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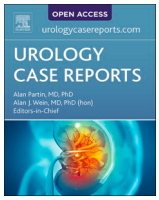

Oncology

Hepatocellular carcinoma metastasis presenting as a pedunculated bladder mass

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A B S T R A C T

Extrahepatic metastasis of hepatocellular carcinoma (HCC) is a sign of advanced disease with poor prognosis. Haematogenous metastasis to the urinary bladder is extremely rare. We describe a case of a 66-year-old male with advanced HCC that developed HCC metastasis to the bladder. There have only been six case reports previously documenting this. Uniquely this is the first case to develop metastatic disease to the bladder after receiving both locoregional and systemic therapy.

1. Introduction

Extrahepatic metastasis of hepatocellular carcinoma (HCC) is a sign of advanced disease. Haematogenous spread to the bladder is exceptionally rare. To our knowledge there have only been six other documented cases in the literature. Majority of these cases present with painless macroscopic haematuria. Clinically and radiologically, they can mimic the symptoms of primary bladder cancer. We describe a unique case of metastatic HCC to the bladder after receiving both locoregional and systemic therapy. Highlighting the importance of completing thorough evaluation of haematuria in patients with HCC.

2. Case report

A 66-year-old male patient with advanced HCC on systemic therapy presented with macrohaematuria, fatigue, weight loss and anorexia. His background is of compensated cirrhosis from previous hepatitis C and alcohol excess. After initially undergoing locoregional therapies for intrahepatic HCC (microwave ablation and transarterial chemoembolization) his cancer progressed with bony and adrenal metastases. He subsequently commenced on systemic therapy with atezolizumab and bevacizumab, as well as receiving external beam radiotherapy to the sites of his metastases. He has never had any bladder instrumentation or trauma. At the time of his current presentation, he had received systemic therapy for 18 months and his alpha foetoprotein (AFP) at this time was 200 kIU/L with no evidence of active intrahepatic or extrahepatic HCC seen on imaging.

In the workup for haematuria the patient's urine cytology was negative for malignant cells however a computed tomography-intravenous pyelogram (CTIVP) showed an 18mm polypoid lesion arising from the right anterior aspect of the bladder (Fig. 1). Cystoscopy demonstrated a right anterior wall bladder lesion with a necrotic surface and narrow neck and he underwent a cystoscopy and transurethral resection of bladder tumour (TURBT). The histopathology demonstrated high-grade HCC, likely extending into the lamina propria to produce an exophytic polypoid lesion (Fig. 2). The patient recovered well from the operation with no further haematuria. He remains on systemic therapy.

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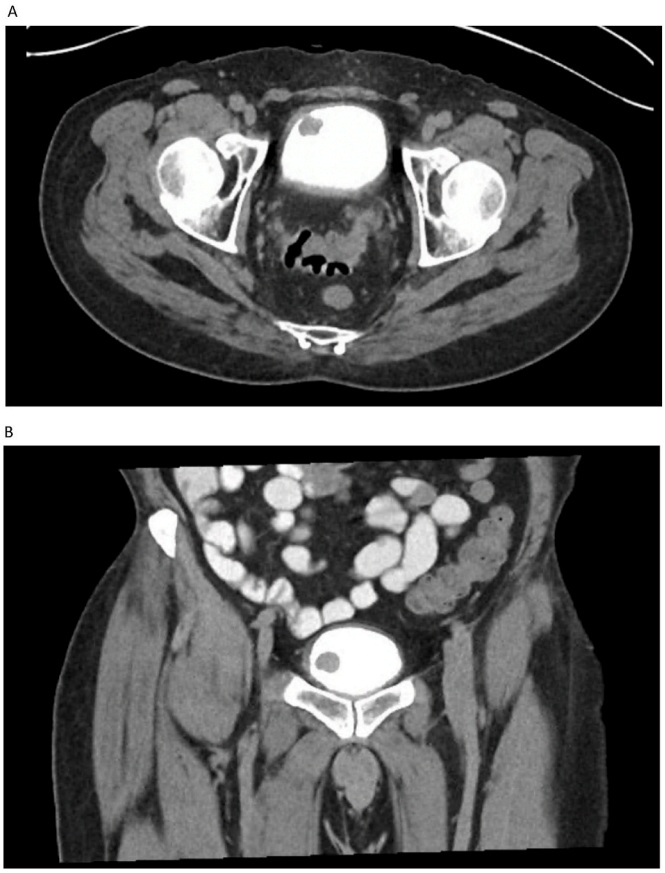

Fig. 1. CT-IVP with (A) axial and (B) coronal views an 18mm polypoid lesion arising from the right anterior aspect of the bladder.

3. Discussion

Extrahepatic metastasis of HCC is a sign of advanced disease with poor prognosis.[1] The most common sites of extrahepatic metastasis of HCC are lung, bone, adrenal glands, lymph nodes and brain.[1,2] Haematogenous metastasis to the urinary bladder is extremely rare. There have only been six case reports previously documenting this. This case is unique as it is the only case to develop metastatic disease to the bladder after receiving both locoregional and systemic therapy.

