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CASE REPORT

Long-term survival after two surgical resections of peritoneal metastases from hepatocellular carcinoma with an interval of 4 years

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Key Clinical Message

We propose that surgical resections of peritoneal metastases arising from hepatocellular carcinoma are an option for selected patients with controlled HCC in the liver, and without metastases in other organs, when the complete removal of such metastases can be achieved, especially in the case of patients with normal liver function.

Keywords

Fluorodeoxyglucose positron emission tomography, hepatocellular carcinoma, peritoneal metastases, surgical resection.

Introduction

Peritoneal metastases arising from HCC are relatively uncommon [1], with an incidence of only 0.6% after hepatectomy in Japan [2]. Traditionally, peritoneal metastases from HCC have been considered to be the advanced stage of HCC. Therefore, surgical resection of such metastases has not been indicated to improve the patient survival. However, some studies have suggested that resection of peritoneal metastases arising from HCC may have significance under limited conditions [3, 4].

We herein report the case of a patient who underwent two resections of peritoneal metastasis from HCC and has survived for more than 10 years since the initial resection.

Case Report

An 80-year-old Japanese female with no history of hepatitis infection, blood transfusion, or alcohol abuse was admitted to our hospital for the second resection of peritoneal metastasis from HCC. Seven years before, enhanced computed tomography (CT) had detected a 6.6-cm early-enhanced lesion in Segment 4 (Fig. 1A), and the laboratory data were as follows: serum total bilirubin, 0.9 mg/dL; aspartate aminotransferase (AST), 25 IU/L; alanine aminotransferase (ALT), 23 IU/L, and indocyanine green retention rate at 15 min, 4%. The serum alpha-fetoprotein (AFP) and des-gamma–carboxy prothrombin (DCP) levels were elevated (AFP: 8470 ng/mL, DCP: 1950 mAU/mL). She was diagnosed with HCC arising in a normal liver, and a left hemihepatectomy was performed. Although there was no apparent rupture of the tumor during the operation, the tumor was exposed to the serosa (Fig. 1B). Grossly, the tumor was a single nodular lesion encapsulated by fibrotic tissue with extranodular growth and a maximum diameter of 9 cm located in Segment 4 (Fig. 1C). Histologically, the tumor was a moderately differentiated HCC (Fig. 1D). The surgical margin was negative (15 mm), and there was no evidence of lymphovascular or perineural invasion. Four months after the hepatectomy, her tumor marker levels increased (AFP: 138 ng/mL, DCP: 610 mAU/mL), and ultrasonography (US) and CT detected a solitary tumor that was 2 cm in diameter in the peritoneum adjacent to the site of previous resection (Fig. 2A). However, the abdominal tumor was asymptomatic. Five months after

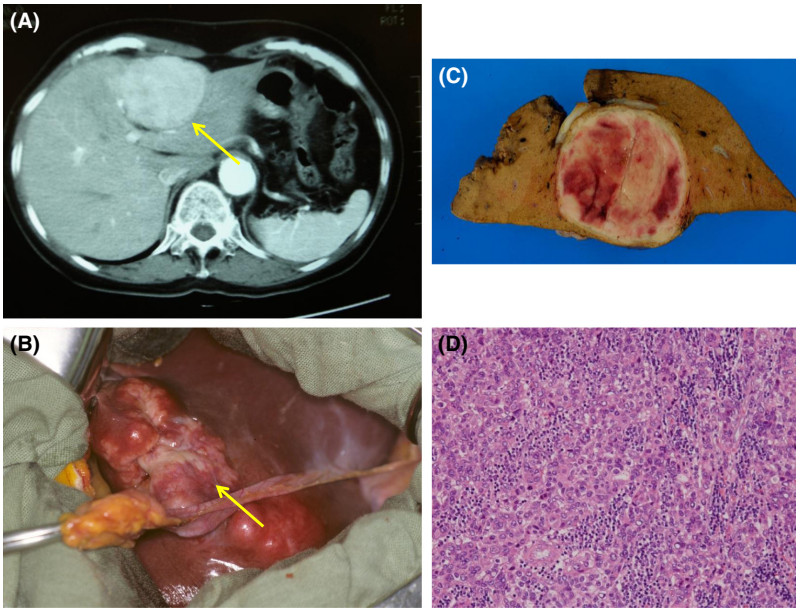

Figure 1. (A) CT revealed an early-enhanced lesion in Segment 4, which was diagnosed as HCC (arrow). (B) The tumor was recognized in Segment 4, and it was exposed to the serosa (arrow). (C) Macroscopically, the liver tumor was encapsulated by fibrotic tissue and was of a single nodular type with extranodular growth. (D) The microscopic findings showed a moderately differentiated HCC (hematoxylin and eosin stain (H&E); original magnification, ×150).

