CASE REPORT

Rare sites of delayed metastasis in renal cell carcinoma

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SUMMARY

Renal cell carcinoma (RCC) is a lethal malignancy with a propensity for metastatic spread to any part of the body. The common sites of metastases from RCC include lungs, adrenals, intestines and brain and most intra-abdominal organs which may present as synchronous or metachronous to the primary tumour. A long follow-up is advised to deal with the risk of delayed metastases even when the primary has been well controlled. There have been few case reports in regard to rare sites of RCC metastasis. In this series of three cases, we present three rarest sites of metastatic RCC reported after 5 years of the primary malignancy.

BACKGROUND

Isolated metastasis occurring after many years and at rare sites stresses the need of long and careful follow-up in the patients treated by radical nephrectomy.^{1 2}

CASE PRESENTATION**Case 1**

A 48-year-old man presented with a right thigh swelling which was painless and slowly progressive since 2 years. The patient had started experiencing some difficulty in walking and sought medical attention. X-Ray of right leg and thigh was indicative of soft tissue swelling. MRI was suggestive of a 13.6×4.3×3.2 cm lesion in the right sartorius muscle in the medial part of right thigh. It was heterogeneous and iso-hyperintense to muscle on T1-weighted (T1W) image and heterogeneous and hyperintense on T2-weighted (T2W) imaging (figure 1). No evidence of other metastases were found. Radical excision of the thigh swelling was performed. Histopathology was reported as metastatic clear cell renal cell carcinoma (RCC) (figure 2). This patient had a right-sided stage 2 (T2aN0M0) RCC, Fuhrmann's grade III and underwent radical nephrectomy 8 years back (figure 3). The patient is doing well at 1 year of follow-up.

Case 2

A 45-year-old woman presented to cardiology department with dyspnoea on exertion and palpitations. Examination revealed raised jugular venous pressure, basal crepitation and pedal oedema. On evaluation with echocardiography, she was found to have a mass lesion in right atrium and right ventricle (figure 4). CT of chest and abdomen confirmed the solitary mass lesion in the right atrium and ventricle and no inferior vena cava (IVC)

Figure 1 (A) T1-weighted MRI showing iso-intense lesion involving right sartorius muscle (B) T1-weighted MRI showing iso-intense lesion involving right sartorius muscle (C) T2-weighted MRI showing hyperintense lesion involving right sartorius muscle.

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Figure 2 Histopathology H&E (magnification ×10).

thrombus or local recurrence in the abdomen. She had undergone radical nephrectomy 6 years back for a left-sided stage 2 (T2bN0M0), which was reported as Fuhrmann's grade III, papillary RCC (Type 2) (figure 5). It was assumed to be a solitary metastasis from RCC and the patient underwent tumour excision under cardiopulmonary bypass (figure 6). Histopathology confirmed it to be a metastatic papillary RCC (figure 7). Adjuvant therapy with sunitinib was started for this patient, but she died owing to refractory cardiac failure because of local recurrence of metastases in heart 6 months after surgery.

Case 3

A 64-years-old woman presented with a history of gross haematuria. On evaluation with a contrast-enhanced CT (CECT), she was found to have a 3×2.5×2 cm polypoidal enhancing mass

Figure 3 (A) Non-contrast CT showing heterogenous lesion in right kidney. (B) Contrast CT showing heterogeneous enhancing lesion in right kidney.

lesion on the posterior wall of the bladder (figure 8). She underwent complete transurethral resection of bladder tumour (TURBT) and histopathology was reported as metastatic clear cell RCC (figure 9). Six years ago, this patient had undergone radical nephrectomy with histopathology showing stage 2 (T2bN0M0), Fuhrmann's grade III clear cell RCC (figure 10). The patient was doing well at 3 years of follow-up.

INVESTIGATIONS

Case 1

MRI was suggestive of a 13.6×4.3×3.2 cm lesion in the right sartorius muscle in the medial part of right thigh. It was heterogeneous and isohyperintense to muscle on T1W image and heterogeneous and hyperintense on T2W imaging. No evidence of other metastases were found.

Case 2

On evaluation with echocardiography, she was found to have a mass lesion in right atrium and right ventricle. CT of chest and abdomen confirmed the solitary mass lesion in the right atrium and ventricle and no IVC thrombus or local recurrence in the abdomen.

Case 3

On evaluation with a CECT, she was found to have a 3×2.5×2 cm polypoidal enhancing mass lesion on the posterior wall of the bladder.

TREATMENT

Case1: Radical excision of the mass

Case2: Excision of right atrial mass under cardiopulmonary bypass

Case3: TURBT of bladder mass

OUTCOME AND FOLLOW-UP

Patients in Cases 1 and 3 are doing well at follow-up at 1 and 3 years. The patient in Case 2 died.

