

T1 Colorectal Cancer with Synchronous Liver Metastasis

Kiichi Sugimoto^a Masaya Kawai^a Kazuhiro Takehara^a
Yoshihiko Tashiro^a Shinya Munakata^a Shun Ishiyama^a
Hiromitsu Komiyama^a Makoto Takahashi^a Yutaka Kojima^a
Michitoshi Goto^a Yuichi Tomiki^a Kazuhiro Sakamoto^a Seiji Kawasaki^b

Departments of ^aColoproctological Surgery and ^bHepato-Biliary-Pancreatic Surgery,
Juntendo University Faculty of Medicine, Tokyo, Japan

Key Words

T1 colorectal cancer · Lymph node metastasis · Synchronous liver metastasis · Distant metastasis · Risk factor

Abstract

The patient was a 68-year-old man who was admitted to our hospital with a liver tumor. Abdominal ultrasonography and computed tomography revealed a liver tumor 30 mm in diameter. On colonoscopy, a pedunculated tumor with a central depression (20 mm in diameter) was observed in the ascending colon, and this tumor was considered to be invading deeply into the submucosal layer. Right hemicolectomy with D3 lymphadenectomy and partial hepatectomy were performed simultaneously. On histopathological examination of the resected specimen, the tumor was a well-differentiated tubular adenocarcinoma with 3,000 µm invasion of the submucosal layer. The liver tumor showed histological findings similar to those of the primary colorectal carcinoma. The pathological stage according to the 7th edition of the TNM classification was stage IV (T1N0M1). Nine months after the operation, computed tomography revealed hepatic hilar lymph node metastases and a great deal of ascites. The patient ultimately died 14 months after the operation.

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Introduction

Colorectal cancer is one of the most common cancers in developed countries [1]. In Japan, it accounts for the largest number of deaths from malignant neoplasms in women and the third largest number in men [1]. However, since the recurrence rate of T1 colorectal

Kiichi Sugimoto
Department of Coloproctological Surgery
Juntendo University Faculty of Medicine
2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421 (Japan)
E-Mail ksugimo@juntendo.co.jp

cancer (invasion no deeper than the submucosa) without lymph node metastasis is approximately 1%, the outcome of T1 colorectal cancer is considered to be good [1]. On the other hand, the incidence of synchronous liver metastases in colorectal cancer has been reported to be about 10% [2], yet T1 colorectal cancer with synchronous liver metastasis is considered to be rare [3, 4]. The form of metastases from T1 colorectal cancer is mainly lymph node metastases. A few patients exhibit hematogenous metastases, such as liver metastases. Therefore, there have been many reports of lymph node metastases, but few reports of the risk factors of synchronous or metachronous distant metastases from T1 colorectal cancer. We report a case of T1 colorectal cancer of the ascending colon with synchronous liver metastasis.

Case Report

The patient was a 68-year-old Japanese man who was admitted to our hospital with a liver tumor that had been detected by abdominal ultrasonography. His medical history included hypertension, diabetes mellitus and gout. Physical examination indicated no significant findings. Laboratory tests showed: erythrocyte count $484 \times 10^4/\text{mm}^3$ (normal 420–554), hemoglobin 15.9 g/dl (normal 13.8–16.6), leukocyte count $8,600/\text{mm}^3$ (normal 3,500–9,000), platelet count $21.8 \times 10^4/\text{mm}^3$ (normal 15.5–36.5), serum total protein 6.5 g/dl (normal 6.3–8.1), total bilirubin 0.69 mg/dl (normal 0.3–1.2), aspartate aminotransferase 28 IU/l (normal 9–38), alanine aminotransferase 27 IU/l (normal 4–36), alkaline phosphatase 224 IU/l (normal 115–359), γ -glutamyl transpeptidase 53 IU/l (normal 4–68), blood urea nitrogen 16 mg/dl (normal 9–21), and creatinine 0.92 mg/dl (normal 0.60–1.20). Hepatitis B surface and hepatitis C antibody were negative. Carcinoembryonic antigen and CA19-9 were both elevated at 23.9 ng/ml (normal 0–3) and 51 U/ml (normal 0–37), respectively.

Abdominal ultrasonography revealed a hyperechoic mass in segment 7 of the liver, 30 mm in diameter, with a circumferential hypoechoic area. Abdominal computed tomography also showed mild enhancement of a liver tumor 30 mm in diameter at the portal phase (fig. 1a). On colonoscopy, a pedunculated tumor with a central depression (20 mm in diameter) was observed in the ascending colon, and this tumor was considered to be invading deeply into the submucosal layer (fig. 1b). Abdominal magnetic resonance imaging showed the liver tumor as a low-intensity mass in the T1 emphasis phase (fig. 1c), as a high-intensity mass in the T2 emphasis phase (fig. 1d) and as a strongly high-intensity mass by administering the contrast medium ferumoxide (fig. 1e). T1 colorectal carcinoma with liver metastasis was suspected, and right hemicolectomy with D3 lymphadenectomy and partial hepatectomy were performed simultaneously (fig. 2a, b). On histopathological examination of the resected specimen, the tumor was a well-differentiated tubular adenocarcinoma with 3,000 μm invasion of the submucosal layer (fig. 2c, d) and venous permeation without tumor budding or lymph node metastasis. The liver tumor showed histological findings similar to those of the primary colorectal carcinoma (fig. 2e). The pathological stage according to the 7th edition of the TNM classification was stage IV (T1N0M1). The patient had an uneventful postoperative course. He took 5-FU drugs orally for 6 months as a postoperative adjuvant chemotherapy. Nine months after the operation, elevation of serum carcinoembryonic antigen was recognized. Computed tomography revealed hepatic hilar lymph node metastases and a great deal of ascites. His general condition worsened, and the patient ultimately died 14 months after the operation.