Kim et al.[3] reported a case of HCC that was initially treated with transarterial chemoembolization. Routine CT imaging discovered a bladder lesion which on cystoscopic evaluation and TURBT confirmed metastatic HCC. The patient was then commenced on lenvatinib. Yasutomi et al.[4] also reported a case report of isolated metastasis of HCC to the urinary bladder. Chung et al.[1] reported a case of a woman with HCC who declined treatment. Five years later, she presented with macroscopic haematuria. Cystoscopic evaluation showed haemorrhagic cystitis and three small lesions that on biopsy revealed metastatic HCC. Miyajima et al.[2] reported a case of oligometastatic HCC following extended right hepatectomy and previous metastasis to the lung and hilar lymph nodes. This patient was also receiving atezolizumab and bevacizumab when they developed macroscopic haematuria, and a bladder lesion was seen on CT. Histopathology from TURBT confirmed metastatic HCC, the patient was then commenced on lenvatinib. Finally, Franks et al.[5] reported a case of HCC that was found at the time of liver transplantation, this patient developed multiple pulmonary metastasis whilst on immunosuppression and systemic therapy. Two years later the patient developed macroscopic haematuria, again a CT showed a pedunculated bladder lesion. Cystoscopic evaluation and resection demonstrated metastatic HCC.

In the majority of these cases, the patients developed intermittent painless macroscopic haematuria. They all proceeded to have dedicated CT imaging, except for Kim et al.[3] who underwent a routine CT for HCC monitoring. Therefore, all patients with HCC and macrohaematuria need prompt investigation which should include microurine, urine cytology, dedicated imaging, and cystoscopy. Clinically and radiologically, there is similarity between bladder cancer and metastatic HCC. In our case, at presentation with macrohaematuria there was an elevated AFP of 200 kIU/L. Therefore, if there is no obvious site of active HCC, performing a urine microscopy or CTIVP may be helpful in identifying a bladder metastasis. Furthermore, our case and previous literature have shown the importance of cystoscopic evaluation, resection, and histopathological evaluation to assess bladder lesions. The morphological features of metastatic HCC as mentioned in the literature can be similar in appearance to a urothelial carcinoma,[1] which further supports the importance of prompt biopsy.

In conclusion, metastatic HCC to the urinary bladder is very rare. The small number of previous case reports over the past 30 years have shown that metastasis can be isolated to the urinary bladder or in addition to other sites of metastasis. This is one of the few cases of advanced HCC with oligometastatic disease on systemic therapy. This case is significant as it reiterates the importance of investigating additional sites of metastasis especially when presenting with painless haematuria and a rising or incongruent AFP.

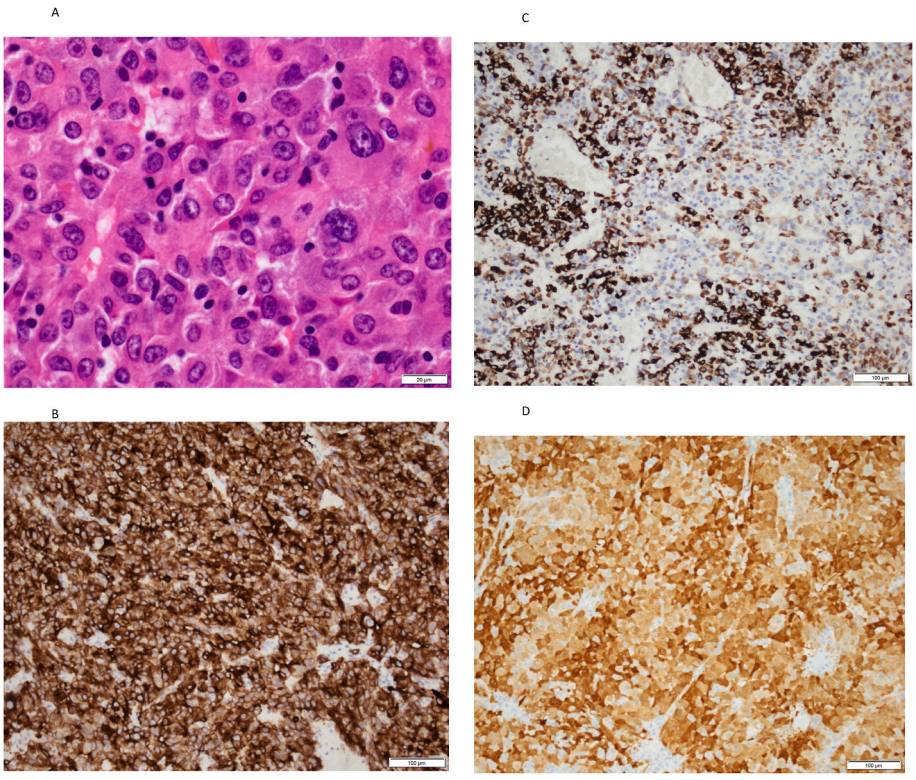

Fig. 2. (a) Cystoscopic resection of the polypoid mass showed metastatic hepatocellular carcinoma. Histologically high-grade, with large cell size, with rounded to irregular nuclei, frequent binucleation, numerous mitoses, and the cytoplasm eosinophilic. Immunochemically positive for (b) HepPAR1, (c) arginase and (d) cytokeratin CAM5.2. The tumour was negative for GATA-3, AE1/AE3 and CK7 and CK20.

Financial and competing interest disclosures

The authors report no conflicts of interest.

Patient's consent

Informed consent in writing was obtained from the patient.

CRediT authorship contribution statement

Sarah Lorger: Data curation, Writing – original draft. **George McClintock:** Writing – review & editing. **Geoffrey Watson:** Data curation, Writing – review & editing. **Ken Liu:** Writing – review & editing. **Nicola Jeffery:** Writing – review & editing.

Abbreviations:

AFP	alpha foetoprotein
CT	computed tomograghy
HCC	hepatocellular carcinoma
IVP	intravenous pyelogram
TURBT	transurethral resection of bladder tumour

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