Anatomical hepatectomy for liver metastasis from rectal adenocarcinoma presenting with intrabiliary extension: a case report

Tetsuo Kon, Hideo Suzuki, Tatsuya Kawaguchi, Kazuyuki Gyoten, Hideki Machishi, Takashi Kurumiya and Yoshikatsu Okada

1 Department of Surgery, Kuwana East Medical Center, Japan
2 Department of Radiology, Kuwana East Medical Center, Japan

Abstract

Liver metastases from colorectal carcinoma commonly form nodular lesions in the liver parenchyma. We report a case of liver metastasis from rectal adenocarcinoma that extended predominantly into the bile duct. A 62-year-old Japanese man underwent low anterior resection for rectal adenocarcinoma 9 years ago. Approximately 3 years later, he underwent radiofrequency ablation therapy for a metastatic liver tumor. Nine years after surgery, a tumor in liver segment III exhibiting intrabiliary extension was discovered; it was unclear if this was a metastatic liver tumor or intrahepatic cholangiocarcinoma. Accordingly, we performed a left hepatectomy with lymph node dissection. The tumor was negative for cytokeratins 7 and 20, and was histologically similar to the primary rectal adenocarcinoma; it was diagnosed as rectal carcinoma metastasis. The patient has survived for 3 years after the hepatic surgery, for 9 years after radiofrequency ablation therapy, and for 12 years after the primary surgery. This case shows that liver metastasis from colorectal carcinoma can present as a predominantly intrabiliary growth that mimics intrahepatic cholangiocarcinoma on imaging. Moreover, our case provides evidence for the superiority of anatomical hepatectomy over partial hepatectomy for metastatic liver tumors with intrabiliary growth arising from rectal adenocarcinomas.

Key words: colorectal adenocarcinoma, liver metastasis, intrabiliary growth, cholangiocarcinoma, anatomical hepatectomy, partial hepatectomy

Introduction

Liver metastases from colorectal carcinoma (CRC) commonly form nodular lesions in the liver parenchyma. However, there have been reports of unusual cases of metastatic liver tumors from CRC that predominantly extend along the intrahepatic bile duct. Such unusual tumors generally mimic intrahepatic cholangiocarcinoma (IHCC) clinically, radiographically, and pathologically. Importantly, it remains unclear whether anatomical or partial hepatectomy is more suitable to treat such tumors. Herein, we report a case of liver metastasis from CRC presenting as an intrabiliary growth, and discuss the clinicopathological considerations that inform selection of the surgical procedure for such tumors.

Case Report

The patient was a 62-year-old Japanese man who had undergone low anterior resection for rectal carcinoma 9 years earlier. The pathological stage of the rectal carcinoma was stage II (T3N0M0). Histologically, the tumor was a well-differentiated adenocarcinoma with lymphovascular invasion (Figure 1a, b). Three years and 2 months after the surgery, a metastatic tumor was found in liver segment VI. The patient chose radiofrequency ablation therapy (RFA) over surgery. During a post-RFA follow-up period of 6 years and 1 month, his serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) levels remained within the normal ranges. However, 1 week before admission, serum CEA and CA19-9 levels were elevated to 6.8 ng/dL (normal range, <5.0 ng/dL) and 40.3 U/mL (normal range, <37.0 U/mL), respectively.

Upon admission to our hospital, the patient exhibited no abnormalities on physical examination. Complete blood
counts and serum chemistry profiles were within normal limits. Abdominal contrast-enhanced computed tomography revealed distention of the superior branch of the bile duct in segment III of the liver (B3) (Figure 2a) as well as a nodule in the same segment (Figure 2b). A slightly enhancing lesion extended along the inferior branch of B3 (Figure 2b). Abdominal magnetic resonance imaging revealed a tumor along the inferior branch of B3, with a low-intensity signal on T1-weighted images (Figure 3a) and an isointense signal with background liver parenchyma on T2-weighted images (Figure 3b). On diffusion-weighted images, the lesion in the inferior branch of B3 exhibited a high-intensity signal (Figure 3c). Based on these findings, the differential diagnoses were metastatic liver tumor from rectal carcinoma and IHCC. Hence, we performed a left hepatectomy with dissection of the lymph nodes in the hepatoduodenal ligament.

