J Hepatobiliary Pancreat Surg (2003) 10:321–324
DOI 10.1007/s00534-002-0835-2

Journal of HBP Surgery

Complete remission of disease for 5 years following initial and repeat resection of the liver for the removal of 22 metastases of colorectal origin

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Abstract
Although liver resection is accepted as the only available treatment that regularly produces long-term survival with possible cure in patients with colorectal carcinoma metastatic to the liver, controversy appears to exist regarding the surgical indication for patients with more than four nodules. Similarly, it may be arguable to perform a repeated hepatic resection for a patient who developed multiple recurrent liver metastases with a short disease-free period after the initial liver resection. During the last 7 years, we have adopted constantly the aggressive surgical approach to patients with colorectal carcinoma metastatic to the liver if the number of tumor nodules identified preoperatively were less than ten and irrespective of the length of disease-free period after the previous resection. Here we report on a patient who underwent hepatic resection twice at an interval of 3 months and in whom a total of 22 metastatic nodules (6 in the initial hepatic resection and 22 in the repeated resection) were removed. The patient is now alive and remains disease-free, 5 years after the first liver resection.

Key words Multiple liver metastases · Colorectal carcinoma · Repeat hepatic resection

Introduction

Liver resection is currently accepted as the only available treatment that is consistently associated with long-term survival with possible cure in patients with colorectal carcinoma metastatic to the liver.[1–3] However, it is arguable whether hepatectomy would still be indicated in patients with four or more metastatic nodules in the liver.[4–6] On the other hand, repeat liver resection for recurrence after the initial resection has come to be widely accepted over the last decade.[7–9] Nevertheless, it is also generally true that surgeons are reluctant to proceed with repeat resection in patients who develop multiple metastases within a short disease-free period after the initial liver resection.

In this communication, we report on a patient in whom we carried out hepatic resection twice at an interval of 3 months and removed a total of 22 metastatic nodules. The patient is now alive and remains disease-free, 5 years 8 months after the first liver resection.

Case report

A 61-year-old man was referred to our department with the diagnosis of carcinoma of the ascending colon with liver metastases. Although helical biphasic computed tomographic (CT) scanning revealed only two nodules in the liver, probably due to fatty infiltration causing a poor contrast effect, ultrasonography (US) delineated a total of four metastatic nodules: 1 nodule extending from segment 5 to segment 8 (20 mm in diameter), 1 in segment 8 (10 mm), and 2 in segment 6 (20 mm and 8 mm) (Fig. 1). On May 13, 1996, we carried out liver resection and right hemicolectomy sinultaneously. Intraoperative inspection, bimanual palpation, and intraoperative ultrasonography (IOUS) revealed the presence of two more nodules, one each in segment 6 (6 mm) and segment 7 (5 mm). All of these six metastatic tumors were removed via multiple limited liver resections (segment 8, segment 7, segment 5, and segment 6 which contained 3 nodules). The postoperative course was uneventful and the patient was discharged 2 weeks after the operation.

The patient was followed up at our outpatient clinic. In July 1996, the serum carcinoembryonic antigen (CEA) level, which had decreased after the operation, was elevated again. Subsequent US revealed the presence of seven metastatic nodules in the right lobe of the liver (Fig. 2). Again CT scan could delineate only 3 of

Offprint requests to: H. Imamura
Received: May 22, 2002 / Accepted: December 12, 2002

