



Metachronous Bladder Metastasis from Clear Cell Renal Cell Carcinoma

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Abstract

Bladder metastasis, either synchronous or metachronous, is an uncommon presentation of renal cell carcinoma. We herein report a metachronous bladder metastasis from renal cell carcinoma of clear cell type, and review the current literature on the presentation, management and prognosis of this kind of metastasis. A 77-year-old man was presented to Queen Mary Hospital, Hong Kong in 2011 with hematuria, subsequently found a renal tumor invading into renal pelvis. Open right radical nephrectomy was performed and the tumor was confirmed to be pT1b clear cell carcinoma of Fuhrman grade 2. He remained asymptomatic all along after nephrectomy, but surveillance ultrasonography (USG) revealed a 2.2 cm bladder neck mass in 23 months after nephrectomy. After patient refused transurethral resection, the mass further enlarged to 3.8cm one year later. Transurethral resection was performed and histopathological examination confirmed clear cell carcinoma, with no fibro-muscular invasion. Multiple pulmonary metastases were also found on computed tomography (CT) of the thorax. He refused target therapy and preferred conservative treatment. He remained symptom-free 2 months after the transurethral resection.

Keywords: Bladder metastasis; Renal cell carcinoma; Ultrasonography

Introduction

It is uncommon for renal cell carcinoma to metastasize to bladder. In this study we presents a man with pT1b clear cell renal cell carcinoma, treated with right radical nephrectomy in 2011, and developed bladder metastasis 23 months after nephrectomy. He has been asymptomatic since the nephrectomy. Literature of on the presentation, treatment options and the prognosis of this kind of bladder metastasis is reviewed.

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Case Presentation

A 77-year-old man was first presented to the Urology Division of Surgical Department, Queen Mary Hospital, Hong Kong in 2011 for hematuria. He had hypertension, diabetes mellitus and pre-existing chronic renal disease, with glomerular filtration rate (GFR) of less than 20 ml/min/1.73 m. Ultrasonography (USG) of the kidneys revealed a 4.7 x 5.2 x 5.9 cm heterogeneous soft tissue mass in right renal pelvis, distorting the normal renal architecture, with intra-lesional colour Doppler flow signals. Flexible ureterorenoscopy found a soft and sludge-like mass within renal pelvis, and biopsy returned clear cell renal cell carcinoma. The renal mass had low-grade F18-fluorodeoxyglucose (FDG) uptake on positron emission tomography - computed tomography (PET-CT), and no distal metastases were found.

He subsequently underwent open right radical nephrectomy in May 2012. Final histopathological examination of the specimen confirmed pT1b clear cell carcinoma of Fuhrman Grade 2, and the resection margin was clear. His renal function remained stable after operation and did not require dialysis.

He was put on regular surveillance with USG of urinary system and chest radiography (CXR). A new 1.3 x 2 x 2.2 cm soft tissue mass was found at the bladder base on USG in April 2015, but he refused either transurethral resection (TUR) or flexible cystoscopy (FC) as he did not have any obstructive symptoms or hematuria. USG was repeated in April 2016, and the mass had enlarged to 3.8 x 3.7 x 2.8 cm (Figure 1). In addition, CXR taken in April 2016, showed a new 1.5 cm nodule at right mid-zone; CT thorax confirmed multiple pulmonary nodules, measuring up to 2.1 x 1.4 cm.

He finally agreed to TUR of the bladder mass, which was performed in July 2016. Intra-operatively a 4cm soft sessile mass was noted at 7-8 O'clock of bladder neck; complete resection was achieved.

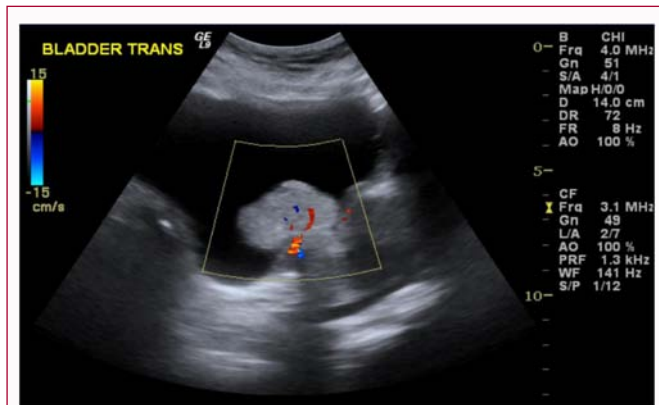


Figure 1: 3.8 x 3.7 x 2.8cm mass at bladder base, with intra-lesional Doppler flow signals on USG.

On histopathological examination, the tumour consisted of nests of round to polygonal cells associated with rich vascular network; the cells had distinct cell borders and possessed clear cytoplasm (Figure 2a and 2b); there was no fibro muscular invasion. Findings were compatible with clear cell renal cell carcinoma.

