—Case Reports—

Rare Case of Synchronous Cystic Duct Metastasis from Renal Cell Carcinoma

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Introduction: The common metastatic sites of renal cell cancer (RCC) are the lung, bone, liver, brain, adrenal glands, and contralateral kidney. Metastasis to the gallbladder is rare, and cystic duct metastasis from RCC has been reported in only one metachronous case. This is the first report of a case of synchronous cystic duct metastasis from RCC.

Case Report: A 72-year-old woman presenting with hematuria had a history of Cushing disease approximately 10 years previously. Enhanced computed tomography of the abdomen showed a mass measuring 5.8 × 3.0 cm in the left kidney, which was strongly enhanced in the early phase and washed out in the late phase. A mass measuring 2 cm in diameter was seen in the left adrenal gland, and a 1.0-cm mass was noted in the right adrenal gland. Multiple tiny masses were detected in the cystic duct. Left renal cell carcinoma, cystic duct metastasis, and bilateral adrenal gland metastases were diagnosed. Because the metastatic tumor was close to the common bile duct, we performed left nephrectomy, bilateral adrenalectomy, cholecystectomy, resection of the extrahepatic bile duct, and hepaticojejunostomy. Pathological findings showed that the renal tumor was clear cell carcinoma, as were the bilateral adrenal tumors and cystic duct tumor. The patient died 30 months after the operation.

(J Nippon Med Sch 2019; 86: 242–247)

Key words: renal cell carcinoma, cystic duct, metastasis

Introduction

Renal cell carcinoma (RCC) accounts for 3% of malignancies in adults and for 90% of renal neoplasms[1]. Cancers of the kidney account for 4% of all newly diagnosed malignancies in men and 3% in women[2]. Approximately one-third of patients with RCC present with metastasis at the time of diagnosis[3], the most common sites of which are the lung, bone, liver, brain, adrenal glands, and contralateral kidney[4]. Gallbladder metastasis from RCC is believed to be rare[5], and cystic duct metastasis from RCC has been reported in only one metachronous case[6]. Herein, we report the first case of synchronous metastasis of RCC to the cystic duct.

Case Report

A 72-year-old woman presenting with hematuria had a past medical history of Cushing disease approximately 10 years previously. Laboratory examination (**Table 1**) showed a serum aspartate aminotransferase (AST) of 278 IU/L (normal: <28 IU/L), serum alanine aminotransferase (ALT) of 394 IU/L (normal range: <33 IU/L), and C-reactive protein of 1.25 mg/dL (<0.3 mg/dL). The tumor markers observed included serial carcinoembryonic antigens (CEA), 5.0 ng/mL (<2.5 ng/mL), and serial CA 19-9, 100.6 U/mL (<37 U/mL). Enhanced computed tomography (CT) of the abdomen showed a mass measuring 5.8 × 3.0 cm in the left kidney. The mass was strongly enhanced in the early phase and washed out in the late phase (**Fig. 1a, b**). A mass measuring 2 cm in diameter was present in the left adrenal gland, and a 1.0-cm mass was observed in the right adrenal gland. Multiple tiny masses observed in the cystic duct were enhanced in the

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https://doi.org/10.1272/jnms.JNMS.2018_86-405
Journal Website (https://www.nms.ac.jp/sh/jnms/)

Table 1 Results of laboratory examinations

Peripheral blood		Blood chemistry			
WBC	10,800 /μL	GOT	278 IU/L	Alb	2.9 g/dL
RBC	363×10⁴ /μL	GPT	394 IU/L	BUN	18.8 mg/dL
Hb	10.3 g/dL	LDH	440 IU/L	Cr	0.85 mg/dL
Ht	31.3 %	ALP	2,285 IU/L	Na	140 mEq/dL
Plt.	23.7×10⁴ /μL	CPK	29 IU/L	K	4.0 mEq/dL
		AMY	55 IU/L	Cl	101 mEq/dL
Serology		T-bil	1.5 mg/dL	FBS	139 mg/dL
CRP	1.25 mg/dL	TP	5.5 g/dL	HbA1c	6.4 %
Tumor markers				Coagulation	
CEA	15.8 ng/mL			PT (%)	106 %
CA19-9	141.6 U/mL			APTT (s)	26.2 s

