

Hepatic Resection of Metastatic Tumor from Serous Cystadenocarcinoma of the Ovary

Metastatic carcinomas are the largest group of malignant tumors of the liver. But parenchymal liver metastasis from cystic ovarian adenocarcinoma is very rare. We report a case in which the resection of metastatic liver neoplasm from ovarian serous cystadenocarcinoma was done 7 yr after initial treatment. A 48-yr-old oriental housewife complained of easy fatigability and right lower quadrant discomfort. The hepatic mass was detected by ultrasonographic examination. Serum albumin, bilirubin, and aspartate aminotransferase/alanine aminotransferase were normal. Alkaline phosphatase level was slightly increased at 146 IU/L. A tumor marker study showed alpha-fetoprotein 0.97 IU/mL, carcinoembryonic antigen 0.965 ng/mL, cancer antigen 125 1,267 ng/mL and CA 19-9 106.1 ng/mL. The operation involved cholecystectomy and segmentectomy VI and VII of the liver. The patient recovered from the surgery without any complication. On the 10th postoperative day, the patient received a single-regimen chemotherapy with paclitaxel (Taxol, 155 mg/m²BSA) and was discharged. She has been carefully followed-up without any evidence of recurrence after completion of the remaining 5 cycles of chemo-therapy, at intervals of three weeks.

Key Words : Ovarian Neoplasms; Cystadenocarcinoma, Serous; Neoplasm Metastasis; Hepatectomy

Jong Hoon Lee, Kyung Sik Kim,
Cheol Woon Chung¹, Young Nyun Park*,
Byong Ro Kim

Department of Surgery, Yonsei University College of Medicine, Seoul; Department of Pathology*, Yonsei University College of Medicine, Seoul; Department of Surgery¹, Pocheon-Jungmun University College of Medicine, Kyungkido, Korea

Received : 10 April 2001
Accepted : 13 August 2001

Address for correspondence

Byong Ro Kim, M.D.
Department of Surgery, Yonsei University College of Medicine, 134 Shinchon-dong, Seodamun-gu, Seoul 120-752, Korea
Tel : +82-2-361-5541, Fax : +82-2-313-8289
E-mail : brkim@yumc.yonsei.ac.kr

INTRODUCTION

Metastatic carcinomas are the largest group of malignant tumors of the liver. The majority arise from bronchogenic, colorectal, prostate, breast, and pancreatic cancers. Ovarian serous carcinoma is the most common form of epithelial ovarian cancer, and accounts for 40% to 50% of all such tumors, which spread to vital organ parenchyma, such as the lung and liver, and occur in 2-3% of the patients. Furthermore, parenchymal liver metastasis from cystic ovarian adenocarcinoma is very rare (1-3). The number of studies that have evaluated the benefit of hepatic resection of metachronous metastases from gynecologic cancer is very small, but recently some authors have reported that hepatic resection of metachronous metastases from gynecologic carcinoma can be performed safely, and may help prolong survival in carefully selected patients (4). We report a case in which the resection of metastatic liver neoplasm from ovarian serous cystadenocarcinoma was done 7 yr after initial treatment.

CASE REPORT

A 48-yr-old oriental housewife was admitted to the Department of Surgery in Severance Hospital, Yonsei University

College of Medicine with mild abdominal discomfort in the right lower quadrant. She had previously received total abdominal hysterectomy with bilateral salpingo-oophorectomy due to serous papillary carcinoma of both ovaries at another hospital in August 1993 and had received 6 cycles of chemotherapy with cisplatin and alkylloxan, after the surgical treatment. She had a history of a pulmonary tuberculosis 20 yr before, which was treated with medication. Her father died from laryngeal cancer and her elder sister had ovarian cancer. She visited a private clinic with mild abdominal discomfort and hepatic mass was detected by ultrasonographic examination. She was transferred to our hospital for further evaluation and treatment.

