

Long-term Survival after Surgical Resection for Liver Metastasis from Gastric Cancer: Two Case Reports

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Surgical resection of colorectal cancer metastasis to the liver results in a 5-year survival rate of around 40%. Liver metastasis from other cancers such as neuroendocrine carcinoma and genitourinary tumors are also treated effectively with combined liver resection. However, hepatic metastasectomy for liver tumor from gastric cancer hasn't been considered as a standard treatment, and the benefit for this treatment has not been established. We report here on two cases of gastrectomy and combined liver resection for synchronous liver metastasis without any evidence of other metastatic lesions,

and these two patients have survived for more than 7 years without evidence of disease recurrence. In conclusion, for patients with hepatic metastasis from gastric cancer, combined surgical resection of the liver metastasis should be considered as a treatment option when metastasis to other sites can be excluded. (*Cancer Res Treat. 2006;38:184-188*)

Key Words: Stomach neoplasms, Liver resection, Long-term survival

INTRODUCTION

The liver is a common site of hematogenous metastasis from gastrointestinal malignancies because it is the first major organ that the venous blood reaches after it drains from the primary site. The benefit of performing hepatic resection for liver metastases has been established in selected patients who are suffering from some malignancies such as colorectal, neuroendocrine and genitourinary cancers, and a consensus has been reached in favor of hepatic metastasectomy.

On the other hand, the prognosis of hepatic metastasis from gastric cancer, when this is recognized, is poor. The tumor is generally scattered throughout both lobes of the liver and this is frequently accompanied with peritoneal dissemination. Thus, in contrast to the hepatic lesions arising from colorectal metastases, curative resection of metastases from gastric cancer is not obtainable in most cases (1). Nonetheless, complete surgical

resection of the primary tumor and the liver metastases appears to be the only option for possibly curing the disease, although the benefits of surgical metastasectomy of gastric cancer are poorly defined.

We report here on two long-term survivors, both who survived more than 7 years and who underwent curative gastrectomy with combined liver resections for synchronous hepatic metastases from gastric cancer.

CASE REPORT

1) Case 1

A 62-year-old male patient initially presented at our hospital with a complaint of dyspepsia for the previous 4 months. He had no history of another chronic illness and no family history of gastric cancer. On admission, the physical examination was unremarkable and his functional performance status was Eastern Cooperative Oncology Group (ECOG) 1. On endoscopic biopsy, he was diagnosed as suffering with gastric adenocarcinoma of Borrmann's type III that involved the antrum. Abdominopelvic computed tomography (CT) demonstrated several enlarged perigastric lymph nodes without other obvious metastatic lesions in the liver, except for the dilated intrahepatic and common hepatic ducts. Abdominal ultrasound showed a small hypoechoic lesion in segment 2 of the liver. In June 1997, radical subtotal gastrectomy (D2 resection) and wedge resection of the liver were performed after intraoperative verification of a 1×1