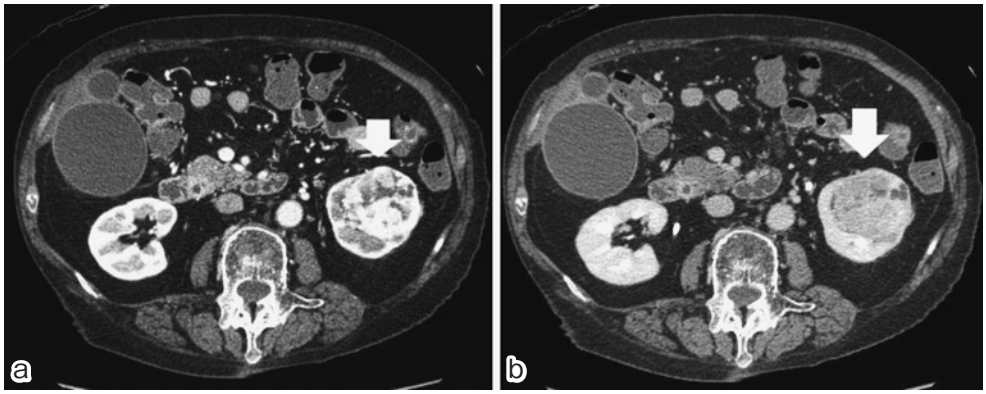

Fig. 1 a, b: Enhanced computed tomography of the abdomen shows a mass measuring 5.8 × 3.0 cm in the left kidney. The mass was strongly enhanced in the early phase and washed out in the late phase (arrow).

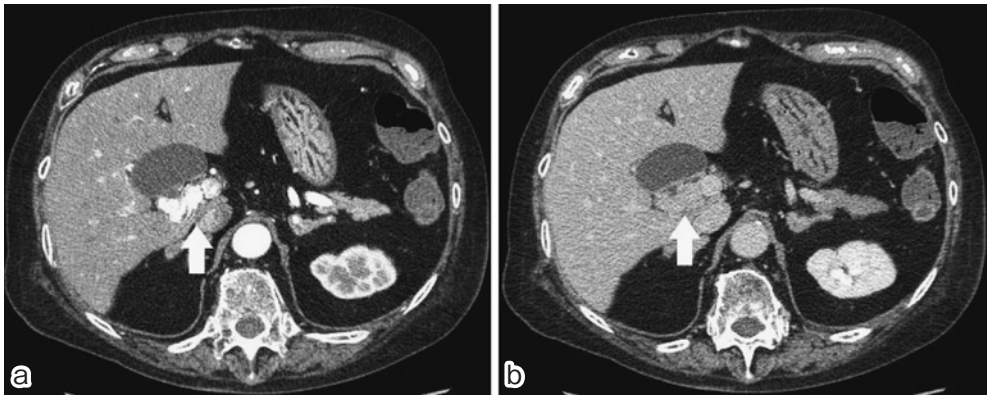

Fig. 2 a, b: Multiple tiny masses were detected in the cystic duct and were strongly enhanced in the early phase and washed out in the late phase (arrow).

early phase and washed out in the late phase (**Fig. 2a, b**). Abdominal ultrasonography revealed tumors in the cystic duct and gallbladder stones. There was no wall thickening of the gallbladder and no accumulation of fluid around the gallbladder. Positron emission tomography (PET) revealed uptake lesions in the renal tumor; however, other metastatic lesions in the adrenal glands and cystic duct showed no radioisotope accumulation. Left renal cell carcinoma, cystic duct metastasis, and bilateral adrenal gland metastasis were diagnosed, and we performed left nephrectomy with left adrenalectomy, right adrenalectomy, cholecystectomy, resection of the extrahe-