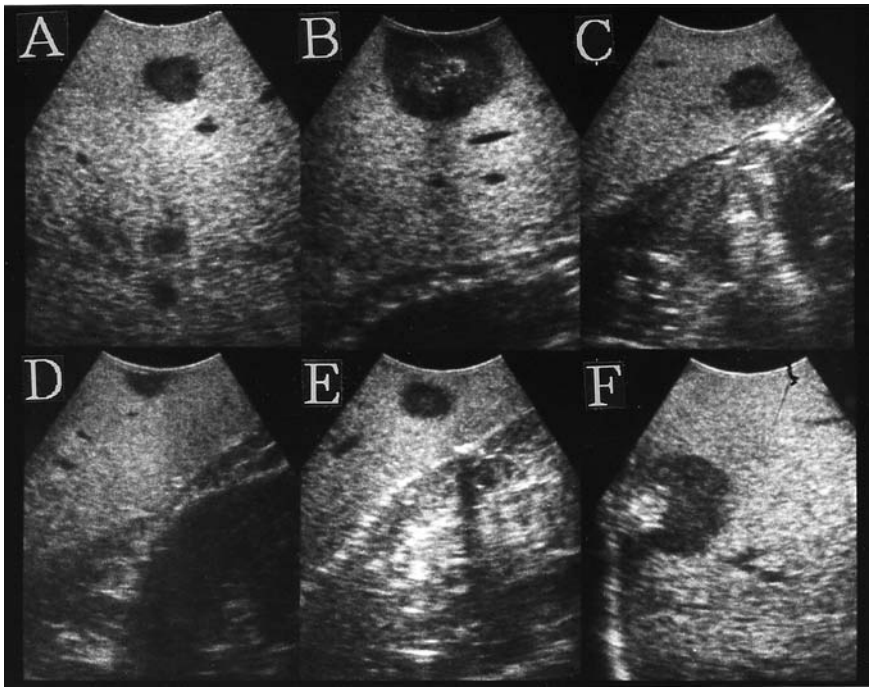

Fig. 1A–F. Intraoperative ultrasonography images at the first hepatectomy. One nodule in segment 5 (**A**), three nodules in segment 6 (**B–D**), and one nodule in segment 7 (**E**) and segment 8 (**F**) are identified

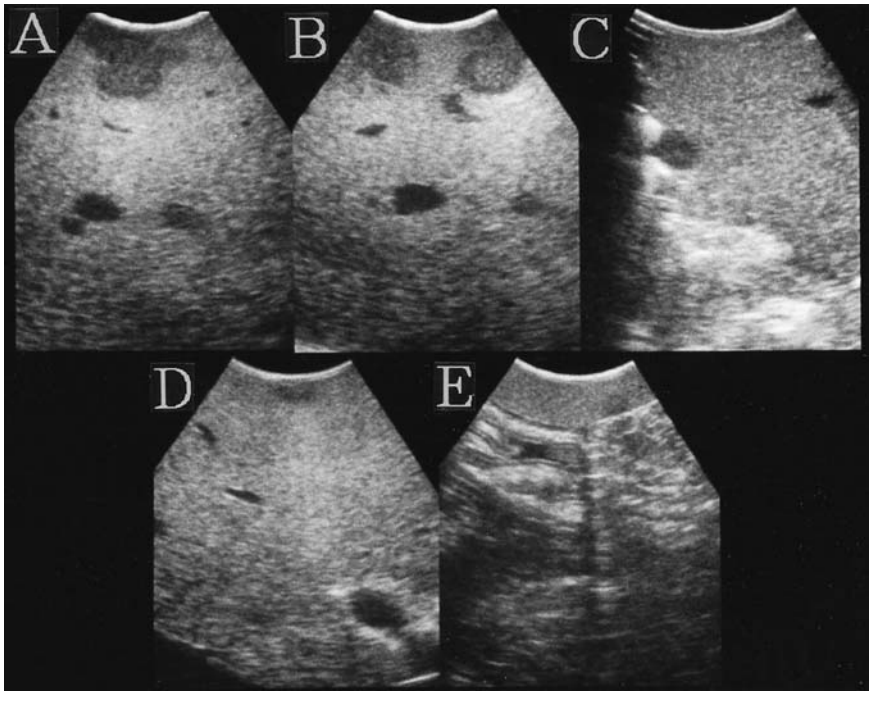

Fig. 2A–E. Intraoperative ultrasonography images at the second hepatectomy. Out of the 16 nodules identified intraoperatively, 7 were revealed: 4 nodules in segment 8 (**A,B**), 2 in segment 4 (**C,D**), and 1 in segment 6 (**E**)

these nodules probably because of the diffuse fatty infiltration (Fig. 2). There was no evidence of extrahepatic metastases. We first conducted preoperative portal vein embolization[10] to the right portal branch to induce compensatory hypertrophy of the left lobe of the liver on August 23, 1996. Then, on September 11, 1996, we carried out a repeat partial hepatic resection. IOUS revealed the presence of 12 small (5–10 mm each) metastatic nodules in the right lobe, and four metastatic nodules (one each in segments 2 and 3, and two in segment 4) in the left lobe of the liver. Right lobectomy plus three partial resections of the left lobe were carried out to remove these tumors. Precise examination of the resected liver confirmed the intraoperative US findings,