The patient complained of easy fatigability and right lower quadrant discomfort. Vital signs on admission showed blood pressure of 110/70 mmHg, body temperature 36.8°C, respiration rate 18/min, heart rate 80/min. The findings from physical examination was unremarkable, except slightly pale conjunctivae and operative scars on the lower midline area. She looked anemic, with a hemoglobin 9.8 g/dL, and hematocrit of 30.4%. Serum albumin, bilirubin, and aspartate aminotransferase (AST)/alanine aminotransferase (ALT) were all within the normal ranges. Alkaline phosphatase level was slightly increased at 146 IU/L. A tumor marker study showed alpha-fetoprotein (AFP) 0.97 IU/mL, carcinoembryonic anti-

gen (CEA) 0.965 ng/mL, cancer antigen (CA) 125 1267 ng/mL, and CA19-9 106.1 ng/mL. Chest posteroanterior radiography examination showed an inactive old tuberculous lesion in the right upper lung field but no metastatic lesions. Abdominal computed tomography revealed a 8.8×7.6 cm-sized lobulated mass lesion in segment VI, VII with central necrosis and minimal heterogeneous peripheral enhancement (Fig. 1). There was no abnormal fluid collection or pathological lymphadenopathy in the peritoneal cavity, and no evidence of metastases on bone scan. ICG R15 examination was 2.5%, and we decided to perform liver resection, under the impression of a metastatic neoplasm of liver. The operation involved cholecystectomy and segmentectomy VI and VII of the liver. During the operation, three resection margins were sent for frozen pathology, and were reported to be negative for tumor extension. The resected liver showed a solid, grayish tan, and firm mass with multifocal necrosis (Fig. 2). The margin of the tumor was irregular and showed infiltrative growth. The mass showed solid sheets of small, uniform, dark cells that often were slightly spindled. The tumor cells showed marked cytological atypia (Fig. 3). The cellular papillae and psammoma bodies were rarely found. The mucin production or sinusoidal pattern of tumor cells was not found microscopically. The pathological features of the ovarian tumors, which had been resected 7 yr before, were reviewed and they were similar to those of the hepatic tumor, although the papillary growth was vague and cellular differentiation was poor in the hepatic lesion than in the previous ovarian tumor. The liver mass was diagnosed as metastatic serous carcinoma from the ovary. The patient recovered from

the surgery without any complication. On the 10th postoperative day, the patient received a single regimen chemotherapy with paclitaxel (Taxol, 155 mg/m^2 BSA) and was discharged. She has been carefully followed up without any evidence of recurrence after completion of the remaining 5 cycles of chemotherapy, at three weeks' intervals.

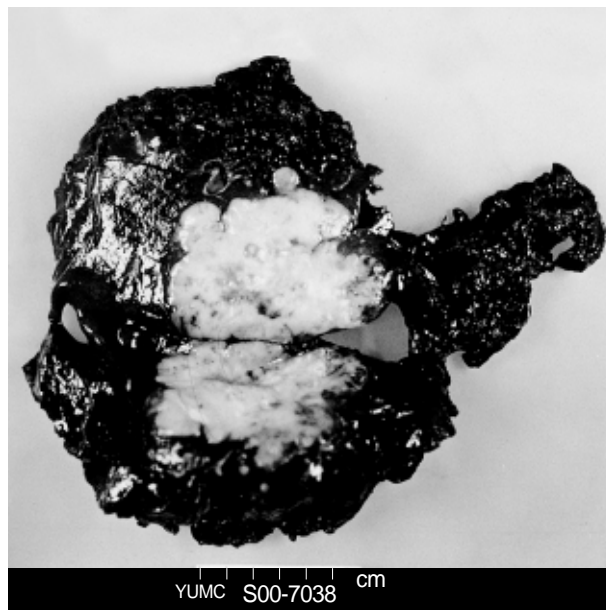


Fig. 2. Gross feature of metastatic serous carcinoma. The resected liver shows a solid, grayish tan, and firm mass with multifocal necrosis.