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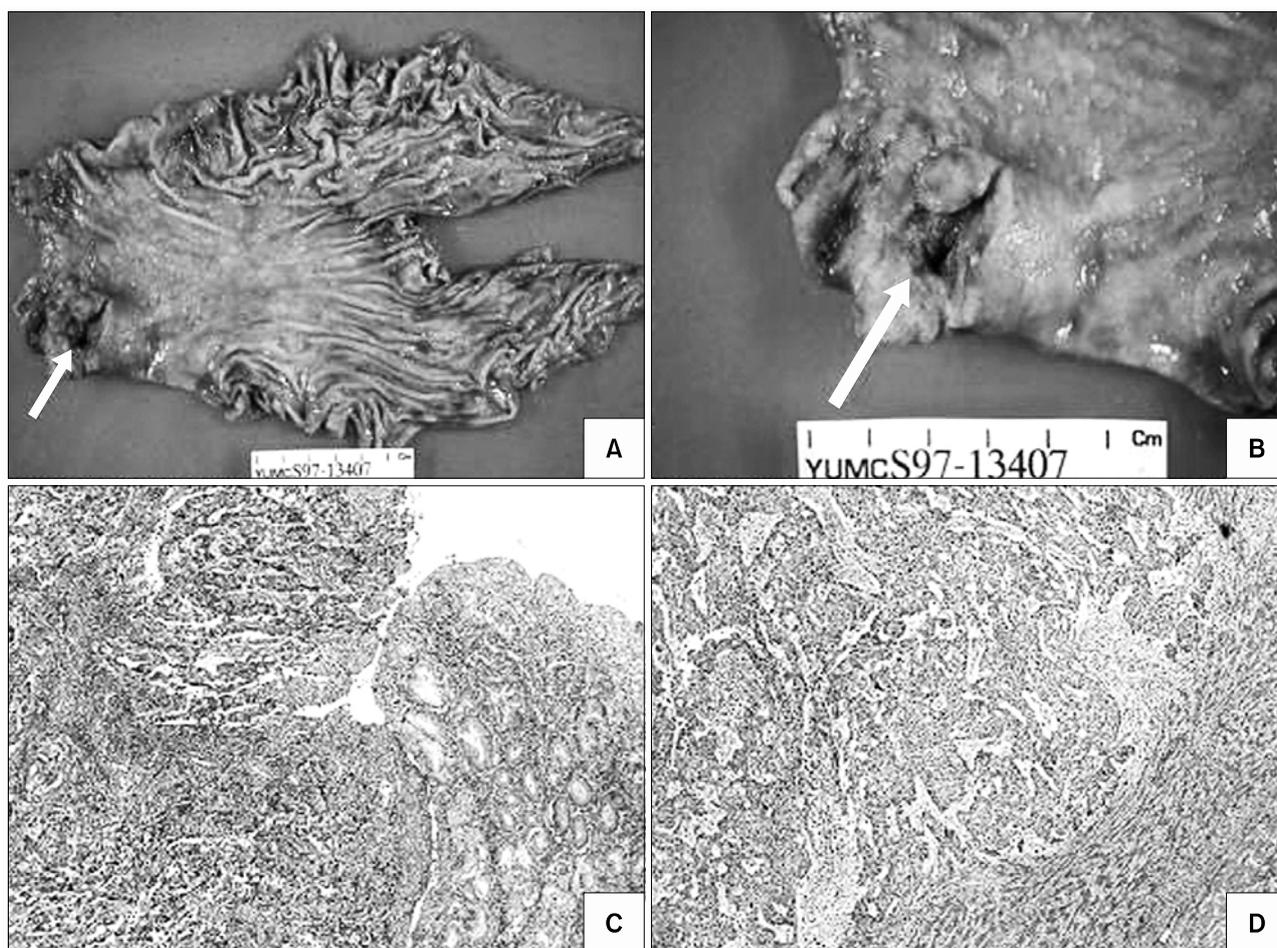


Fig. 1. The macroscopic and microscopic finding of the first case. (A) and (B), gross findings of the gastrectomized stomach showing an ulcerofungating mass (arrow) that measured 3.5×4.0 cm on the posterior wall of the antrum. (C) Poorly differentiated adenocarcinoma with lymphocytic infiltrates in the surrounding stroma of the stomach (H&E, ×40). (D) Microscopic findings of the metastatic adenocarcinoma of the liver (H&E, ×40).

cm sized palpable nodule that was highly suspicious for metastasis. Macroscopically, the stomach revealed a 3.5×4.0 cm sized ulcerofungating mass located at the posterior wall of the antrum, and the diameter of the resected liver mass was 0.8×0.6 cm. Microscopic examination revealed that the gastric mass was a poorly differentiated adenocarcinoma that expanded to the proper muscle along with metastases in 28 of the 44 lymph nodes. As shown in Fig. 1, the resected liver mass was a poorly differentiated adenocarcinoma that showed the same pathology as that of stomach mass, which was compatible with the liver metastasis. The procured tumor-free resection margin of the liver was only 0.2 mm. The patient's final stage was pT2N3M1, and he underwent postoperative combination chemotherapy with 6 cycles of a 5-fluorouracil, etoposide, and cisplatin (FEP) regimen. He has survived for more than 9 years (109+months) without any evidence of recurrence, and the last follow was July 2006. The case is summarized in Table 1.

