J Hepatobiliary Pancreat Surg (2008) 15:209–212
DOI 10.1007/s00534-007-1226-5

Journal of HBP Surgery

Renal cell carcinoma with unusual metastasis to the gallbladder

Hiroyuki Nojima[1], Akihiro Cho[1], Hiroshi Yamamoto[1], Matsuo Nagata[1], Nobuhiro Takiguchi[1], Osamu Kainuma[1], Hiroaki Souda[1], Hisashi Gunji[1], Akinari Miyazaki[1], Atsushi Ikeda[1], Ikuko Matsumoto[1], Takehide Asano[1], Munemasa Ryu[1], Naoki Nihei[2], and Masayuki Maruoka[2]

[1]Department of Gastroenterological Surgery, Chiba Cancer Center Hospital, 666-2 Nitona-chou, Chuo-ku, Chiba 260-8717, Japan
[2]Department of Urology, Chiba Cancer Center Hospital, Chiba, Japan

Abstract
Gallbladder involvement in patients with renal cell carcinoma (RCC) is extremely rare. We present a report of a 61-year-old man with a synchronous RCC metastasis to the gallbladder presenting as an intraluminal polypoid mass simulating primary gallbladder carcinoma. Enhanced abdominal computed tomography demonstrated a well-enhanced polypoid lesion in the gallbladder. Intraoperative rapid pathological examination of the gallbladder tumor showed clear cell-type cancerous cells. Microscopically, tumor cells of both the resected kidney and gallbladder had round uniform nuclei, clear cytoplasm, and well-defined cytoplasmic borders, forming alveolar patterns. Immunohistochemically, the tumor cells were negative for cytokeratin 7 (CK7) and carcinoembryonic antigen (CEA), which is usually positive in primary clear cell carcinoma of the gallbladder. Therefore, the final diagnosis was RCC with a synchronous gallbladder metastasis.

Key words Renal cell carcinoma · Gallbladder · Metastasis

Introduction

Renal cell carcinoma (RCC) is well known to metastasize to distant organs such as the lung, lymph nodes, bone, liver, and adrenal glands,[1] and approximately 30% of patients present with metastatic disease on initial examination.[2,3] However, gallbladder (GB) involvement in patients with RCC is extremely rare, being present in fewer than 0.6% of autopsies.[4,5] GB is rarely the site of distant metastasis of RCC, and in most cases, malignant melanoma is the primary tumor.[1] We herein present a rare case of premortem-diagnosed GB metastasis from RCC, which was completely resected.

Offprint requests to: H. Nojima
Received: February 14, 2007 / Accepted: March 16, 2007

Case report

A 61-year-old man was referred to our hospital with left lower quadrant abdominal pain radiating to the back, and bloody urine. Abdominal ultrasonography revealed a hypoechoic lesion, 30 mm in diameter, in the right kidney. Enhanced abdominal computed tomography (CT) demonstrated a 30-mm hypervascular right renal tumor with caval thrombosis. In addition, CT showed a well-enhanced 20-mm polypoid lesion in the GB (Fig. 1). Magnetic resonance imaging (MRI) also revealed a polypoid lesion in the GB, which showed low signal intensity on a T1-weighted image and high signal intensity on a T2-weighted image. Blood biochemistry results were in normal ranges, including carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9). Under the diagnosis of right renal cell carcinoma (RCC) and a presumptive diagnosis of metastatic GB tumor from RCC, the patient underwent a right radical nephrectomy with removal of the caval thrombosis, and cholecystectomy. Because a primary GB cancer could not be excluded, intraoperative rapid pathological examination of the GB tumor was performed, which showed clear cell-type cancerous cells. Macroscopically, the resected specimen of the right kidney showed an expansive mass with a false membrane, $45 \times 35 \times 30$ mm in diameter (Fig. 2) and the GB tumor showed a 15-mm-sized polypoid lesion (Fig. 3). Pathological findings of the renal tumor showed clear cell carcinoma (Fig. 4). Microscopically, the tumor of the GB was located in the submucosal layer, lifting the surrounding mucosa of the GB; the surface of the elevation had localized ulceration (Fig. 5). The GB mucosal cells had no atypia. The tumor cells had round uniform nuclei, clear cytoplasm, and well-defined cytoplasmic borders, forming alveolar patterns (Fig. 6). There were no foci of mucin production nor ordinary adenocarcinoma patterns of digestive organs. Immunohistochemically, the tumor cells were negative for cytokeratin 7 (CK7; Fig. 7) and CEA.