Macroscopically, a whitish nodule, measuring 1.5 × 1.0 cm, was found in the parenchyma of segment III adjacent to the inferior surface of the liver (Figure 4). The tumor involved the inferior branch of B3 and extended along it. The superior branch of B3 and the bile duct in segment II were preserved.

Histological examination revealed that an adenocarcinoma showed predominantly intraductal papillary growth replacing the bile duct epithelium (Figure 5a, b, c). The tumor cells showed abrupt transition to the adjacent bile duct, which in turn showed no cellular atypia (Figure 5b, c). The tumor cells of the liver contained pencil-like hyperchromatic nuclei (Figure 5d). These histological findings were consistent with liver metastasis from primary rectal adenocarcinoma. The intrahepatic arteries and portal veins were preserved. The tumors (Figure 6a) were negative for cytokeratin (CK) 7 and CK20 on immunohistochemical analysis (Figure 6b, c), whereas the normal biliary epithelium was positive for CK7 and negative for CK20 (Figure 6b, c). CA19-9 was absent in the tumor cells, but present in the biliary epithelial cells (Figure 6d). Because both the original and metastatic tumors demonstrated strikingly similar histological appearances, the tumor was diagnosed as a liver metastasis from rectal carcinoma.

The patient had an uneventful postoperative course and received adjuvant chemotherapy with capecitabine. He has not exhibited any signs of recurrence in the liver or any other organ, and is functioning well 3 years after the most recent surgery. The patient provided written informed consent for reporting this case.

Discussion

In the present case, a metastatic tumor from CRC involved the inferior branch of B3 and extended predominantly along this branch, with an intraductal papillary growth pattern. Comparison between computed tomography images obtained 6 months before admission and those obtained on admission showed the growth of the tumor (Figure 7a, b). On images obtained 6 months before admission, a nodule with a slightly low attenuation, measuring 1.5 × 1.0 cm in diameter, was retrospectively discovered close to the inferior surface of the liver (Figure 7a, right). Neither enlargement of the superior branch of B3 nor tumor extension along the inferior branch of B3 was observed 6 months prior to admission (Figure 7a; left, center, and right). At the time
of admission, this nodule had already involved the inferior branch of B3 (Figure 7b). Owing to a tumor embolism in the bifurcation of B3, the superior branch of B3 was enlarged on admission (Figure 7b). The increased tumor volume and bile duct obstruction may explain the slight elevation of the serum CEA and CA19-9 levels, respectively.

Liver metastases from CRC occasionally involve the bile duct and show intraductal papillary growth. According to a study by Okano et al., 10% of liver metastases from CRC show intrabiliary growth macroscopically⁵. Similarly, Kubo et al. reported that 10.6% (23/217) of liver metastases from CRC presented with macroscopic intrabiliary growth⁶. A
Liver metastasis from CRC with intrabiliary growth is associated with a better prognosis than other forms of liver metastases. Okano et al. reported that patients with macroscopic bile duct invasion had a better 5-year survival rate (80%) than those with microscopic bile duct invasion (48%) or no bile duct invasion (57%)². They also identified macroscopic invasion as an independent prognostic variable ². Moreover, Kubo et al. reported a significant difference between patients with and without macroscopic intrabiliary extension in terms of the interval between initial colectomy and hepatectomy (37.4 ± 25.4 vs. 6.1 ± 7.2 months, respectively)⁹. These different outcomes may be explained by the fact that most tumors with intrabiliary growth are well-differentiated adenocarcinomas. This feature is characteristic of less aggressive tumors and results in tumor colonization of the bile duct; the normal biliary epithelium is replaced with tumor cells, which grow along an intact basement membrane without penetrating it. The clinical course of the patient presented here was consistent with that of a less aggressive tumor; he had a well-differentiated adenocarcinoma with intrabiliary extension and has survived for 3 years after the hepatic surgery, for 9 years after RFA, and for 12 years after the primary surgery of the rectum.