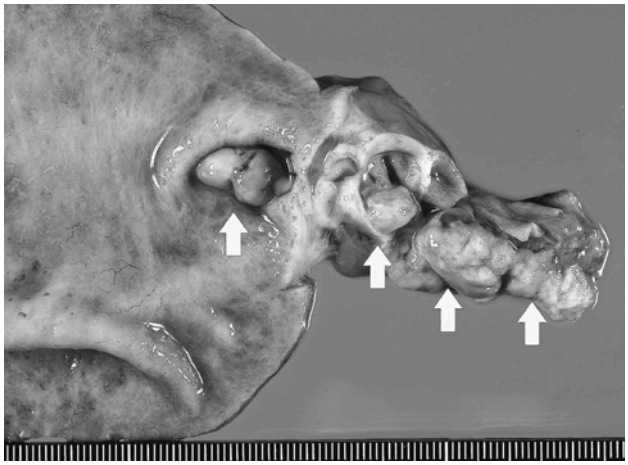

Fig. 3 Cystic duct metastasis from renal cell carcinoma (RCC) (arrows).

patic bile duct, and hepaticojejunostomy because the metastatic tumor was close to the common bile duct. The tumors in the cystic duct were smooth and yellow (**Fig. 3**). The postoperative course was uneventful, and liver function recovered after the operation. The patient was discharged on postoperative day 21. Pathological findings showed that the renal tumor consisted of clear cell carcinoma (**Fig. 4a**), as did the bilateral adrenal tumors and cystic duct tumor (**Fig. 4b, c**).

Only cystic duct metastasis was detected in the hepatobiliary system. No metastatic cancer cells were found in the gall bladder or the extrahepatic bile duct. However, microscopic vascular invasion was detected. Immunohistochemical staining of the primary RCC and cystic duct tumors yielded a positive result for CD10 and a negative result for PAX8, which suggests that these two tumors share an immunophenotype (**Fig. 5**). The pathological findings were consistent with a diagnosis of left renal cell carcinoma, cystic duct metastasis, and bilateral adrenal gland metastasis. The Union for International Cancer Control (UICC) pathological staging was T1bN0M1 Stage IV. The patient was followed postoperatively in the outpatient clinic and received no adjuvant therapy. At 10 months postoperatively, lung metastasis, liver metastasis, and bone metastasis were detected. We performed molecularly targeted therapy, and there was no evidence of disease progression. The patient died 30 months after the operation.

Discussion

We encountered a rare case of synchronous cystic duct metastasis from RCC. Cystic duct metastasis from a malignant tumor is rare[6]. A PubMed search with the key words "Cystic duct metastasis" identified only five previous cases. The primary diseases of these five cases were breast cancer (n=2) and RCC, rectal cancer, and melanoma (n=1 each). These cases are summarized in **Table 2**[6–10]. In the present case, cystic duct metastasis from RCC was diagnosed preoperatively. Enhanced CT showed a hypervascular tumor in RCC[11]. In addition, metastases of RCC suggested the presence of a hypervascular tumor. We were able to detect the metastasis preoperatively, which was possible for only two of the six previous cases of RCC metastasis. Although we assumed that cystic duct metastases would cause cholecystitis, the previous case reports indicated that only half the patients presented with cholecystitis. In our patient, cystic duct metastasis from RCC did not cause cholecystitis.

The therapeutic strategy for cystic duct metastasis from RCC is unclear. In gallbladder metastasis from RCC, cancer cells may spread to multiple organs[3]. However, some reports indicated that about 40% of cases of gallbladder metastasis from RCC remained free of recurrent disease after cholecystectomy (longest duration of follow-up, 6 years)[12]. Our therapeutic strategy for gallbladder metastasis from RCC included cholecystectomy. We thus considered the same strategy for treatment of cystic duct metastasis from RCC.