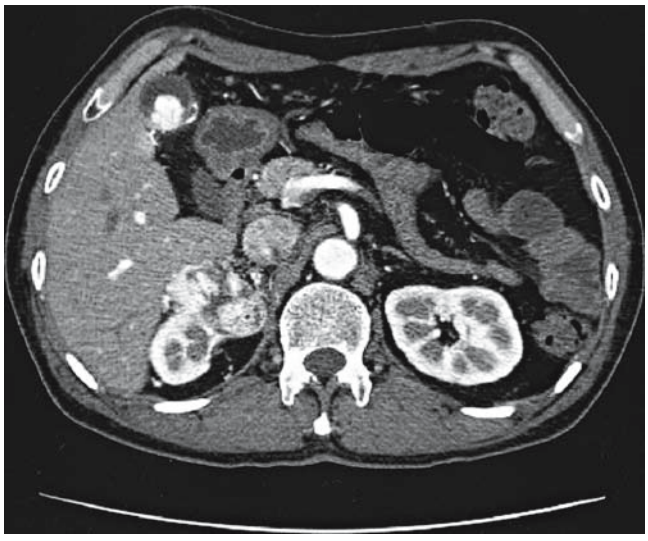

Fig. 1. Enhanced computed tomography (CT), showing a well-enhanced 20-mm polypoid lesion in the gallbladder (GB)

Fig. 2. Resected specimen of the right kidney, showing an expansive mass with a false membrane, 45 × 35 × 30 mm in diameter

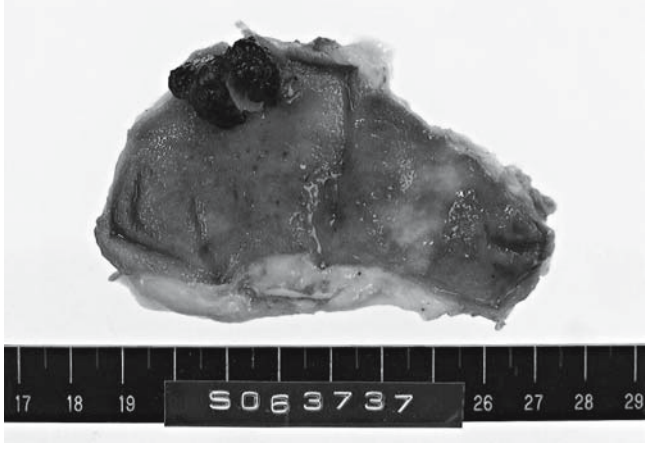

Fig. 3. The resected GB specimen, showing a 15-mm-sized polypoid lesion

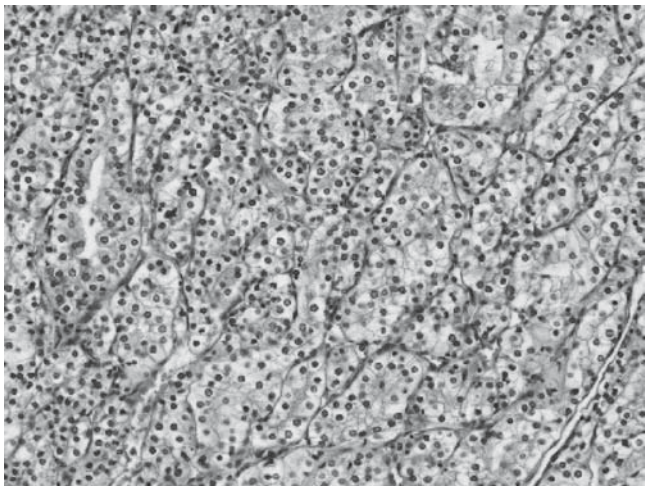

Fig. 4. Pathological findings of the renal tumor showed clear cell carcinoma. H&E, ×40

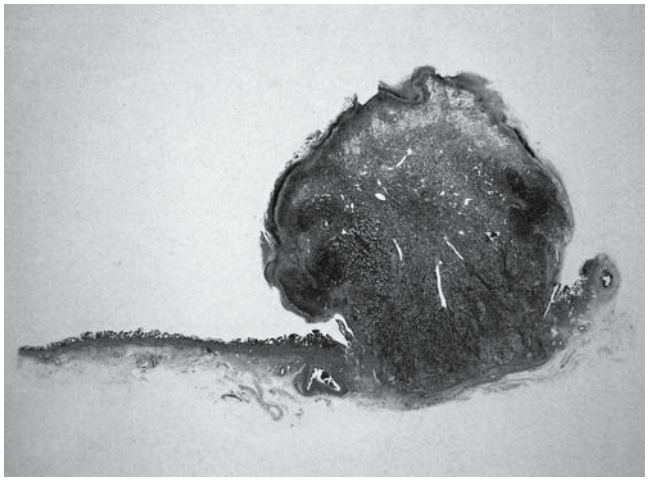

Fig. 5. The tumor of the GB was located in the submucosal layer, lifting the surrounding mucosa of the GB; the surface of the elevation had localized ulceration. H&E, ×4

