Renal metastasis from intrahepatic cholangiocarcinoma

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Abstract

Metastases to the kidney are extremely rare and intrahepatic cholangiocarcinoma (ICC) is difficult to treat. In this study, we report a case of renal metastasis from ICC. A 72-year-old man who had been followed-up for chronic hepatitis C was diagnosed with ICC in the segment 8 and underwent S8 segmentectomy in 2014. During follow-up, the serum levels of carcinoembryonic antigen and carbohydrate antigen 19-9 were slightly elevated, and abdominal contrast-enhanced computed tomography revealed a low-density mass preceded by rim enhancement in the arterial phase measuring 1.5×1.5 cm in the segment 6, and a hypovascular mass measuring 2.2×2.0 cm in the upper pole of the left kidney in 2017. He underwent partial hepatectomy and partial nephrectomy. Based on postoperative histological findings combined with immunohistochemical analysis, the tumors both in the liver and kidney were diagnosed as recurrent ICC.

Keywords Intrahepatic cholangiocarcinoma · Malignancy · Nephrectomy · Renal metastasis

Abbreviations

ICC	Intrahepatic cholangiocarcinoma
CEA	Carcinoembryonic antigen
CA19-9	Carbohydrate antigen 19-9
ICG-R15	Indocyanine green retention rate at 15 min
CT	Computed tomography
PET	Positron-emission tomography

Background

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver malignancy after hepatocellular carcinoma and accounts for approximately 4% of all primary liver cancers [1]. The incidence and mortality rates of ICC have significantly increased worldwide [2, 3]. Although the only potentially curative treatment is complete resection, postoperative recurrence rates are high, and the most frequent site of recurrence is intrahepatic, followed by

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simultaneous intra- and extrahepatic disease, and extrahepatic disease [4]. However, renal metastasis from ICC is extremely rare. Herein, we report a case of renal metastasis from ICC which was surgically resected.

Case report

A 72-year-old man who had been followed-up for chronic hepatitis C was detected with a liver tumor measuring 4.0×2.5 cm in the segment 8 of the liver and was referred to our hospital in 2014. Abdominal contrast-enhanced computed tomography (CT) revealed a low-density mass preceded by rim enhancement in the arterial phase measuring 3.2×3.0 cm in the segment 8. Positron-emission tomography (PET)–CT revealed that the liver lesion demonstrated significant uptake of fluorodeoxyglucose with a maximum standardized uptake rate (SUVmax) of $5.6 \rightarrow 6.2$, and no other uptake lesions were observed. He was diagnosed with intrahepatic cholangiocarcinoma (ICC) and underwent S8 segmentectomy with lymph node sampling of No. 8 and 12. Histopathological findings of the resected specimen resulted in moderately differentiated ICC without lymph node metastasis, staged as pT3N0M0 pStage III. The patient did not receive any adjuvant chemotherapy and remained without any sign of disease relapse during follow-up, until 2017 at the age of 75, when his serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) were slightly elevated. A physical examination revealed no remarkable findings except for an inverted L operation scar on the abdomen from a previous surgery. A laboratory analysis provided the following results: platelet count, 14.0×10^4 /

μL (normal range, $15.8\text{--}34.8 \times 10^4/\mu\text{L}$); serum aspartate aminotransferase, 25 U/L (normal range, 13–30 U/L); alanine aminotransferase, 12 U/L (normal range, 10–42 U/L); total bilirubin, 0.9 mg/dL (normal range, 0.4–1.5 mg/dL); albumin, 4.4 g/dL (normal range, 4.1–5.1 g/dL); prothrombin time, 11.4 s (normal range, 11.0–15.2 s); and activated partial thromboplastin time, 32.9 s (normal range, 25.2–35.2 s). Hepatitis B surface antigen was negative, while hepatitis C virus antibody was positive. The serum level of CEA was 5.1 (normal range, <5 ng/mL) and CA19-9 was 59.8 U/mL (normal range, <37 U/mL). The Indocyanine green retention rate at 15 min (ICG-R15) was 25.7%.

Abdominal CT revealed a low-density mass preceded by rim enhancement in the arterial phase measuring 1.5×1.5 cm in the segment 6 (Fig. 1a–c), and a hypovascular mass measuring 2.2×2.0 cm in the top of the left kidney (Fig. 1d–f). PET–CT revealed that both lesions demonstrated significant uptake of fluorodeoxyglucose with a maximum standardized uptake rate (SUVmax) of $3.2 \rightarrow 3.3$ (liver) and $2.3 \rightarrow 2.7$ (kidney) (Fig. 2). The renal tumor was indistinguishable from primary renal neoplasms, such as hypovascular renal cell carcinoma. The patient underwent left partial nephrectomy simultaneously with partial hepatectomy of the segment 6.

