



## Renal metastasis from primary hepatocellular carcinoma: a case report

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### Abstract

We report a rare case of renal metastasis from primary hepatocellular carcinoma (HCC). A mass in the right kidney of a 71-year-old man was detected by follow-up computed tomography (CT) for HCC. He was diagnosed as having primary HCC 18 years ago and had undergone partial hepatectomy, transarterial chemoembolization, and pulmonary segmentectomy for primary HCC and its metastasis over 10 years. Eight years after this, follow-up CT revealed a right kidney mass, and laboratory testing showed an elevated level of protein induced by vitamin K absence II (PIVKA-II). We performed laparoscopic radical nephrectomy for the right kidney mass. Histopathology revealed renal metastasis from primary HCC. To date, only a small number of cases of renal metastasis from HCC have been reported.

**Keywords** Renal metastasis · Hepatocellular carcinoma · Neoplasmas · Acarboxyprothrombin

### Abbreviations

HCC	Hepatocellular carcinoma
CT	Computed tomography
PIVKA-II	Protein induced by vitamin K absence II
AFP	Alpha-fetoprotein
MRI	Magnetic resonance imaging
Hep-par1	Hepatocyte-paraffin 1
GPC3	Glypican 3

peritoneum and bone [2], there are very few reports of renal metastasis from HCC [1]. In this case report, we present the clinical course of renal metastasis from HCC after 8 years of metastasis-free survival and review the previously reported cases. To our best knowledge, this is the 10th case of renal metastasis from HCC to be published in the literature.

### Case report

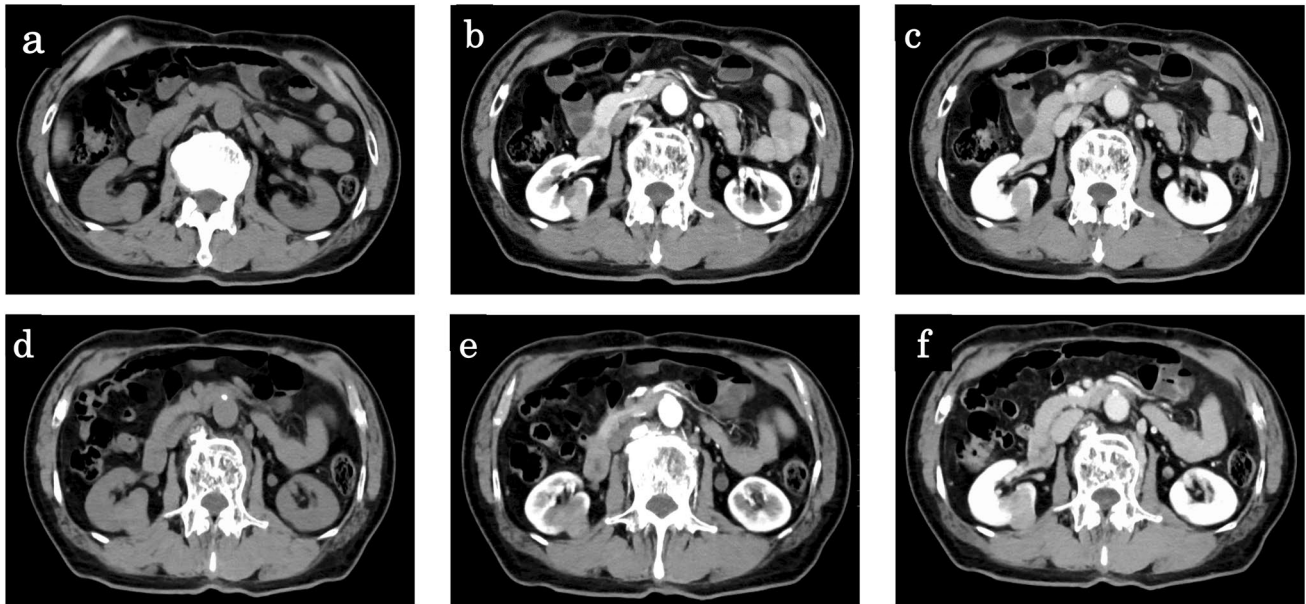
A 71-year-old man presented with an incidental right renal mass revealed by follow-up computed tomography (CT) for HCC in July 2019. The patient had suffered from hepatitis B and developed HCC in 2001. He underwent partial hepatectomy in July 2001, transarterial chemoembolization in August 2009, partial hepatectomy again in July 2010 for intrahepatic metastasis, and pulmonary segmentectomy for lung metastasis in January 2011. Follow-up CT examinations showed no recurrence or metastasis for almost 8 years. In July 2019, however, a CT scan showed a 21 × 14-mm mass in the right kidney with enhancement in the early phase and washout in the late portal phase (Fig. 1a–c). Protein induced by vitamin K absence II (PIVKA-II), one of the markers of HCC, was elevated from 34 mAU/mL (normal range, < 40 mAU/mL) in July 2018 to 100 mAU/mL in July 2019 (Fig. 2). The level of alpha-fetoprotein (AFP) was maintained under the reference value. His liver function showed