Discussion

A multicenter study in Japan reported that 153 (8.5%) of 1,806 patients with T1 colorectal cancer had lymph node metastases and 40 (2.2%) of 1,806 patients had synchronous or metachronous distant metastases [3]. Among them, the incidence of liver metastases was 1.2%. Furthermore, when the focus was restricted to synchronous liver metastases, the incidence was 0.2%. Okano et al. [4] also reported that the incidence of liver metastases from T1 colorectal cancer was 3.3% and that of synchronous liver metastases 0.9%. Thus, the form of metastases from T1 colorectal cancer is mainly lymph node metastases. However, a few patients exhibit hematogenous metastasis, such as liver metastases. Moreover, synchronous liver metastases are thought to be extremely rare. Therefore, to date, there have been many reports of lymph node metastases but few reports of distant metastases.

With respect to the risk factors of lymph node metastasis in T1 colorectal cancer, Sakuragi et al. [5] reported that the depth of submucosal invasion ($\geq 2,000$ μm) and lymphatic invasion significantly predicted the risk of lymph node metastasis in multivariate analysis. In addition, the depth of submucosal invasion ($\geq 1,000$ μm) [6], lymphovascular invasion [6], histological grade [7, 8] and budding at the invasive front of the tumor [7, 8] were thought to be significantly associated with lymph node metastasis. On the other hand, with respect to the risk factors of synchronous or metachronous distant metastases from T1 colorectal cancer, nodal metastases, depth of invasion and venous invasion are considered to be risk factors [3]. Okano et al. [4] also reported that venous invasion was closely related to liver metastasis. These risk factors of distant metastasis are often common to those of lymph node metastases. It is considered that the highly malignant potential of T1 colorectal cancer, which can invade the submucosal layer broadly or exhibit poor differentiation, allows the tumor to invade the venous plexus of the submucosal layer and then develop distant metastases. In our case, submucosal invasion (3,000 μm) and venous invasion were recognized as risk factors. Consequently, this case had multiple risk factors of distant metastasis.

Liver resection for resectable liver metastases is recommended as the most effective therapy [9]. It has also been reported that the 5-year survival rate after liver resection in patients with synchronous liver metastases is 19–38%, and that the prognosis of patients with resectable synchronous liver metastases is better than that of those with non-resectable liver metastases [10]. However, even after curative resection, some cases have a poor prognosis for recurrence in the remnant liver and exhibit extrahepatic recurrence. In our case, postoperative adjuvant chemotherapy was undertaken for 6 months, however the prognosis was poor because of extrahepatic recurrence 9 months after the operation. Hayaishi et al. [11] reported that extrahepatic recurrence was a prognostic factor after curative liver resection and noted that postoperative adjuvant systemic chemotherapy is necessary for patients with synchronous liver metastases because liver metastases should be considered equivalent to systemic disease. Moreover, expert consensus statements by the American Hepato-Pancreato-Biliary Association also concluded that adjuvant systemic chemotherapy after curative liver resection must be supported because most patients with synchronous liver metastases concurrently exhibit extrahepatic metastases [12]. However, the regimens and periods of postoperative adjuvant systemic chemotherapy were not fixed because of the absence of consensus for adjuvant chemotherapy after curative liver resection. Further investigations are necessary in order to judge the usefulness of postoperative adjuvant chemotherapy. There are few well-organized reports because T1 colorectal cancer with synchronous liver metastasis is extremely rare. On the other hand, the prognosis is often poor in patients with metachronous liver metastases after surgery for T1 colorectal cancer [13–15]. Therefore, it is predictable that the prognosis of patients with synchronous

liver metastasis is also poor. It is necessary to establish postoperative surveillance and a plan for adjuvant chemotherapy for T1 colorectal cancer with synchronous liver metastasis.

We consider this case to be rare, and it is necessary to accumulate more cases to further elucidate the risk factors for liver metastasis from T1 colorectal cancer.

Disclosure Statement

The authors declare no conflict of interests for this article.