Therefore, the final diagnosis was RCC with a synchronous GB metastasis. The postoperative course was uneventful, and the patient has been well with no recurrence noted during the 10 months of follow-up, without any additional therapies.

Discussion

Distant metastases of RCC are present in about 25%–35% of patients at the time of diagnosis.[6] The reported 5-year survival rate of RCC patients is approximately 50%,[7] while that of the patients with distant metastases is approximately 10%.[6] The metastatic behavior of RCC

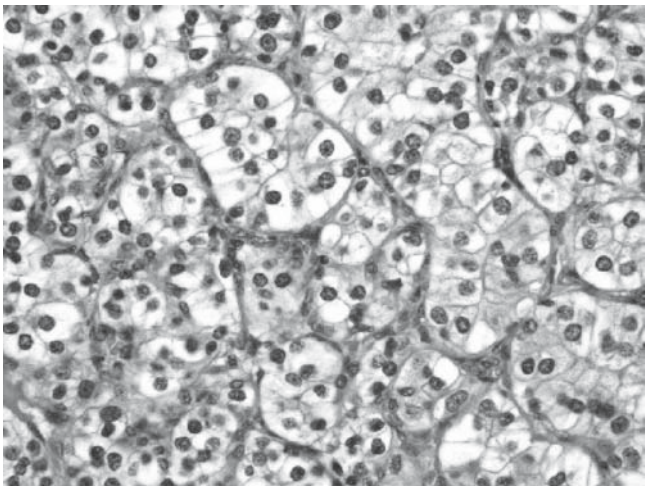

Fig. 6. Histologically, the tumor cells had round uniform nuclei, clear cytoplasm, and well-defined cytoplasmic borders, forming alveolar patterns. H&E, ×40

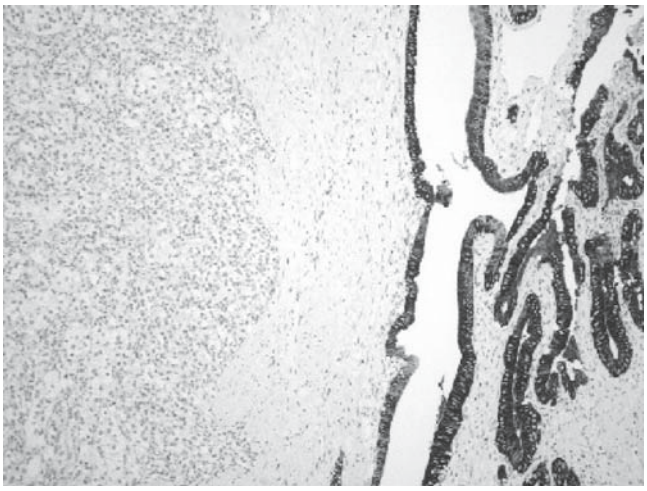

Fig. 7. Immunohistochemically, the tumor cells were negative for cytokeratin 7 (CK7). In contrast, the mucosa of the GB was positive for CK7, ×10

Table 1. Reported cases of gallbladder metastasis of renal cell carcinoma

Case no.	Age (years)/Sex	Symptom	Syn or Meta Interval	Operative procedures	Macroscopic findings	Outcome
1[8]	46 M	–	Meta/11 M	Cholecystectomy	Polypoid	Alive, 16 M
2[9]	73 M	–	Meta/5 Y	Cholecystectomy	Pedunculated	Alive, 2 Y
3[10]	64 M	–	Meta/1 Y	Cholecystectomy	Polypoid	NR
4[11]	48 M	–	Meta/2 Y	Cholecystectomy	Polypoid	NR
5[18]	63 M	–	Meta/27 Y	Cholecystectomy	Polypoid	Alive, 6 Y
6[18]	80 M	–	Meta/8 Y	Cholecystectomy	Pedunculated	Alive, 2 Y
7[16]	73 M	+	Syn	Rad nephrectomy and chole	Polypoid	Dead, 1 M
8[12]	46 M	+	Meta/3 Y 8 M	Cholecystectomy	Polypoid	Dead, 4 Y
9[17]	41 M	–	Meta/3 M	Cholecystectomy	Pedunculated	Alive, 7 M
10[13]	62 M	–	Syn	Rad mephrectomy and chole	Round	Alive, 3 Y
11[14]	64 M	+	Syn	Rad nephrectomy and chole	Polypoid	Alive, 26 M
12[15]	71 M	–	Meta/1 Y	Cholecystectomy	Polypoid	Alive, 19 M
13[Present patient]	61 M	+	Syn	Rad nephrectomy and chole	Polypoid	Alive, 10 M