2) Case 2

The second case is a 43-year-old male patient who visited

our hospital with complaints of hunger pains for the previous 5 months. His physical examination and laboratory findings were unremarkable, and his performance status was ECOG 1. He was diagnosed as having stomach cancer of Borrmann's type II involving the upper body, and adenocarcinoma was confirmed by endoscopic biopsy. Abdomino-pelvic CT scan showed a single low-attenuated mass in segment 8 of the liver without evidence of other metastasis. Considering the patient's favorable general condition and single hepatic metastasis, radical total gastrectomy (D2 resection) with combined liver resection was performed. The patient also underwent coincidental splenectomy due to intraoperative detection of an enlarged splenic hilar lymph node. On operation, a single 4×4 cm sized mass was discovered in segment 8 of the liver without other evidence of intra-abdominal metastasis. Macroscopically, the gastric specimen was an ulcerative lesion that measured 7×9 cm, and it was located at the posterior wall of the cardia and upper body. On multiple cut sections of the liver mass, the parenchyma revealed a 4×4 cm sized well-circumscribed, friable gray tan nodular area that grossly abutted to one of the surgical margins. Histopathologic

Table 1. Clinico-pathological characteristics of the long-term survivors who underwent gastrectomy and combined hepatic metastasectomy

| Case | 1 | 2 |
|--|--------------------------------------|------------------------------|
| Gender/age | Male/62 | Male/43 |
| Size of liver metastasis (long diameter, cm) | 0.8 | 4.0 |
| Depth of invasion of the stomach wall | Proper muscle | Perigastric fat |
| Lymph nodes metastasis (positive/dissected) | 28/44 | 13/38 |
| Pathologic type | Poorly differentiated adenocarcinoma | Moderately adenocarcinoma |
| Type of metastasectomy | Wedge resection | Segmentectomy |
| Resection margin of liver resection | Negative (0.2 mm) | Negative (0.2 mm) |
| Timing of diagnosis and resection | Synchronous | Synchronous |
| Chemotherapy | FEP* (6 cycles) | FAM† (12 cycles) |
| Outcome after surgery | 109+months without recurrence | 94+months without recurrence |

*5-Fluorouracil-Etoposide-Cisplatin, † 5-Fluorouracil-Adriamycin-Mitomycin-C.

