

Sequential unusual site metastases in renal cell cancer: Saga of repeated tumor implantation and prolonged survival without systemic therapy

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Abstract

Renal cell cancer (RCC) is known to produce metastasis to unusual sites both synchronously and metachronously several years after the primary treatment. We report a rare case of RCC with three different, sequential, and each time isolated rare site metastasis to ureteric stump, surgical site, and urinary bladder over a period of 6 years after radical nephrectomy. At each recurrence, metastasectomy was carried out and no systemic therapy was administered. Eleven years after radical nephrectomy and 5 years after last resection, the patient remains disease free. Multiple recurrences can occur in RCC and complete surgical resection results in disease free survival.

Key Words: Bladder renal cell cancer, metachronous metastasis, metastasectomy in renal cell cancer, renal cell cancer with rare site metastasis, ureteric renal cell cancer

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INTRODUCTION

Renal cell cancer (RCC) is one of the most aggressive genitourinary cancers. Distant recurrences years after presumed curative resection are known in RCC. The usual distant spread is hematogenous to lung, liver, and bones. Ureter, bladder, head and neck, skin, surgical scar and heart are unusual sites of metastasis and usually are involved as a part of diffuse systemic spread in late stages of the disease. Isolated metachronous metastasis to these unusual sites is rare with only a handful of cases reported in English literature. We report a case of RCC with histologically proven separate recurrences in sequential metachronous fashion to three unusual sites over a period of

6 years post radical nephrectomy managed by surgical resection only. Currently, 11 years after surgical resection of the renal mass and 5 years after last recurrence, she is disease free.

CASE REPORT

A 28-year-old female with previously treated tubercular lymphadenitis presented with left flank pain and gross painless hematuria of 15 days duration. On evaluation with contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis there was a 4.4 cm × 2.9 cm × 4.4 cm heterogeneous enhancing mass in the interpolar region of

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left kidney [Figure 1]. She underwent left open radical nephrectomy via flank incision and the histopathology specimen revealed clear cell carcinoma Fuhrman grade II confined to the kidney ($T_{1B}N_0M_0$). She recovered well from surgery and was on regular 3 monthly follow-up with clinical examination, serum chemistries and ultrasonography when she noticed gross painless hematuria 2 years after radical nephrectomy. CECT was normal and urine cytology was inconclusive. On cystoscopy bloody efflux was seen from left ureteric orifice and retrograde pyelogram and ureteroscopy identified a mass lesion in residual ureteric stump. Using a Gibson's incision the ureteric stump and cuff of bladder were excised and there was a 1 cm × 0.5 cm clear cell cancer Fuhrman grade II similar to primary RCC extending up to submucosa and deep muscles were free. One year after the resection, she presented with a 2 cm × 2 cm firm mobile nodule in left iliac fossa at the margin of Gibson incision [Figure 2a]. Fine-needle aspiration cytology revealed clear cell cancer and it was widely excised and was localized to subcutaneous tissue. Final histopathology was clear cell cancer Fuhrman grade II similar to primary tumor. She was kept on close surveillance and was asymptomatic for 2 years when she again developed gross painless hematuria with passage of clots. CECT showed two small lesions on the posterior wall of urinary bladder as the only abnormality [Figure 2b]. On cystoscopy, there was a solitary 1 cm × 1 cm pedunculated growth in midline over interureteric bar with overlying calcification, which was completely resected and deep muscle and random bladder biopsies taken. On histopathology, the tumor was RCC Fuhrman grade II, deep muscle was not involved and random bladder biopsies showed normal urothelium. Currently, 11 years postnephrectomy, with 3 histologically documented recurrences and 5 years after the last recurrence she is disease and symptom free with normal chest and abdominal computed tomography scan and continues on 1 yearly regular follow-up.

DISCUSSION

Metachronous metastasis after radical nephrectomy for presumably localized disease is well-documented in RCC. Usually, there is diffuse systemic involvement and the prognosis is dismal despite systemic therapy. Ureteric stump, surgical scar



Figure 1: Contrast-enhanced computed tomography of abdomen depicting renal cell cancer in interpolar region of left kidney (arrows)

site, and bladder are considered rare sites for recurrence and only few cases have been reported.