Syn, synchronous; meta, metachronous; rad, radical; chole, cholecystectomy; NR, not reported; M, mouths; Y, years

is often bizarre and unpredictable, and it is known to metastasize mainly to the lung, lymph nodes, bone, brain, liver, adrenal glands, the other kidney, and rarely to organs such as the vertebrae, stomach, spleen, pancreas, and diaphragm.[5] However, GB metastasis of RCC is seldom detected, being present in fewer than 0.6% of autopsies.[4,5]

In our review of the English-language literature, we found 12 reported cases of GB metastasis of RCC (summarized in Table 1).[8–18] The presumed mode of GB involvement from intraperitoneal organs is usually direct invasion or peritoneal implantation, while metastases from extraperitoneal organs, such as the lung, kidney, breast, and malignant melanoma, follow a hematogenous route.[15,19] Hematogeneous metastases to GB initially occur as small flat nodules below the mucosal layer and then they grow as a pedunculated nodule and resemble a primary GB carcinoma.[16] It is well known that cholecystectomy is not sufficient treatment and more radical surgery is required for GB carcinoma with muscular-layer invasion or more advanced disease.[20–23] Furukawa et al.[24] reported that 1 of 31 resected GB polypoid lesions of less than 3 cm was a metastasis from RCC, which was detected on both unenhanced and enhanced CT scans. Dynamic contrast-enhanced CT is useful in the differential diagnosis between metastatic GB tumor from RCC and primary GB carcinoma, because the former is hypervascular, as is primary RCC, while the latter is not so hypervascular.[17] In the present patient, contrast-enhanced CT

showed high density on an arterial dominant phase image, and MRI showed high signal intensity on a T2-weighted image. However, the density of primary GB lesions compared with the density of liver parenchyma on enhanced CT was not shown to be specific.[25] Therefore, we performed intraoperative rapid pathological examination. For the final differential diagnosis between primary and secondary GB tumors, immunohistochemical evaluation is necessary. Immunohistochemically, primary clear cell carcinoma of the GB is strongly positive for CEA and CK7, and moderately positive for CK10, but negative for vimentin. On the other hand, metastatic RCC of the GB is positive for vimentin, but negative for CEA, CK7, and CK10.[18,26] Because our immunohistochemical findings were nearly consistent with the reported findings, we finally diagnosed metastatic GB tumor from RCC rather than primary clear cell carcinoma of the GB. Although metastatic RCC to the GB is unusual, the possibility of GB metastasis from RCC should not be excluded in patients with RCC or a known history of RCC, which is relatively easy to diagnose based on the findings of a pathological examination, including immunohistochemical staining.