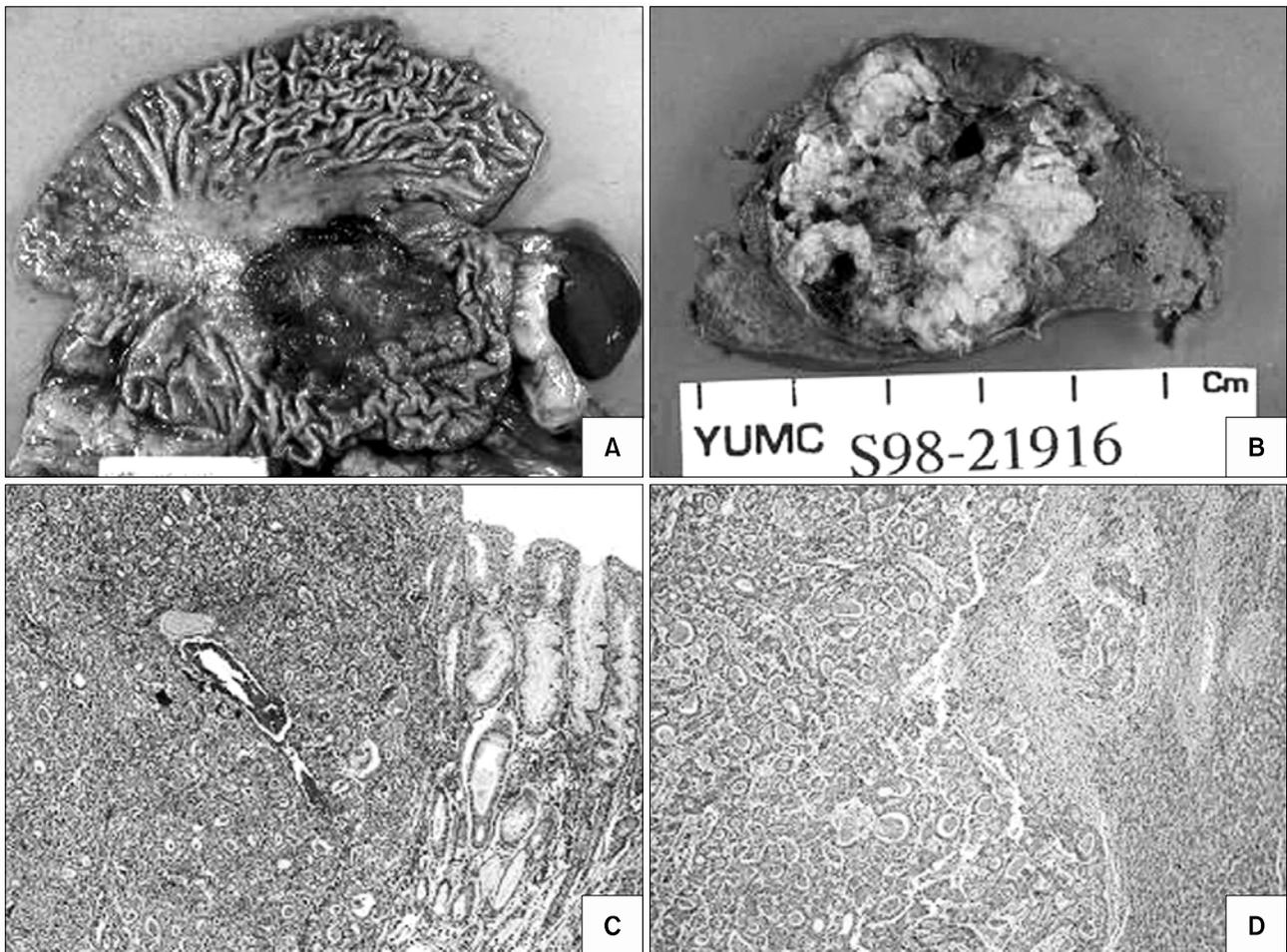


Fig. 2. The macroscopic and microscopic findings of the second case. (A) Removed stomach and spleen with a 7×9 cm sized ulcerative lesion on the posterior wall of the cardia and upper body. (B) The resected segment 8 of the liver showing a well-circumscribed 4×4 cm sized, friable gray tan nodular area on the cut section. It grossly abuts to one of the surgical margins. (C) Moderately differentiated adenocarcinoma of stomach (H&E, ×40). (D) Metastatic adenocarcinoma of the liver (H&E, ×40).

examination showed moderately differentiated adenocarcinoma extending to the perigastric fat tissue and lymphovascular permeation with metastasis to 13 of the 38 lymph nodes. The re-

sected liver showed a moderately differentiated adenocarcinoma that exhibited the same pathology as that of the stomach mass, which was compatible with the liver metastasis from the gastric

cancer (Fig. 2). The final stage was pT3N2M1, and the patient received 12 cycles of postoperative combination chemotherapy of 5-fluorouracil, doxorubicin and mitomycin-C (FAM). The patient has survived for 8 years (94+months) without evidence of recurrence with the last follow-up in July 2006. The case is summarized in Table 1.

DISCUSSION

Gastric cancer with liver metastasis remains a non-curative disease; the median survival duration rarely exceeds 7 months and even intensive systemic chemotherapy does not achieve a satisfactory survival benefit. The liver is the major site of metastasis from gastric cancer, and the incidence of liver metastasis has been reported to be 5~10% (2,3). Therefore, liver metastasis is a significant prognostic factor for the survival of gastric cancer patients.

