CASE REPORT

Complete pathological response of multiple huge liver metastases of colon cancer: a case report

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Abstract

We report a case of a pathological complete response (pCR) with chemotherapy for multiple huge liver metastases from colon cancer. A 59-year-old woman presented with anorexia and weight loss. Laboratory tests revealed elevated liver enzyme levels and tumor markers. A computed tomography/positron emission tomography-computed tomography scan revealed a transverse colon tumor and unresectable liver masses measuring 9.0 cm in maximum diameter in segments 7 and 8, with another mass in segment 6. She underwent laparoscopic colectomy and was administered FOLFOX + Bev. After 11-cycles of chemotherapy, the liver masses became resectable with a partial response, so hepatectomy was performed. On the final histopathological analysis, all lesions were fibrotic without any viable cancer cells. The patient is alive without recurrence 2 years after resection. We believe this is the largest tumor of unresectable colorectal liver metastasis (CRLM) that has ever resulted in pCR with chemotherapy. FOLFOX + Bev was thus found to be an effective treatment for unresectable CRLM.

INTRODUCTION

More than 50% of patients with colorectal cancer will develop liver metastases. For patients with initially unresectable metastases, modern chemotherapy treatment allows ~13% of them to achieve resectability, and the 5-year survival rates after resection are reported to exceed 30% [1].

The incidence of pathological complete response (pCR) of colorectal liver metastasis (CRLM) following chemotherapy remains insufficient and is considered rare. In addition, a smaller tumor size may be associated with a higher incidence of pCR [2, 3]. Indeed, in previous reports, a solitary mass size of 5.7 cm was the maximum size of CRLM detected as pCR [4].

We herein report the case of a patient who achieved pCR for multiple unresectable CRLMs about 9.0 cm in maximum diameter from transverse colon cancer with chemotherapy of 5-fluorouracil and leucovorin (LV) combined with oxaliplatin and bevacizumab (FOLFOX + Bev).
CASE REPORT

A 59-year-old woman initially presented with anorexia and weight loss. Her medical history and family history were unremarkable. Laboratory tests revealed elevated levels of liver enzymes (AST 103 IU/L, ALT 18 IU/L, LDH 1331 IU/L, ALP 496 IU/L, γ-GTP 99 IU/L, LAP 85 IU/L) and tumor markers (CA19-9 40.5 U/ml, CEA 86.6 ng/mL). Her Child-Pugh stage was A. A Computed tomography/positron emission tomography-computed tomography (CT/PET-CT) revealed a transverse colon tumor and multiple masses in segments 6, 7, and 8 of the liver (1.0 cm in segment 6, 9.3 cm in segment 7 and 9.0 cm in segment 8). Colorectal endoscopy and a biopsy revealed adenocarcinoma of transverse colon cancer. The liver masses were considered to be unresectable metastases because of her residual functioning volume being <30% (Fig. 1) [5].

She underwent laparoscopic transverse colectomy due to our prediction of obstruction in the near future. The histopathological findings were as follows: type 3, 70 mm × 58 mm in size, moderately differentiated adenocarcinoma, 13 lymph node metastases. She then started chemotherapy with FOLFOX + BV.

Because of her grade 3 peripheral neuropathy, the oxaliplatin dosage was reduced once from the fifth cycle and then stopped altogether from the seventh cycle. Other severe side effects did not occur, and chemotherapy (5FU/LV + BV) was continued roughly as scheduled. CT scan after 9 cycles revealed a reduction in the size of the liver tumors except one in segment 6 (9.3 cm → 3.8 cm in segment 7, 9.0 cm → 4.4 cm in segment 8, 1.0 cm → 1.0 cm in segment 6), and PET-CT revealed no FDG accumulation at all on liver tumors. Her liver residual functioning volume also increased. (Fig. 2).

The liver tumors were considered to be resectable therefore, and chemotherapy was continued without bevacizumab (5FU/LV) for elective operation for two cycles, after which extended right liver lobectomy was performed. While the preoperative radiological response was partial, on the final histopathological analysis, all lesions were found to be fibrotic and devoid of any viable cancer cells (pCR) (Fig. 3). No postoperative liver complications occurred. The patient is alive without recurrence 2 years after resection.

DISCUSSION

Recently, systemic chemotherapy for unresectable CRLM has progressed remarkably, and ~13% of cases achieve resectable status during treatment [1]. It has also been reported that neoadjuvant chemotherapy for initially resectable CRLM before

Figure 1: Enhanced CT and PET-CT revealed multiple large masses measuring about 9.0 cm in maximum diameter in segments 7 and 8 of the liver.

Figure 2: Enhanced CT and PET-CT performed after chemotherapy revealed a reduction in the size, contrast effect and FDG accumulation of all liver metastases after the ninth cycle of chemotherapy.
hepatectomy can improve the disease-free survival rate [6]. The NCCN guidelines for unresectable CRLM recommend the combination of fluorouracil and LV with oxaliplatin or irinotecan (FOLFOX/FOLFIRI) ± bevacizumab [7], so we started the present patient on FOLFOX + bevacizumab.

After chemotherapy, CT/PET-CT revealed a reduced size of the liver as well as FDG accumulation. The preoperative radiological response was partial, but the pathological response was complete. Confirming pCR before performing liver surgery remains difficult because of the lack of conformity between the histopathological response and the radiological response, with only 20% of radiologic complete response lesions detected to show a pCR [8]. In a previous report in patients who showed pCR, the average diameter of their liver masses before chemotherapy was 2.9 cm, and 71% of the masses were less than 3.0 cm in diameter; these findings suggest that a smaller size may be associated with a higher incidence of pCR [2]. Furthermore, four factors have been reported to be independent predictive factors of pCR: ≤ 60 years of age at diagnosis, metastases measuring ≤ 3 cm at diagnosis, CEA level ≤ 30 ng/mL at diagnosis, and the occurrence of an objective response following chemotherapy [2]. The present patient met the age qualification and showed an objective response following chemotherapy, but the size of her metastasis was much larger and her CEA level also higher than the cut-offs.

In previous reports, the maximum size of CRLMs that showed pCR with chemotherapy was a solitary 5.7 cm mass [4]; this contrasts starkly with the two 9.0-cm liver metastases that showed pCR in the current case. These tumors are the largest to show pCR among unresectable CRLMs with chemotherapy.

Another report suggested that chemotherapy with oxaliplatin administered before hepatectomy may cause hepatic sinusoidal obstruction syndrome (SOS) or severe postoperative complications such as liver failure, especially in cases that involve major hepatectomy, and liver complications have also been reported in patients who have received more than nine cycles of chemotherapy before surgery [9]. In contrast, bevacizumab is reported to protect against SOS [10]. In the present case, the patient received more than nine cycles of chemotherapy including seven cycles oxaliplatin, however, no postoperative liver complications occurred. Previous reports have shown a 5-year survival rate of ~75% in patients with pCR [2]. This patient is also expected to enjoy a superior prognosis.

We herein reported the case of a patient who showed pCR with multiple 9.0-cm-diameter CRLMs following FOLFOX + Bev. This is the largest case of pCR with unresectable multiple CRLMs, and we successfully demonstrated the efficacy of FOLFOX + Bev for unresectable CRLM.

CONFLICT TO INTEREST STATEMENT
The authors declare no conflicts of interest in association with this report.

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ETHICAL APPROVAL
The design of this report has been approved by our institute ethical committee.

CONSENT
Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent form is available for review by the Editor-in-Chief of this journal.

GUARANTOR
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