoneal adenopathy. A chest radiograph was negative for metastatic disease. Endoscopic examination revealed a large ulcerated mass on the high posterior wall of the bladder to the left of midline, Figure 3. Complete transurethral resection was performed with pathological analysis revealing metastatic RCC, clear cell type, with extensive mucosal ulceration.

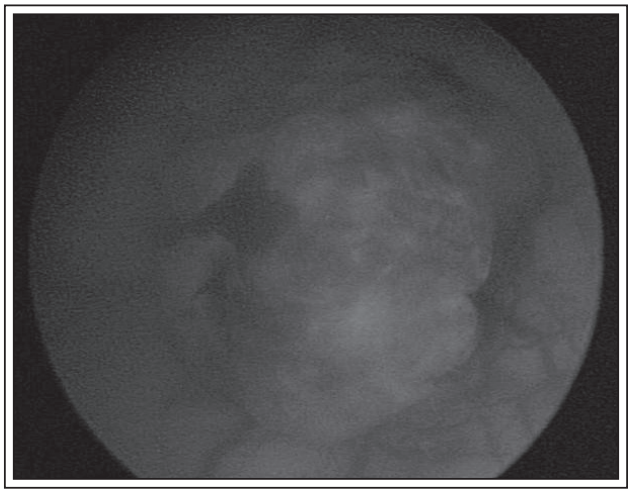

**Figure 3.** Cystoscopic image demonstrates a large ulcerated mass on the posterior wall of the bladder to the left of midline.

After complete discussion of options for management, the patient elected to undergo a right radical nephrectomy and partial cystectomy. She had an uneventful postoperative course and was discharged home on postoperative day four. Pathologic analysis of the kidney specimen revealed a 7.5 cm clear cell RCC, Fuhrman grade II, confined to the renal capsule with ureteral and vascular margins negative for tumor. Histologic examination of the bladder specimen demonstrated bladder wall with extensive ulceration, inflammation, and granulation tissue with no tumor seen. At the time of this report, the patient is alive without evidence of disease 7 months after definitive surgery.

## Discussion of diagnosis

Synchronous metastasis to the ureter or the bladder from RCC represents an extremely rare event. To our knowledge, there are 52 cases of ureteral metastasis of RCC but only nine previously reported cases of synchronous ipsilateral ureteral metastases.[1,2] Interestingly, this is the first case where a patient with synchronous ipsilateral ureteral metastasis from RCC did not present with gross hematuria. In terms of bladder metastasis from RCC, asynchronous metastasis is far more common than synchronous metastasis.[3] In fact, there have only been six reported cases of solitary synchronous metastasis of RCC to the bladder.[4-6]

The mechanism of RCC dissemination to other parts of the genitourinary tract is controversial. Some have argued for retrograde tumor dissemination by the lymphatics. A hematogenous route is another possibility but does not seem to explain solitary bladder or ureteral metastases. Abeshouse wrote one of the earliest case reports of RCC metastasizing to the ureter and bladder.[7] He hypothesized that the left renal vein allows for more access to other pelvic organs through its sophisticated venous network and cited the left kidney as the site of the primary tumor in 81% of cases of RCC metastases to other genitourinary organs. An intriguing theory is one of direct extension and implantation referred to as "drop metastases".[8] This is an attractive way to explain RCC metastasis to the ipsilateral ureteral orifices and ipsilateral ureteral metastases.

In case 1, the patient had a left sided mass with other systemic metastases. One could employ any of the aforementioned hypotheses to explain this patient's ureteral metastasis. However, case 2 is more perplexing. This patient had a right sided renal mass which negates Abehouse's theory. Hematogenous spread seems unlikely to explain a solitary synchronous metastasis to the bladder. The theory of a drop metastasis is difficult to employ in this patient with a midline dome metastasis rather than a metastasis near the ipsilateral ureteral orifice or on the ipsilateral side of the bladder.

Perhaps certain renal tumors possess genetic alterations that increases metastatic predilection for the urinary tract. There may be a mutation within certain malignant cells that results in expression of certain cell adhesion molecules (CAMs) specific for the urinary tract. Or perhaps there is some undiscovered polymorphism causing certain individuals to possess altered CAM receptors within the urothelium itself such that renal epithelium adheres more readily. This could explain the disparity between the frequent finding of renal tumor cells in the urine and the exceedingly rare incidence of genitourinary tract metastases. Over the last decade our understanding of the genetics of renal cell carcinoma has increased exponentially. Future genetic analysis of these rare metastatic lesions may provide further insight into their mechanisms of dissemination.

## Treatment and management

Systemic metastases from RCC portend a poor prognosis with overall 5 year survival of 5%-30%.[9,10] Patients presenting with synchronous metastases seem to do even worse.[11,12] In a large metastasectomy series from The University of Texas M.D. Anderson Cancer Center, patients with metachronous solitary metastasis fared better than those with synchronous solitary metastasis (5 year overall survival rates of 39% of 22%, respectively) regardless of site of metastasis.[11]

Although the prognosis for patients with metastatic RCC is poor, there is a role for metastasectomy in highly selected patients. Complete metastasectomy results in favorable long term survival over conservative treatment.[13] In 1998, Kavolius et al reported a 44% 5 year overall survival rate in 278 patients who underwent a curative metastasectomy for the first recurrence of RCC.[12] Consistent favorable predictors of survival between several series include solitary metastasis, metastasis to the lungs compared to other locations, metachronous presentation, and disease free interval 12 to 24 months.[12,14]

Less contemporary reports of bladder metastasis from RCC cite a dismal prognosis for these patients, with most dying less than 1 year following diagnosis of bladder metastasis.[3,15] More recent case reports have shown improved survival with resection of the metastatic lesion. Specifically, one case report described a patient with metachronous bladder metastasis who was alive and disease free at 6 years

following transurethral resection.[8] Another case report describes a patient with solitary synchronous bladder metastasis free of recurrence at 24 months.[4]

Given the rarity of RCC metastases to the urinary tract, there is no consensus as to the most appropriate surgical management for these lesions. Esrig et al reported two patients with contralateral ureteral metastases (on synchronous and one metachronous) from a renal primary and both were managed with total ureterectomy and construction of an ileal ureter.[2] As mentioned previously, there are several reports of both bladder metastasis from a renal primary managed with palliative transurethral resection. Matsuo et al reported a case of solitary metachronous metastasis of a renal primary to the bladder managed with partial cystectomy.[4] Chinegwundoh et al reported a case of metastatic RCC metastasis to the bladder invading the detrusor muscle managed by a radical cystoprostatectomy with ileal conduit diversion.[15]

Although the rarity of these lesions precludes definitive recommendations, one can argue that the different proposed mechanisms of spread dictate different surgical management. For example, if a ureteral lesion is more likely due to a drop metastasis, it follows the most appropriate management would seem to be total ureterectomy with bladder cuff excision. If the lesion is due to hematogenous spread, then simple excision should suffice. Transurethral resection may be appropriate in select cases for superficial papillary bladder metastases while partial cystectomy seems more appropriate for invasive lesions.

## Conclusions

The genitourinary tract is an extremely rare site of metastasis from renal cell carcinoma. The mechanism of dissemination is not fully understood. Synchronous lesions, although less common, are associated with a worse prognosis. At present, surgical resection of metastatic RCC to the urinary tract, if possible, is recommended as the most likely intervention to afford prolonged, disease free survival. □

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