### Introduction

Renal metastasis is rare from primary tumors. Lung, breast, stomach and contralateral kidney are reported as primary tumor sites [1]. Although metastasis from hepatocellular carcinoma (HCC) occurs mainly in the lung, lymph nodes,

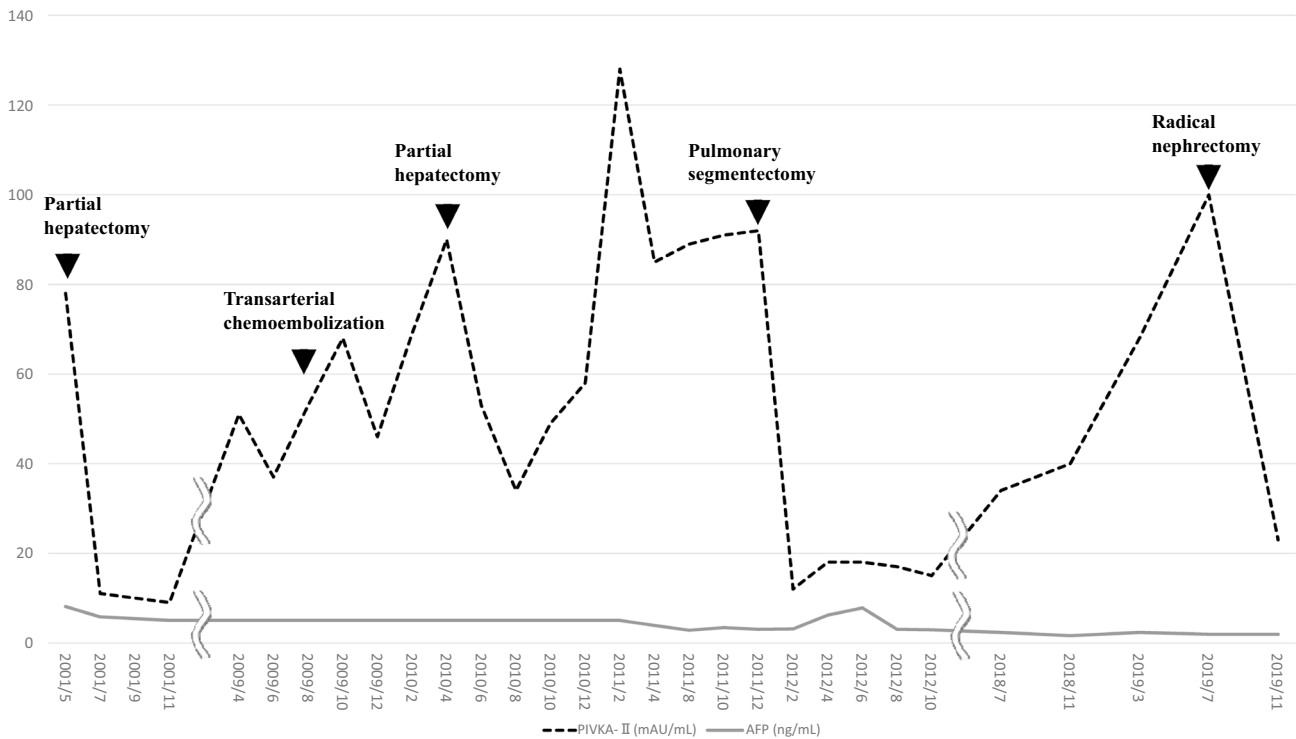
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**Fig. 1** Triple-phase abdominal computed tomography (CT) for a right kidney tumor. **a** Plain phase in July 2019. A 21×14-mm mass was located in the right kidney. **b** Arterial phase in July 2019. Kidney mass shows partly enhancement. **c** Portal phase in July 2019.