Some recent studies showed that cytoreductive nephrectomy improved antitumor immune system response and overall survival rate for patients with metastatic RCC who underwent the procedure before treatment with interferon alfa[13,14]. However, cytoreductive nephrectomy is controversial for the management of metastatic RCC in the targeted therapy era[15]. Good performance status is a predictor of better overall survival after cytoreductive nephrectomy[16]. Moreover, complete resection of metastatic disease greatly improves survival[17–19]. Metastasectomy could allow patients to forgo systemic therapy[15]. The present patient's performance status was good, and complete resection of metastatic disease was thus indicated and performed.

The mechanism of cystic duct metastasis from RCC is unclear. We investigated the mechanisms of hematogenous, lymphatic, and direct metastasis. In our patient, cystic duct metastasis from RCC occurred via hematogenous dissemination, as no lymph node metastasis to regional lymph nodes in the bilateral kidney or gallbladder was observed, and microvascular invasion was present.

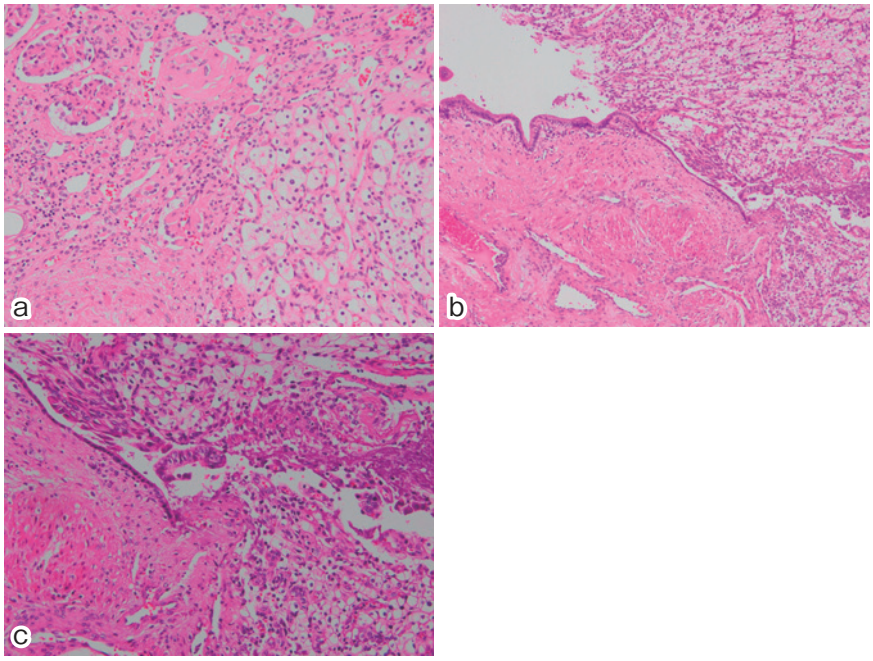

Fig. 4 a: Pathological examination revealed that the renal tumor was composed of clear cell carcinoma (×400).
b, c: The cystic duct tumor was also composed of clear cell carcinoma (b: ×100, c: ×200).