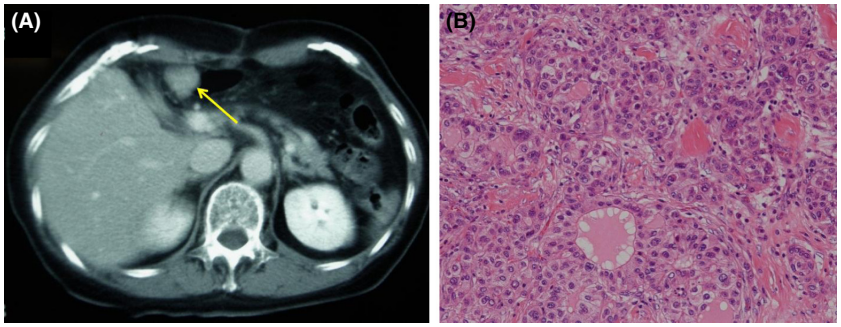

Figure 2. (A) CT detected a solitary tumor in the peritoneum near the region of the previous resection (arrow). (b) Macroscopically, the tumor was whitish and solid and was histologically diagnosed as a peritoneal metastasis from the primary tumor (hematoxylin and eosin stain (H&E); original magnification, ×150).

the hepatectomy, surgical resection of the peritoneal tumor was performed. The tumor was whitish and solid and histologically diagnosed as a peritoneal metastasis from the primary hepatic tumor (Fig. 2B).

Four years after the first resection of the peritoneal metastasis, the serum level of AFP gradually began to increase again. Although we had been following the patient by US every 3 months, and surveillance CT was performed upon noting the elevation of the AFP level, no intrahepatic recurrences or peritoneal disseminations were revealed. Since the serum level of AFP continued to increase up to 920 ng/mL by 3 years after the initial increase of AFP, the patient underwent fluorodeoxyglucose positron emission tomography (PET)/CT. The PET–CT scan revealed a solitary lobular tumor approximately 5 cm in diameter in the lower left abdomen (Fig. 3A), and no other lesions were found in further investigations, such as US and magnetic resonance imaging (MRI). As a result of the preoperative examination, the patient was diagnosed with solitary peritoneal metastasis of HCC with controlled HCC in the liver without any metastases in other organs. Seven years after the first resection of peritoneal metastasis, a second resection of a peritoneal tumor was performed, and the pathological

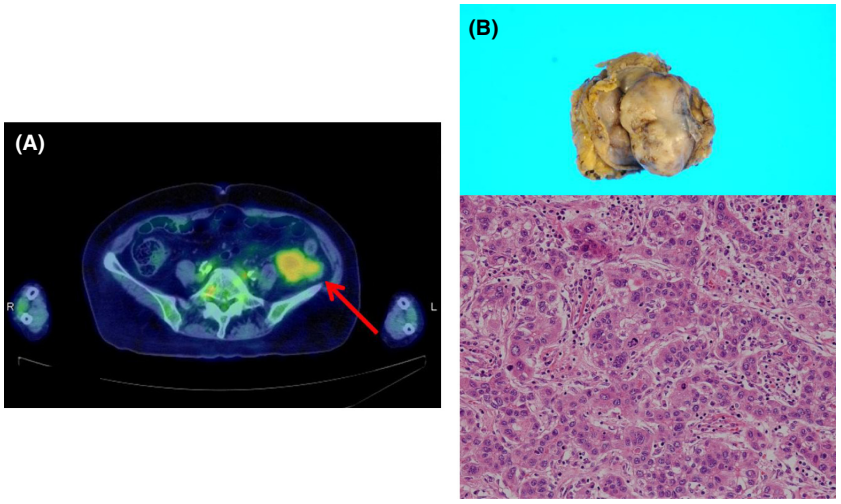

Figure 3. (A) PET–CT revealed a solitary lobular tumor in the lower left abdomen (arrow) 3 years after tumor marker elevation was noted, and was effective for the diagnosis. (B) Macroscopically, the tumor was whitish and solid. The microscopic findings revealed moderately differentiated carcinoma, which was the same finding of the initial liver tumor (hematoxylin and eosin stain (H&E); original magnification, ×150).

examination revealed moderately differentiated carcinoma, which was the same as the original tumor (Fig. 3B). Accordingly, this tumor was diagnosed as another peritoneal metastasis from the initial HCC. After the resection, follow-up US and CT scanning has not detected any intrahepatic recurrence or peritoneal metastasis from the primary HCC. The patient is currently doing well and did not have any findings of recurrence 10 years after the first resection of the peritoneal metastasis from HCC.