On macroscopic examination, the surgical specimen of the liver revealed a whitish mass measuring 23×20 mm in size. On histological examination, this tumor revealed moderately differentiated tubular adenocarcinoma with a confluent glandular and solid nest pattern. Immunohistochemical analysis revealed that the tumor cells were diffusely positive for CK7, partially positive for CK19, and negative for CK20 (Fig. 3). Morphological features and staining patterns

Fig. 1 Abdominal contrast-enhanced CT revealed a low-density mass preceded by rim enhancement in arterial phase measuring 1.5×1.5 cm in the segment 6 of the liver (a–c), and hypovascular mass measuring 2.2×2.0 cm in the top of the left kidney (d–f)

Fig. 2 PET-CT revealed that the both tumors in the liver and kidney showed significant uptake of fluorodeoxyglucose with standardized uptake rate max of 3.2→3.3 (liver) and 2.3→2.7 (kidney), respectively

Fig. 3 On histological examination, the liver tumor revealed moderately differentiated tubular adenocarcinoma with confluent glandular and solid nest pattern. Immunohistochemical analysis showed that the tumor cells were diffusely positive for CK7, partially positive for CK19, whereas were negative for CK20, suggesting that the liver tumor was recurrent ICC. On the contrary, the histology of the

renal tumor was solid, clear boundary and contained eosinophilic cytoplasm and revealed moderately differentiated tubular adenocarcinoma. Immunohistochemical analysis revealed that tumor cells were diffusely positive for CK7, partially positive for CK19, whereas were negative for CK20, PAX8 (Fig. 3). Based on these findings, the renal tumor was ultimately diagnosed as metastasis from ICC

of the tumor cells resembled to those of previously resected specimens of primary ICC, suggesting that the liver tumor was recurrent ICC. The surgical specimen from the kidney demonstrated a yellowish white mass measuring 29×22 mm in size. The histology of the mass revealed that it was solid, had a clear boundary, contained eosinophilic cytoplasm, and revealed moderately differentiated tubular adenocarcinoma. Based on these observations as well as the clinical and pathological findings, the renal tumor was ultimately diagnosed as metastasis from ICC.

The patient's postoperative course was uneventful, and he was discharged on postoperative day 12. Four months after the operation, bone and lung metastases were detected, and the patient started to receive a systemic chemotherapy

with gemcitabine and cisplatin. Currently, he is still alive for 30 months after second surgery and undergoing chemotherapy.

Discussion

Despite high blood flow and profuse vascularity, metastases to the kidney are rare. Abrams et al. reported that the kidney was the 12th most frequent organ involved with metastatic diseases, with an incidence of 12.6% in their series of 1000 autopsies in 1950 [5]. In a study on 11,328 autopsies in 1979, Bracken et al. reported that renal metastasis was detected in 7.2% patients, and the most common

primary tumors in decreasing order of frequency were lung; breast; skin; and tumors of genitourinary, gastrointestinal, and gynecological tracts, respectively [6]. In general these metastatic tumors are discovered during autopsy, and there are few studies examining such tumors diagnosed before the patient's death. Recently, Zhou et al. reported 151 patients who were diagnosed with a primary non-renal malignancy with renal metastasis, and the most common primary tumor sites were the lung (43.7%); colorectal region (10.6%); ear, nose, and throat (6%); breast (5.3%); soft tissue (5.3%); and thyroid (5.3%) [7].

In the present case, the hypovascular renal tumor was detected in the top of the left kidney during the course of regular follow-up after hepatectomy for ICC. There are no specific radiological findings to distinguish a secondary renal tumor from a primary renal cell carcinoma [8]. Although there is no report demonstrating that biopsy of renal tumor is associated with tumor dissemination, there are some reports demonstrating that biopsy of liver tumor such as HCC is associated with tumor dissemination, including peritoneal dissemination and needle tract seeding [9–12]. Therefore, we decided to perform partial nephrectomy in combination with hepatectomy without biopsy of the renal tumor, to avoid the risk of tumor cell dissemination.