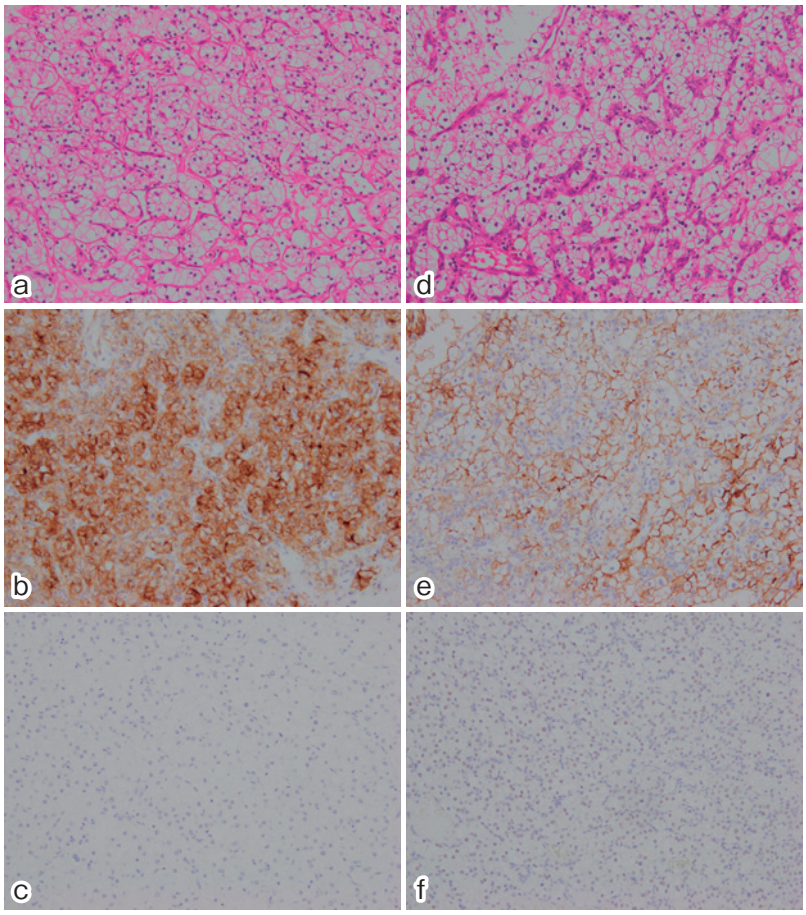

Fig. 5 a, RCC (×200, HE) b, RCC (×200 CD10) c, RCC (×200 PAX8) d, Cystic duct tumor (×200 HE) e, Cystic duct tumor (×200 CD10) f, Cystic duct tumor (×200 PAX8): CD10 was positive in the primary RCC tumor and cystic duct tumor; PAX8 was negative in both tumors.

Table 2 Summary of cases of cystic duct metastasis

	Age (years)	Sex	Primary cancer	Synchronous/ Metachronous	Operation	Diagnostic findings	Other metastasis	Outcome	Survival (months postoperatively)
1	59	F	Breast	Metachronous	Cholecystectomy	Cholecystitis	None	Dead	60
2	73	F	Breast	Metachronous	Cholecystectomy	Cholecystitis	Lymph node, Liver	Dead	12
3	52	F	Melanoma	Metachronous	Cholecystectomy	Cholecystitis	Lymph node, Liver	-	-
4	67	M	Rectal	Synchronous	Colon and Liver resection, Cholecystectomy	Intraoperative appearance	Liver	Dead	12
5	69	M	Kidney	Metachronous	Cholecystectomy	Preoperative imaging findings	None	Alive	7
present case	72	F	Kidney	Synchronous	Left nephrectomy, Bilateral adrenalectomy, Cholecystectomy, Resection of extrahepatic bile duct, Hepaticojejunostomy	Preoperative imaging findings	Left kidney Bilateral adrenal glands	Dead	30

Conclusion

This is the first report of synchronous cystic duct metastasis from RCC. The patient underwent complete resection including the primary kidney with ipsilateral adrenal gland, contralateral adrenal gland, and cystic duct metastatic lesions. Although the patient later developed lung, liver, and bone metastases, she survived for 30 months after surgical resection, with no disease progression. RCC and its metastases were completely resected. When RCC is diagnosed, a general assessment of the patient's condition, and complete resection, are necessary.

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(Received, July 5, 2018)
(Accepted, March 1, 2019)
(J-STAGE Advance Publication, April 26, 2019)