Discussion

In general, peritoneal metastases arising from gastrointestinal malignancies spread widely throughout the peritoneal cavity, with numerous tumor nodules, thus leading to the development of malignant ascites. The resection of such metastases has been considered to offer no significant improvement in the patient survival or quality of life. In contrast, several studies have reported that the resection of peritoneal metastases arising from HCC may be of value because they are more localized [3, 5].

The risk factors for peritoneal metastasis from HCC have not yet been completely clarified, except for the rupture of exophytic HCC, and iatrogenic factors, such as local ablation therapy or percutaneous tumor biopsy [6, 7]. Nakashima et al. [1] reported that the occurrence of peritoneal metastases does not depend on etiologic factors. With regard to the pathological findings of the primary HCC, poorly differentiated HCCs are more likely to develop peritoneal metastases than well-differentiated ones [8], and the presence of microscopic hepatic vein invasion is an independent prognostic factor for the occurrence of extrahepatic recurrence after hepatectomy [9]. However, in this case, the precise mechanism of peritoneal metastasis arising from the HCC is unclear, because the patient has no history of hepatitis infection, and the pathological findings of the primary HCC was moderately differentiated HCC without vascular invasion. We considered that microscopic peritoneal metastases may have existed at the time of the initial hepatectomy because tumor invasion to the serosa of the primary HCC lesion was grossly recognized during surgery.

The optimal treatment of peritoneal metastases arising from HCC has not yet been established. Because these tumors have been considered to represent the disseminated stage of HCC, surgical resection is traditionally not considered to improve the patient survival. Therefore, systemic chemotherapy for HCC has been accepted and widely used for peritoneal metastases from HCC [10]. However, some studies have reported the limited indication and prognostic factors for the surgical resection of peritoneal metastases arising from HCC. In 1999, Nakayama et al. [3] indicated that surgical resection may be of particular value for patients with HCC when the number of metastatic nodules is fewer than four, when there is metachronous occurrence of metastases, and when the AFP values are less than 200 ng/mL. In 2012, Hashimoto et al. [4] reported that the poor prognostic factors for patients who undergo surgical resection of peritoneal

metastases from HCC after hepatectomy are incomplete control of the intrahepatic HCC, the presence of extrahepatic metastases in locations other than the peritoneum, or an incomplete resection of the peritoneal metastases. In the present case, the reasons for the long-term survival, which has been more than 10 years after the initial hepatectomy, may include the isolated peritoneal metastases, metachronous occurrence of the metastases, and no recurrence of the intrahepatic HCC. In addition, our patient's normal liver function without hepatitis infection [11], complete removal of the peritoneal metastases, and the tumor encapsulation by fibrous tissue (which indicates that it was less invasive) may have contributed to improving the patient's survival.

Peritoneal metastases from HCC can be detected by elevated serum AFP levels or based on imaging findings [12]. Although CT is better than US for revealing extrahepatic metastases from HCC, it is sometimes difficult to detect the metastatic masses located in the peritoneal cavity, because peritoneal metastases from HCC usually do not reveal typical findings of peritoneal carcinomas, such as peritoneal thickening with enhancement or enhancing nodules [13]. In contrast, PET/CT is extremely effective for the detection of the recurrence of HCC [14–17]. In our case, the lower abdominal metastasis was missed, because the surveillance CT targeting the remnant liver did not extend to the lower abdomen. The use of PET/CT allowed the detection of the second peritoneal metastasis 3 years after the initial increase in the serum AFP level. This experience strongly suggested that it is important to extend the field of the surveillance CT or perform PET/CT at an earlier time after noting an increase in tumor marker levels, in order to detect peritoneal metastases when a recurrence of HCC is suspected.

In conclusion, we propose that repetitive surgical resections of peritoneal metastases arising from HCC are an option for selected patients with controlled HCC in the liver, and without metastases in other organs, when the complete removal of such metastases can be achieved, especially in the case of patients with normal liver function. Moreover, it is effective to perform PET/CT examinations when a recurrence of HCC is suspected due to tumor marker elevation.

Conflicts of Interest

No conflicts of interest exist regarding this manuscript.

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