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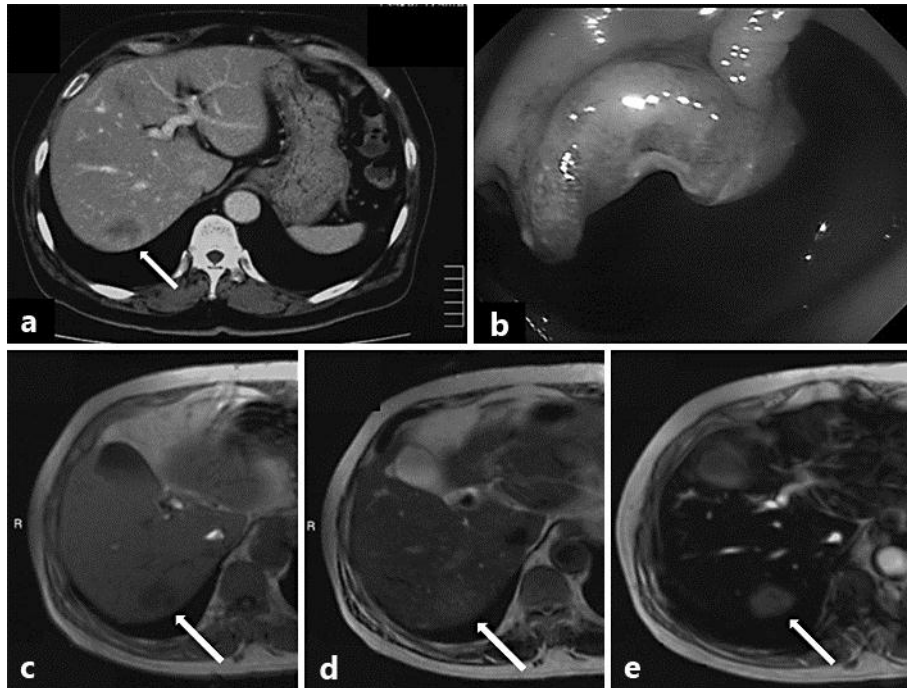


Fig. 1. **a** Abdominal computed tomography showed mild enhancement of a liver tumor 30 mm in diameter. **b** On colonoscopy, a pedunculated tumor with a central depression (20 mm in diameter) was observed in the ascending colon. **c–e** Abdominal magnetic resonance imaging showed the liver tumor as a low-intensity mass in the T1 emphasis phase (**c**), as a high-intensity mass in the T2 emphasis phase (**d**) and as a strongly high-intensity mass by administering the contrast medium ferumoxide (**e**).

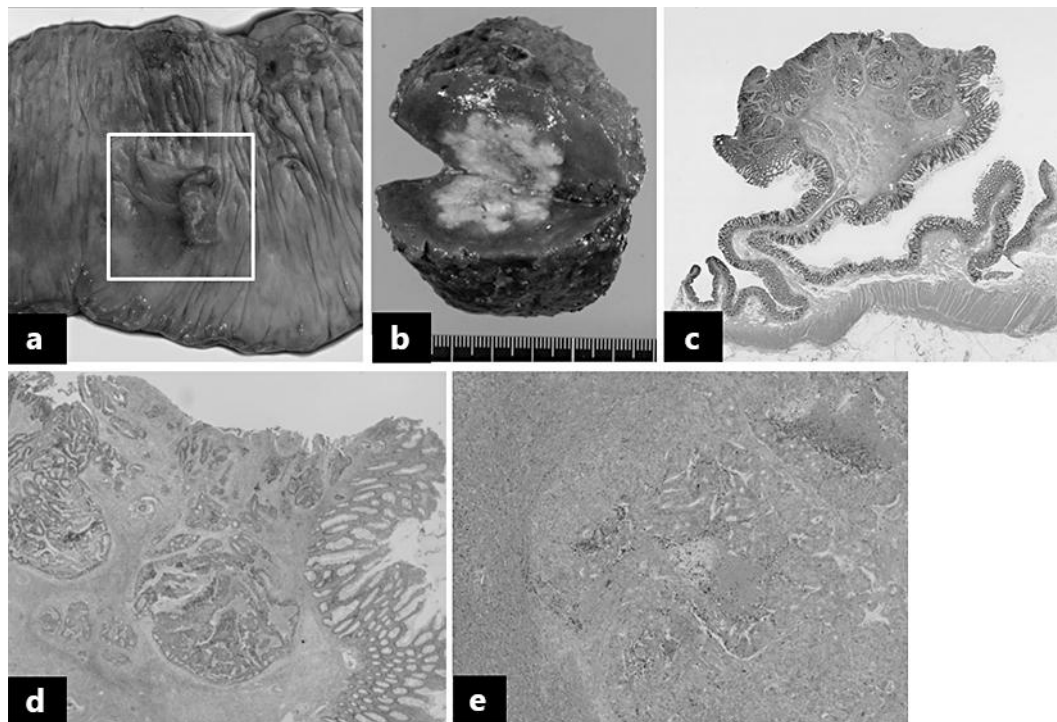


Fig. 2. **a, b** Right hemicolectomy and partial hepatectomy were performed simultaneously. **c, d** The tumor was a well-differentiated tubular adenocarcinoma with 3,000 μm invasion of the submucosal layer (**c**: loupe; **d**: HE, $\times 40$), without tumor budding or lymph node metastasis. **e** The liver tumor showed histological findings similar to those of the primary colon carcinoma (HE, $\times 40$).