DISCUSSION

The incidence of late recurrence of metastatic RCC is 11% in patients surviving for 10 years after the initial diagnosis.³ Therefore, a regular yearly check-up is advisable in such cases postradical nephrectomy. Levy *et al*⁴ reported that 23.8% patients developed metastatic RCC after radical nephrectomy (26.5% for T2 N0 M0).⁴ The risk for development of recurrent malignant disease was greatest during the first three post-operative years. Surveillance for recurrent malignant disease after radical nephrectomy for RCC can be tailored according to the initial pathological tumour stage. For patients with stage T2 N0 M0 tumours, a chest radiograph every year and an abdominal CT scan every 2 years are recommended.⁴ Postoperative bone scans, bone plain films and head CT scans are necessary only in the presence of related symptoms. This surveillance scheme is cost-effective and enables early detection of most cases of recurrent RCC after radical nephrectomy for localised disease.⁵ Isolated skeletal muscle metastasis is a rare condition in RCC.⁶ These isolated tumours may be painless, and hence may go unnoticed when they are small.⁷ There have been few published reports for metastatic RCC to the gluteus maximus-muscle.⁸⁻⁹ Metastatic RCC must be differentiated from benign primary soft-tissue tumours. In the current case, the MRI for metastatic RCC were beneficial because MRI features of metastatic RCC to the skeletal muscle may show high-signal intensity on T1W and T2W sequence,¹⁰ as seen in the current case, that

Figure 4 (A) Echocardiography showing right atrial mass lesion. (B) Echocardiography showing right ventricular mass lesion. (C) CT of chest showing the solitary mass lesion in the right atrium and ventricle and no inferior vena cava (IVC) thrombus or local recurrence in the abdomen. (D) CT of chest showing the solitary mass lesion in the right atrium and ventricle and no IVC thrombus or local recurrence in the abdomen.

is, isohyperintense on T1W and heterogeneously hyperintense on T2W. These signal intensities seem to be characteristic for metastatic RCC to the skeletal muscle. MRI seems to be important in differentiating metastatic RCC from primary tumours arising from the muscle. Preoperatively either open or needle biopsy can differentiate it from other cases of soft tissue

tumour. In this case, histopathology after open biopsy was diagnostic of metastatic RCC to the skeletal muscle. It was successfully treated with wide excision in our patient. Surgical

Figure 5 Contrast-enhanced CT showing large heterogeneous enhancing lesion in left kidney.

Figure 6 (A) Intraoperative picture of tumour removal from right atrium and ventricle. (B) Intraoperative picture of tumour removal from right atrium and ventricle.

Figure 7 (A) Histopathology showing papillary renal cell carcinoma (RCC) H&E (magnification $\times 100$) (B) Histopathology showing papillary RCC H&E (magnification $\times 40$).

resection of metastatic RCC reportedly improves the outcome of patients with metastatic RCC, and 5-year survival rates are between 35% and 50% after surgical therapy for solitary metastasis.¹¹ Adjuvant targeted therapy was offered to the patient who could not afford it owing to financial constraints. The patient had uneventful follow-up at 1 year following excisional surgery. There have been rare reports of solitary late metastasis to the heart with the right ventricle being the preferred chamber involved.¹² Cardiac metastases from RCC are extremely rare, and usually occur by two mechanisms. The first employs a venous haematogenous pathway through the renal vein to the right heart. In patients with isolated disease and delayed disease progression to the right heart, with no involvement of the IVC, microdissemination through a venous

Figure 8 Contrast-enhanced CT showing lesion arising from posterior wall of bladder.

Figure 9 Histopathology-clear cell renal cell carcinoma H&E (magnification $\times 40$, $\times 100$).

haematogenous pathway remains the most probable mode of metastasis.^{13–15} The second is through the lymphatic vessels of the thorax, and then through the reversed lymphatic flow caused by metastasis to the nodes, metastatic RCC can spread to the pericardium and the left myocardium.^{15–17} The first pattern of metastatic spread seems more probable in this case. Histopathology was reported as metastatic papillary RCC. This patient succumbed to the disease 6 months later despite targeted therapy with sunitinib because of refractory cardiac failure owing to metastasis in left chamber of heart. Isolated bladder metastasis from RCC is another rare metastatic recurrence that was encountered. Bladder metastasis account for less than 2% of all bladder tumours.¹⁸ The most common associated primaries are malignant melanoma and stomach and breast cancers.¹⁹ Metastatic bladder cancer is classified radiologically and morphologically into two types: protuberant and diffuse type. Most are protuberant, with symptoms of gross haematuria,²⁰ as seen in our case. There can be two modes of dissemination of metastasis to bladder; haematogenous and lymphatic along the urothelial lining from kidney to bladder. The lesion was completely resected by TURBT and proved to be metastatic RCC. Check cystoscopies performed at 6 and at 1 year were normal. Rare cases with extensive involvement of bladder may require radical cystectomy. About one-third of patients diagnosed with RCC develop metastatic disease. Metastatic RCC can present as a solitary metastatic lesion or as widespread systemic disease. A solitary metastatic lesion eventually develops into a systemic pattern of recurrent disease.²¹ Although there have been advances in chemotherapy, the median survival time of patients with metastatic RCC is 6–12 months, and the 5-year survival rate is only 9%.²² Late isolated solitary metastasis have better prognosis than widespread metastasis. Metastatic RCC is

Figure 10 Contrast-enhanced CT showing large enhancing lesion arising from right kidney.

highly resistant to chemotherapy, hormones and radiotherapy, and the treatment of metastatic RCC remains ineffective. Sunitinib is currently the most widely used oral vascular endothelial growth factor receptor kinase inhibitor in the initial treatment of metastatic clear cell RCC.^{2,3} But in developing countries, it is unaffordable to the high cost involved. Currently, combination therapy that includes surgery and targeted therapy provides the best chance of palliation and cure.

Learning points

- ▶ Metastatic renal cell carcinoma (RCC) can occur in low-stage and low-grade tumours even after many years.
- ▶ Patients with RCC should be on follow-up for at least 10 years after surgery to detect any metastasis.
- ▶ Any isolated mass with history of radical nephrectomy should be evaluated for metastatic disease in such patients.
- ▶ Prognosis depends upon the site and the presence of other metastasis.

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