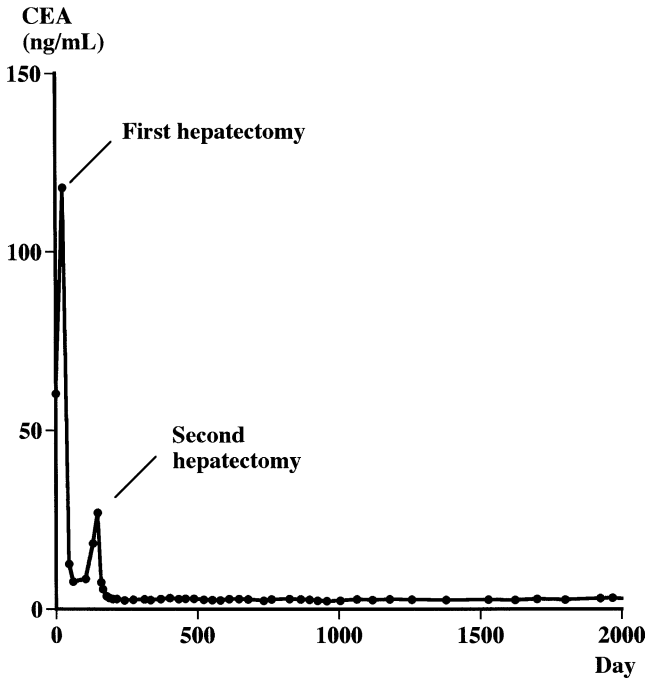

Fig. 3. Chronological profile of the serum carcinoembryonic antigen (*CEA*) level. The serum CEA value decreased from 118 to 7.6 ng/ml following the first hepatectomy. It increased again up to 26.9 ng/ml before the second hepatectomy, but decreased after the operation and has remained within the normal range for 5 years 8 months up to the present

i.e., the presence of a total of 16 metastatic nodules. The postoperative course was uneventful and the patient was discharged 2 weeks after the operation.

The patient has been followed up at our outpatient clinic until the present, i.e., 5 years 4 months after the second partial hepatectomy. Until the time of manuscript submission, there had been no evidence of tumor recurrence. Figure 3 demonstrates the chronological changes in the serum CEA level. While the value was high before the initial and the repeat resections, it declined after both, and has remained within the normal range until the present.

Discussion

During the last 10 years, we have consistently adopted the aggressive surgical approach for the treatment of both initial and recurrent hepatic metastases of colorectal origin. In brief, hepatic resection was considered when the number of nodules detected by preoperative imaging modalities was ten or less, regardless of the interval from any previous hepatectomy, provided that there were no extrahepatic metastases except for resectable lung metastases, and if it was envisaged that an acceptable amount of the liver could be left after the resection. Accordingly, since October 1994, when one of the authors (M.M.) headed our division, 45 cases have been operated upon once, 16 twice, 8 three time, and 1 case four times. At the first hepatectomy, 22 patients had a solitary hepatic lesion, 13 had two, 2 had three, and 22 had four or more (up to 30) nodules. Including in repeat resections, a single nodule was removed in 23 patients, two were removed in 11, three in 4, four in 7, five in 8, six in 4, seven in 1, eight in 2, 12 in 1, 13 in 2, and 14, 18, 20, 22 (the present case), 24, and 47 deposits were removed in one patient each.

In most previous reports in which the presence of four or more nodules was a contraindication for hepatectomy,[1,4–6] the number of cases was too small to permit any definitive conclusion and the number of nodules removed was ten at the most. We consider that the decreased survival of patients with multiple metastases reported in former studies is attributable, at least in part, to the fact that the resection of multiple metastases is more likely to be associated with the presence of additional lesions in the residual liver or other organs. The former situation can be largely prevented by the systematic use of IOUS.

Considering the indication for repeat liver resection, it may not be generally advocated that reoperation be performed in a patient such as the present one in whom more than ten metastases had developed within 3 months after the initial operation. Alternatively, it is sometimes suggested that the doctor watch and wait for a few months in order to observe the biological behavior of the metastases before determining their resectablity.[8] We do not favor either of these policies. First, since newly recognized metastases after hepatic resection simply represent a progression of disease not identified at the first liver resection, the same treatment strategy as that for the initial liver resection should, in theory, be applied. In this context, we would like to emphasize again that thorough IOUS is an essential operative adjunct for screening the liver and minimizing the number of "missed" metastases both at the first and the repeat resections. Second, liver metastases themselves may lead to the development of secondary metastases from the metastatic nodules if they are left unresected.

In conclusion, we have reported a case of colorectal carcinoma metastatic to the liver in a patient in whom a total of 22 metastases were removed at the first resection and a repeat liver resection performed after an interval of 3 months of the first operation. The patient remains alive and disease-free 5 years 4 months after the repeat hepatic resection. The present case appears to address, at least partly, the controversy concerning the treatment strategy for multiple and recurrent hepatic metastases of colorectal origin.

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