Mass enhancement shows slight washout. **d–f** Plain, arterial, portal phase in October 2019 right before the nephrectomy. Tumor size was 25×25 mm



**Fig. 2** Time course of the tumor marker values during the treatment period. Protein induced by vitamin K absence II (PIVKA-II) and alpha-fetoprotein (AFP) were measured every 2–4 months

Child–Pugh class A. Three months later, in October 2019, the tumor had increased to 25×25-mm size (Fig. 1d–f). We

decided to perform radical nephrectomy, considering that the right kidney mass might be derived from HCC, because the

tumor size had rapidly increased and the level of PIVKA-II was elevated. The patient thus underwent retroperitoneal laparoscopic radical nephrectomy. Surgical findings revealed no evidence of invasion to the peri-renal fat and diaphragm. The procedure resulted in 15 mL of blood loss and no peri-operative complications. Hematoxylin and eosin staining revealed that the tumor had a trabecular cell pattern and large nuclei, which were similar to the findings from the primary HCC (Fig. 3a–b). Immunohistochemical staining showed the tumor to be positive for hepatocyte-paraffin 1 (Hep-par1) and glypican 3 (GPC3) (Fig. 3c–d). Hep-par1 is normally positive for hepatocytes, and GPC3 is specific for fetal liver [3, 4]. According to these findings, the tumor was diagnosed as renal metastasis from HCC. The patient was discharged 8 days after the operation. Abdominal magnetic resonance imaging (MRI) performed 1 month after surgery showed no recurrence. The patient's level of PIVKA-II decreased to 23 mAU/mL, within the normal limit, 25 days after the radical nephrectomy (Fig. 2).

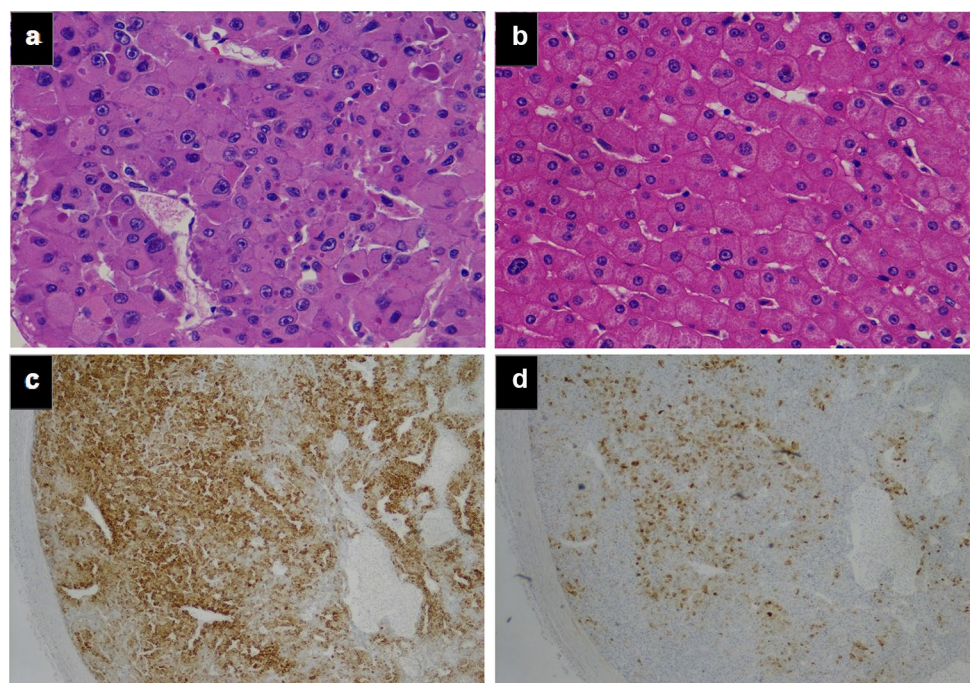
## Discussion

Renal metastasis is very rare, and its rate of occurrence is reported to be 7.2% from autopsies of patients with any malignant disease [5]. The primary tumor is reported to be the lung (19.8%), breast (12.3%), stomach (11.1%) and contralateral kidney (8.6%) [1]. Renal metastasis from HCC is also uncommon. In search of the literature using PubMed, we could only find nine reported cases of renal metastasis from HCC [6–14]. Among these nine cases, the precise