The benefit of metastasectomy in gastric cancer has not yet been well defined, and it is not considered as a standard treatment. This is because hepatic metastases from gastric cancer are usually multiple lesions scattered to both lobes of the liver, and it is also accompanied with widespread peritoneal dissemination. However, if complete surgical resection of the primary tumor and liver metastases is possible, it could be the only treatment modality that offers the potential for cure. Nevertheless, further information on the indications and patient selection is still lacking, and the debate on hepatic metastasectomy in gastric cancer is ongoing.

The rationale of combined hepatic resection is well established for some cancers such as colorectal cancer. The reported 5-year survival rate after curative resection for liver metastases of colorectal cancer ranges from 30% to 51% (4~8). From these data, a consensus has been made in favor of hepatic metastasectomy in the case of unilobar involvement together with three or fewer metastatic nodules (1,9). Moreover, some authors have also expanded its indications to include all technically resectable metastases irrespective of the numbers (6~8).

Some reports favor performing metastasectomy for advanced gastric cancer whenever possible. However, little is known about factors influencing the prognosis after resection of hepatic metastasis from gastric cancer because of the small number of cases. A consensus has not yet been reached, and there is a definite need for further study. The first point to consider for the indications of performing combined hepatic resection of metastatic gastric cancer is the attainable resection margin. Miyazaki et al. reported a significant survival difference according to the tumor-free hepatic resection margin. He demonstrated significantly longer survival in the group that procured a resection margin of more than 10 mm (10). In our cases, we could guarantee R0 resection, but the tumor free hepatic resection margin was only 0.2 mm in both the two cases. An inadequate surgical margin could influence the subsequent treatment strategy. Our patients did not received radiotherapy, but they received postoperative systemic chemotherapy for the purpose of eradicating micrometastasis. The role of the radiotherapy and/or chemotherapy after metastasectomy remains to be established, and the influence of the resection margin on the prognosis in such patients need further studies.

The second point is the number of hepatic nodules. Okano

et al. reported survival rates of 56% for single metastasis, but they didn't report any survival rates for multiple metastases after hepatectomy (11). Another report also suggested the importance of the number of liver metastases as a prognostic factor (10). It is no wonder that the number of hepatic nodules is related to the postoperative hepatic reservoir and the feasibility of resection. Although our two patients had only a single hepatic nodule, respectively, it is hard to draw any conclusions on the relationship between the number of metastases and its influence on the survival because there were only two patients in our study. However, it can be suggest that patient with a single metastasis could be a candidate for combined metastasectomy.

The third point is the timing of the diagnosis of liver metastasis and its resection. Some authors showed more favorable outcomes for patients with metachronous metastasis as compared to patients with synchronous metastasis (11~13). On the other hand, other authors reported conflicting results that favored long-term survival for synchronous metastasis (1,14,15). In our cases, both of the patients had synchronous metastasis and they have survived for more than 7 years, suggesting that even in case of synchronous metastasis from gastric cancer, hepatic resection should be considered if curative resection is possible.

The last point is the size of metastatic lesion. It is logical to assume that a patient with a larger metastatic tumor will have a poor prognosis. However, the relationship between the size of metastatic tumor and patient outcome is as of now unclear.

In Korea, Roh et al studied about 11 patients who underwent hepatic resection and gastrectomy, and they found that 2 patients (18%) obtained long-term survival (15). The first survivor has submucosa-limited carcinoma with synchronous liver metastasis, and this patient survived for 102 months after combined resection. The other survivor had metachronous hepatic metastasis that was detected 37 months after gastrectomy. Segmentectomy of liver was performed and the patient survived for over 9 months after hepatic resection (15). These findings suggest that there could exist a certain subgroup of patients that can benefit from hepatic metastasectomy, although it is not considered as a standard treatment for gastric cancer. More data and clinical experiences are required to clarify the role of hepatic metastasectomy in gastric cancer, and also to determine its indications.

Thanks to the recent development of imaging tools such as positron emission tomography (PET), it is possible to detect metastasis more accurately at a relatively early stage. In conclusion, surgical hepatectomy should be considered as a treatment option when metastasis to other site can be excluded.

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