Preoperative differentiation between liver metastasis from CRC with intrabiliary growth and IHCC is difficult. There are no clinical symptoms that are highly characteristic of liver metastasis from CRC with intrabiliary growth⁸,⁹. While elevated CEA and serum alkaline phosphatase levels are common findings on laboratory tests⁸,⁹, these markers can also be elevated in IHCC patients¹⁰,¹¹. The computed tomography findings of liver metastasis from CRC with intrabiliary growth are usually nonspecific, although a thickened portal tract, intrahepatic bile duct dilatation, and a wedge-shaped area with contrast enhancement are characteristic features of this type of tumor¹². On the other hand, cholangiocarcinoma presents with a broad range of appearances on radiography¹³,¹⁴.

Importantly, this case provides evidence for the superiority of anatomical hepatectomy over partial hepatectomy for metastatic liver tumors with intrabiliary growth arising from rectal adenocarcinomas. When liver metastases from CRC form nodular lesions in the liver parenchyma, partial hepatectomy may be a sufficient treatment¹⁵; however, when the tumor shows intrabiliary spreading, as seen in the present case, partial hepatectomy alone may not com-
pletely excise the tumor because of the extension along the bile ducts10. Although there is no consensus regarding the most appropriate procedure for such patients, anatomical hepatectomy tends to be preferred over regional liver resection7, 9, 17–19. This is primarily to guard against the possibility of residual tumor cells on the cut margin of the bile duct7, 9, 17–19. Moreover, anatomical hepatectomy is the logical choice because of the aforementioned difficulty in preoperatively differentiating between a liver metastasis with intrabiliary growth arising from CRC and IHCC. In the present case, we performed a left hepatectomy with sufficient margins in the bile duct that resulted in good postoperative outcome; the patient has survived for a relatively long period.

Pathological discrimination between liver metastasis from CRC and IHCC should be performed carefully, based on both conventional histological examination using hematoxylin and eosin staining and immunohistochemical staining with antibodies against CK7 and CK20. This procedure is particularly important to determine the need for, and the selection of, chemotherapy. It is also important in prognosis prediction. Metastatic liver tumors from CRC with macroscopic intrabiliary growth show a histologically abrupt transition from the adjacent bile duct epithelium to tumor tissue: cellular atypia is absent in the normal bile duct epithelial cells9. On immunohistochemical analysis, a typical CK7−/CK20+ expression pattern is generally observed in CRC20–22. In contrast, biliary epithelial cells show a CK7+/CK20− pattern19–22. However, according to Tot et al., 9% (18/206) of metastatic liver tumors from CRC were negative for both CK7 and CK20 expression20. Similarly, Sasaki et al. reported that 16% (4/25) of liver metastases from CRC were CK7−/CK20−23. Whereas Rullier et al. reported that no CK7−/CK20− cholangiocarcinomas were found among their cases (0/29)24. In the present case, the liver tumor showed a histological appearance similar to that of the primary tumor, as well as an abrupt change from the normal bile duct epithelium to the adenocarcinoma. Immunohistochemical analysis revealed a CK7−/CK20− expression pattern. The tumor was ultimately diagnosed as a metastasis from the primary CRC.

However, intrahepatic recurrence of the segment VI metastatic lesion treated with RFA 6 years before admission cannot be completely ruled out. Intrahepatic recurrences after treatment of metastatic liver tumors from CRC show diverse patterns, including local recurrence, multiple hepatic nodules, and intrahepatic distant metastases25. Therefore, it is possible that ours is a rare case of intrahepatic recurrence.

In conclusion, we report an unusual case of liver metastasis from rectal adenocarcinoma that presented with intrabiliary growth (Figure 8). During follow-up, physicians should consider the possibility of liver metastasis with intrabiliary growth for patients with a history of CRC. Moreover, our patient’s long survival time suggests that anatomical hepatectomy is a more effective treatment than partial hepatectomy for metastatic liver tumors from CRC with intrabiliary growth.

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