We reviewed English medical publications in PubMed using keyword; “intrahepatic cholangiocarcinoma”, “recurrence,” “renal metastasis” or “metastasis to the kidney.” Consequently, this search yielded only one case report on renal metastasis from ICC, where histological examination revealed squamous cell carcinoma [13]. In addition, we found nine studies regarding surgical treatment for recurrent ICC and reviewed in Table 1 [14–22]. Among them, there are two case series including a case of renal metastasis which was treated with surgical resection. Kamphues et al. reported 13 cases who underwent repeat hepatic resection, and one of them underwent right nephrectomy in combination with hepatic resection for renal metastasis from ICC [15]. Yoh et al. reported 15 cases who underwent repeat surgery for recurrent ICC, one of them underwent resection of renal metastasis from ICC [20]. Both studies demonstrated the efficacy of surgical resection for recurrent ICC, but not included the detail descriptions of renal metastasis from ICC.

Immunohistochemical analysis is commonly used to differentiate between primary and metastatic renal tumors. In

the present case, morphological features and immune profiles resembled liver and renal tumors, i.e., diffusely positive for CK7, partially positive for CK19, and negative for CK20. In addition, cancer cells of the renal tumor were negative for PAX8. Based on these results, the tumor in the kidney was diagnosed as recurrent ICC.

Although the treatment strategy for the metastatic renal tumor is according to that for primary tumor, little is known about the outcome of the metastatic renal tumor after resection because of the rarity of the disease. Zhou et al. reported that survival appeared to be longer in patients who were candidates for and treated with surgery, with a median survival of 4.81 years from primary tumor diagnosis and 2.24 years from renal metastasis diagnosis [7]. For recurrence after hepatectomy, aggressive surgical treatment led to prolonged survival in selected patients [16, 17, 23]. However, due to the lack of large-scale case studies on its treatment, there is no established treatment strategy for renal metastasis of ICC, and indication of surgical resection is uncertain. Our patient developed recurrence in remnant liver, lung, and bone 4 months after surgery; however, he is still alive and has received 30 months of chemotherapy. Surgical resection of renal metastasis from ICC should needs careful attention.

Conclusions

Renal metastasis from ICC is extremely rare and we have presented a case of metastasis of ICC to the kidney, which was surgically resected. Preoperative diagnosis of renal metastasis by imaging modalities is difficult for distinguishing from a primary renal tumor, and histopathological examination combined with immunochemical analysis is helpful. Although extremely rare, when renal tumors are detected after hepatectomy for ICC, metastasis to the kidney should be considered and accurate diagnosis should be made so that the appropriate treatment can be administered.

Data availability

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

Table 1 Literature review of surgery for recurrent intrahepatic cholangiocarcinoma

Author (year)	Total no. of pts	No. of recurrent pts	Recurrence site	Surgery for recurrence	Renal metastasis
Yamamoto et al. [14]	54	25	Liver (14), peritoneum (6), lymph node (5), bile duct (2), lung or bone (5)	7 pts liver (7)	None
Kamphues et al. [15]	107	71	ND	13 pts liver (12), paracaval (1)	1 pts developed renal metastasis after repeat hepatectomy
Sulpice et al. [16]	87	45	Liver only (25), localized extrahepatic (adrenal gland (1), peritoneum (1)), general (18)	4 pts liver (4)	None
Souche et al. [17]	125	76	Liver (39), lymph node (9), peritoneum (7), multiple sites (21)	11 pts liver (10), liver transplantation (1)	None
Park et al. [18]	128	81	ND	10 pts liver (4), liver transplantation (1), muscle (2), diaphragm (2), peritoneum (1)	None
Yamashita et al. [19]	356	214	Liver (104), lymph node (81), lung (40), peritoneum (33), others (26)	43 pts liver (25), lymph node (8), lung (7), bone (1), adrenal gland (1), brain (1)	None
Yoh et al. [20]	161	108	ND	15 pts liver (7), lung (5), kidney (1), chest wall (1), lymph node (1)	1
Hu et al. [21]	920	607	Liver only (323), extrahepatic only (90) (lymph node (46), peritoneum (34), bone (13), adrenal gland (5)), Both (194)	88 pt details ND	None
Nickkholgh et al. [22]	190	87	Liver only (54), Extrahepatic only (18) (lymph node (6), bone (3), mesenteric vein (3), lung (2), peritoneum (2), pancreas(2), Both (15)	25 pts liver(20), lymph node(5)	None

ND not described

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest in association with this study.

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

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