Ureteric stump recurrence is commonly seen after transitional cell cancer, but is rare after RCC. The spread can be by hematogenous, lymphatic, or urogenous route and recurrence can occur 2 months to 8 years after resection of primary tumor.^[1] In the present case, ureteric metastasis was identified 2 years after radical nephrectomy for RCC involving pelvicaliceal system and was limited to mucosa and submucosa suggesting drop metastasis via urinary tract as the most plausible mechanism.

Recurrence of RCC at the surgical site is again unusual and incidence ranges from 0.9% to 1.8%.^[2] Improper specimen handling or poor surgical technique with breach of capsule or spillage of contents are major causative factors. Our patient presented with a small subcutaneous nodule at margin of Gibson's incision 1 year after surgery without any evidence of muscle invasion or distant metastasis and was managed by wide local resection.

Urinary bladder metastasis can be synchronous or metachronous and is reported in <2% of RCC cases.^[3] Isolated bladder metastasis has been rarely reported and can be managed by transurethral resection or partial cystectomy and have significantly better survival.^[4,5] We noted isolated bladder metastasis 6 years after radical nephrectomy and managed it with transurethral resection. After 5 years of transurethral resection, she is disease free.

Isolated metachronous recurrence to multiple rare sites in a sequential pattern, like in our case, has never been reported previously and adds to the ever increasing and varied presentations for recurrent RCC. The sequence and site of recurrences in our case raises suspicion of tumor implantation each time with interval gap of 1–2 years between each presentation. The similar histopathological appearances

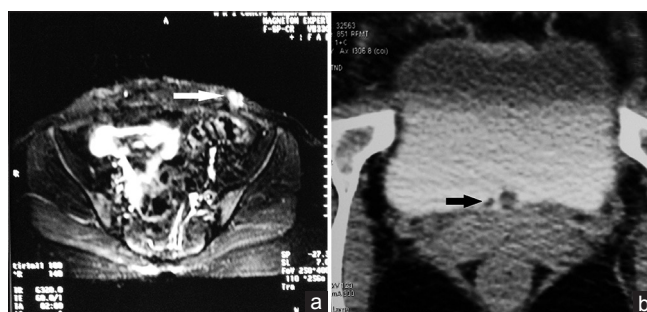


Figure 2: (a) Magnetic resonance imaging of abdomen showing subcutaneous nodule in left iliac fossa (arrow) which was a recurrence at the margin of Gibson's incision. (b) Contrast-enhanced computed tomography scan depicting two small nodules on the posterior wall of urinary bladder (arrow)

each time and no other metastasis until 6 years postlast metastatectomy tends to support the suspicion of tumor implantation. Studies in mice have shown different and poorer growth potential for human RCC cells when implanted in subcutaneous tissue versus implantation in renal subcapsular tissue, suggesting the limited scope of tumor implantation and growth outside of renal milieu.^[6] The good prognosis after complete metastatectomy in such cases including our case may be explained based on this theoretical explanation. This case also brings to light the potential for tumor seeding and the need to minimize tumor spillage even in cases of RCC.

In addition, the role of metastatectomy in RCC must be highlighted. Patients with metastatic RCC should be offered metastasectomy, if the chance of complete resection is high, as the 5 years survival after surgical resection of solitary metastasis ranges between 35% and 60%.^[5,7] Patients with metachronous metastasis fair better than synchronous metastasis in terms of survival. For those with bladder metastasis, 3 years survival after resection of solitary metastasis is 80%, for multiple metastases is 20%, but patients with systemic metastasis along with bladder metastasis usually succumb to their disease within 1 year.^[5,7]

CONCLUSION

RCC has an unpredictable course and local and distant relapse can occur years after primary surgery for presumably localized disease. Urinary tract can be involved by drop metastasis or

implantation, especially if the pelvicaliceal system was involved by the tumor. If possible, this isolated implantation must be completely resected, which can provide long term disease free survival possibly better than that for isolated distant metastasis, without the need for systemic therapy. But, one should be vigilant for further recurrences.

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Conflicts of interest

There are no conflicts of interest.

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