clinical course was reported in five cases (Table 1) [10–14], four of men and one of a woman. The kidney tumor size in three reports was over 40 mm (meeting the National Comprehensive Cancer Network criteria of T1b), and the kidney tumor had ruptured in two cases. Only one case reported the clinical course of tumor markers, including PIVKA-II and AFP [14]. In that case, the elevation of PIVKA-II was related to the emergence of intrahepatic and lung metastases. In our case, the level of PIVKA-II also changed depending on the status of the metastasis (Fig. 2), but the AFP remained below the standard value. The outcome in three cases was death within 3 months after initial treatment: two patients were treated with transarterial embolization and the other chose palliative care. The outcome in the other two cases was survival of more than 3 months after initial treatment: One patient was treated with open radical nephrectomy, and the other underwent transarterial embolization. Sorafenib was administered as further treatment in these two patients. Drugs target vascular endothelial growth factor receptor2 (VEGFR2) are reported as treatments for unresectable hepatocellular carcinoma. Recent clinical trials has shown that sorafenib and lenvatinib significantly improves overall survival in unresectable HCC [15] [16]. In our case, we will administer sorafenib or lenvatinib if other metastasis occur in the future.

In summary, we reported the case of a 71-year-old man with renal metastasis from HCC and elevation of PIVKA-II after 8 years of metastasis-free survival. We performed radical nephrectomy, because the tumor had rapidly increased in size and the level of PIVKA-II was elevated. Sorafenib or lenvatinib remain choices for further treatment if metastasis

**Fig. 3** Histopathological findings of the right kidney tumor and original HCC. Tumor cells obtained by radical nephrectomy. A trabecular cell pattern and large nuclei are seen (hematoxylin and eosin [H&E] staining) (a). Tumor cells from the partial hepatectomy performed in 2011 (H&E staining) (b). Positive staining for hepatocyte-paraffin 1 (c) and glypican 3 (d) of the tumor obtained by the present radical nephrectomy. Pictures a and b were showed in original magnification  $\times 400$ . Pictures c and d were  $\times 100$



**Table 1** Reports of renal metastasis from hepatocellular carcinoma

References	Age	Sex	Size (mm)	Initial presentation	Other metastasis	Initial treatment	Further treatment	Diagnosis	Outcome following initial treatment
Fukushima et al. [10]	52	M	78×86	Gross hematuria	Intrahepatic	Transarterial embolization	Interferon-α	Needle biopsy	Died of disease at 2 months
Mezawa et al. [11]	67	M	None	Back pain	Intrahepatic, lung, brain	Transarterial embolization	Palliative	Autopsy	Died of disease at 3 months
Aron et al. [12]	74	M	None	Gross hematuria and back pain	None	Palliative	None	Needle biopsy	Died of disease at 6 weeks
Ong et al. [13]	70	M	55×45	None (routine MRI)	Intrahepatic, lung	Open radical nephrectomy	Sorafenib	Nephrectomy	Alive with disease for over 3 months
Kinoshita et al. [14]	76	F	80×60	Back pain	None	Transarterial embolization	Sorafenib	CT and tumor marker	Alive with disease for over 12 months
Present case	71	M	21×14	None (routine CT)	None	Laparoscopic radical nephrectomy	None	Nephrectomy	Alive with disease for over 3 months

CT computed tomography, MRI magnetic resonance imaging

recurs. Clinicians need to be aware of the potential occurrence of a renal tumor in patients with a past medical history of HCC. Further accumulation of evidence from additional reports is required to reveal a proper strategy for treating renal metastasis from HCC.

**Author contributions** YR, SY, GK, IS and TJ performed the operation and managed the patient postoperatively. BT, SK and YW performed the pathological analysis. YR and SY drafted the manuscript. All authors read and approved the final manuscript.

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**Data availability** Data and material will be available on request to the corresponding author.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflicts of interest.

**Informed consent** Informed consent was obtained from the patient for the publication of this case report.

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