Option of target therapy with tyrosine kinase inhibitor (TKI), pazopanib, was offered by the clinical oncologist, and he decided not for any systemic treatment. He had no symptoms, for instance hematuria or dyspnea, from the metastases 2 months after transurethral resection.

Discussion

Bladder is an uncommon site of metastasis for renal cell carcinoma. 1,451 autopsy cases of renal cell carcinoma only revealed 1 case of isolated bladder metastasis, and 23 (2%) multi-organ metastases with bladder involvement [1]. The mode of spread to bladder is still uncertain. Some postulated tumour spread via hematogenous route from systemic circulation or retrograde metastasis through the gonadal vein, from the left renal vein, to the bladder [2]. Retrograde tumour dissemination by the lymphatic system is also possible. Another theory is antegrade spread of renal tumours to the ureter and bladder [3], especially for metastasis confined to the bladder mucosa. In our case we believe an antegrade spread via the urinary tract is the most possible route, since the initial renal tumour had invaded into the renal pelvis, which facilitated tumour dissemination into the collecting system, and the tumour was limited to bladder mucosa only. Hematogenous spread was another possibility for our case as the man also developed multiple pulmonary metastases.

Metastases were predominantly of clear cell type in reported literature. Zhang et al. [4] reported 11 cases of bladder metastases, and noted long disease-free survival was possible for solitary metastasis, but prognosis was poor for those with other distal metastases, with survival ranging from 5 -71 months. Matsumoto et al. [5] has reviewed another 65 published cases, in which 33 of them had metachronous metastasis, with median time to metastasis of 33 months (1-204 months). With a median follow-up time of 15 months, 34% died of renal cell carcinoma. 2 reported cases had survival more than 5 years after resection of solitary bladder metastasis. They identified metastasis within 1 year from nephrectomy and presence of other distal metastases as adverse factors on survival, with hazard ratio of 2.30 and 3.61, respectively.

Most of the bladder metastases, unlikely our case, were presented

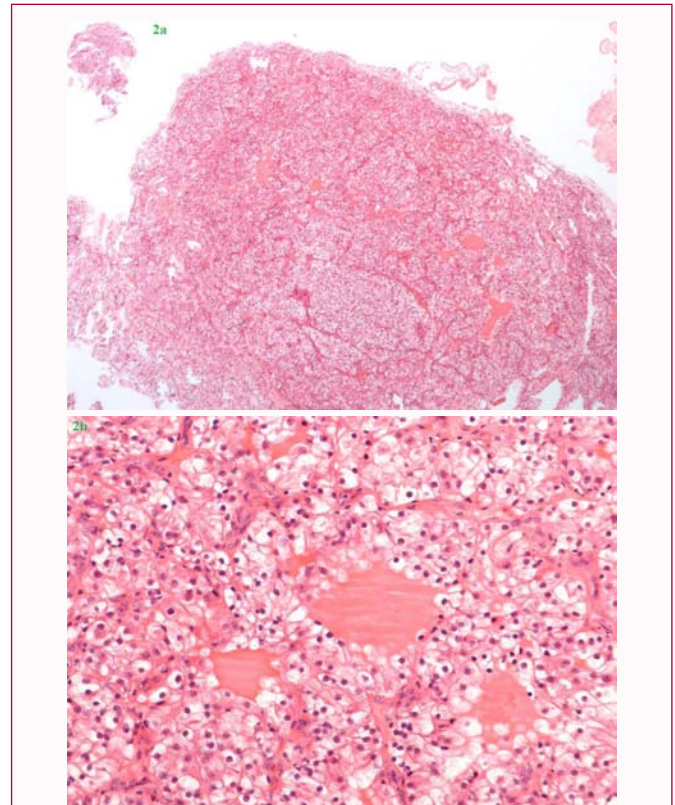


Figure 2a & 2b: Hematoxylin and eosin (H&E) stained sections, taken at 40x (Figure 2a) and 200x (Figure 2b) magnification respectively. The tumor consists of nests of round to polygonal cells associated with a rich vascular network. The cells have distinct cell borders and possess clear cytoplasm. Their nuclei are mostly round and hyperchromatic, some with distinct nucleoli.

with symptoms, mostly hematuria (75%), flank pain (15%), and fever (5%). Only 13% were asymptomatic [5].

Due to the scarcity of reported cases, treatment is not standardized for bladder metastasis; TUR, partial or total cystectomy have been reported. Nonetheless, if the tumor is resectable, complete metastectomy should be attempted as resection of metastasis of other sites has shown improved survival. The 5-year survival after metastectomy of pulmonary [6] or pancreatic metastasis [7] can be up to 50% and 75%, respectively.

In conclusion, bladder metastasis from renal cell carcinoma is rare. Solitary metastasis and latemetachronous metastasis with complete resection may have good prognosis and survival. However, majority are accompanied with distal metastases and the prognosis is generally poor.

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