References

1. Saitoh H. Distant metastasis of renal adenocarcinoma. Cancer 1981;48:1487–91.
2. Lokioch J, Harrison JH. Renal cell carcinoma: natural history and chemotherapeutic experience. J Urol 1975;114:371–4.
3. de Kernion JB, Belldegrum A. Renal tumors. In: Walsh PC, Retik AB, Stamey TA, Vaughan ED Jr, editors. Campbell's urology. 6th ed. Philadelphia: WB Saunders; 1992. Chapter 2, p. 1053–93.
4. Bennington JL, Kradjan RM. Distribution of metastases from renal carcinoma. In: Renal carcinoma. Philadelphia: WB Saunders: 1967. p. 156–70.
5. Weiss L, Harlos JP, Torhorst J, Gunthard B, Hartveit F, Svendsen E, et al. Metastatic patterns of renal carcinoma: an analysis of 687 necropsies. J Cancer Res Clin Oncol 1988;114:605–12.
6. Dekernion JB, Ramming KP, Smith RB. The natural history of metastatic renal carcinomas: a computer analysis. J Urol 1978; 120:148–52.
7. Silverberg E, Lubera JA. Cancer statistics. CA Cancer J Clin 1989;39:3–20.
8. Pandey D, Kane SV, Shukla PJ, Shrikhandle SV, Tongaonkar HB. Isolated gall bladder metastasis from renal cell carcinoma. Indian J Gastroenterol 2006;25:161–2.
9. Ishizawa T, Okuda J, Kawanishi T, Kitagawa T, Yakumaru K, Sekikawa T. Metastatic renal cell carcinoma of the gallbladder. Asian J Surg 2006;29:145–8.
10. Limani K, Matos C, Hut F, Gelin M, Closset J. Metastatic carcinoma of the gallbladder after a renal cell carcinoma. Acta Chir Belg 2003;103:233–4.
11. Park JS, Chae YS, Hong SJ, Shin DH, Choi JS, Kim BR. Metastatic renal cell carcinoma of the gallbladder. Yonsei Med J 2003;44:355–8
12. Sparwasser C, Krupienski M, Radomsky J, Pust RA. Gallbladder metastasis of renal cell carcinoma. A case report and review of the literature. Urol Int 1997;58:257–8.
13. King DH, Centeno AS, Saldivar VA, Sarosdy MF. Renal cell carcinoma metastatic to the gallbladder or prostate: two case reports. Urology 1995;46:722–5.
14. Pagano S, Ruggeri P, Franzoso F, Brusamolino R. Unusual renal cell carcinoma metastasis to the gallbladder. Urology 1995;45: 867–9.
15. Satoh H, Iyama A, Hidaka K, Nakashiro H, Harada S, Hisatsugu T. Metastatic carcinoma of the gallbladder from renal cancer presenting as intraluminal polypoid mass. Dig Dis Sci 1991; 36:520–3.
16. Celebi I, Guzelsoy M, Yorukoglu K, Kirkali Z. Renal cell carcinoma with gallbladder metastasis. Int J Urol 1998;5:288–90.
17. Furukawa H, Mizuguchi Y, Kanai Y, Mukai K. Metastatic renal cell carcinoma to the gallbladder: color Doppler sonography and CT findings. AJR Am J Roentgenol 1997;169:1466–7.
18. Andoh H, Kurokawa T, Yasui O, Shibata S, Sato T. Resection of a solitary pancreatic metastasis from renal cell carcinoma with a gallbladder carcinoma: report of a case. Surg Today 2004;34: 272–5.
19. Murguia E, Quiroga D, Canteros G, Sanmartino C, Barreiro M, Herrera J. Gallbladder metastases from ductal papillary carcinoma of the breast. J Hepatobiliary Pancreat Surg 2006;13: 591–3.
20. Rodriguez Otero JC, Proske A, Vallilengua C, Lujan M, Poletto L, Pezzotto SM, et al. Gallbladder cancer: surgical results after cholecystectomy in 25 patients with lamina propria invasion and 26 patients with muscular layer invasion. J Hepatobiliary Pancreat Surg 2006;13:562–6.
21. Yagi H, Shimazu M, Kawachi S, Tanabe M, Aiura K, Wakabayashi G, et al. Retrospective analysis of outcome in 63 gallbladder carcinoma patients after radical resection. J Hepatobiliary Pancreat Surg 2006;13:530–6.
22. Araida T, Yoshikawa T, Azuma T, Ota T, Takasaki K, Hanyu F. Indications for pancreatoduodenectomy in patients undergoing lymphadenectomy for advanced gallbladder carcinoma. J Hepatobiliary Pancreat Surg 2004;11:45–9.
23. Srikanth G, Kumar A, Khare R, Siddappa L, Gupta A, Sikora SS, et al. Should laparoscopic cholecystectomy be performed in patients with thick-walled gallbladder? J Hepatobiliary Pancreat Surg 2004;11:40–4.
24. Furukawa H, Kosuge T, Shimada K, Yamamoto J, Kanai Y, Mukai K, et al. Small polypoid lesions of the gallbladder: differential diagnosis and surgical indications by helical computed tomography. Arch Surg 1998;133:735–9.
25. Furukawa H, Takayasu K, Mukai K, Inoue K, Kyokane T, Shimada K, et al. CT evaluation of small polypoid lesions of the gallbladder. Hepatogastroenterology 1995;42:800–10.
26. Bittinger A, Alterkrugar I, Barth P. Clear cell carcinoma of the gallbladder. a histological and immunohistochemical study. Pathol Res Pract 1995;191:1259–65.