Fig. 1. Enhanced CT showing 8.8×7.6 cm sized lobulated mass lesion on segment VI and VII of the liver. The mass shows central necrotic area and minimal, heterogenous peripheral enhancement.

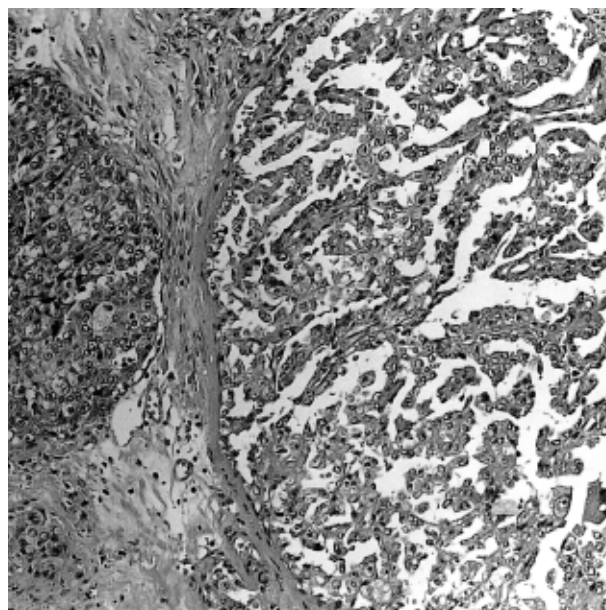


Fig. 3. Microscopic feature of metastatic serous carcinoma. The larger nodule shows characteristic cellular papillae (H&E, $\times 100$).

DISCUSSION

The liver is the commonest site of blood-borne metastases from the abdominal viscera, and the most frequent site for metastatic growths, other than the lymph nodes (5). Metastatic carcinoma occurs much more frequently in the liver than primary hepatocellular carcinoma. Patients with metastatic involvement of the liver present with major symptoms, including hepatic pain, hepatomegaly, ascites, and jaundice. Anorexia and weight loss are almost constant findings. Hepatomegaly and hepatic tenderness are frequently noted and palpation may reveal a distinct nodularity of the liver in about half the cases. The alkaline phosphatase level is increased in over 80 percents of patients and the AST level is increased in approximately two-thirds of the patients. Serum AFP determination is a good tumor marker for primary hepatocellular carcinoma but in metastatic carcinoma it is negative (6). Serial follow-up for the tumor markers of specific tumors, such as CEA, CA 19-9, and CA 125, is helpful for diagnosis. In our patient, the CA 125 level was highly elevated at 1,267 ng/mL and the CA 19-9 was also elevated at 106.1 U/mL. Although CA 125 can be observed in a variety of benign conditions and other nongynecologic malignancies, it is elevated in 80% of epithelial ovarian cancers. These tumor markers may be useful in helping to predict the potential for malignancy preoperatively. If elevated, they can be used to monitor the response to therapy and detect early recurrence (3).

Imaging studies also play an important role in determining liver metastases. The hepatic metastatic tumor from cystic ovarian carcinoma may manifest as a well-defined cystic lesion or as a solid mass, and this solid mass shows delayed enhancement on contrast-enhanced CT imaging. Furthermore, rapid cystic formation and subcapsular extension is frequently seen (7). CT findings of our patient were compatible with the above descriptions. The level of specific tumor marker of primary cancer was useful and imaging studies were very helpful for the diagnosis of metastatic lesions in the liver from ovarian serous cystadenocarcinoma.

Hepatic resection for a secondary malignant growth can be performed safely with a real possibility of cure in selected instances (8). Surgical treatment of hepatic metastases should be considered only if (a) the control of the primary tumor is accomplished or anticipated, (b) there are no systemic or intra-abdominal metastases, (c) the patient's condition is compatible with the major operative procedure, and (d) the extent of hepatic involvement is such that resection and total extirpation of the metastases is feasible (6). Resection of hepatic metastases from carcinomas of the colon and rectum appear to extend the survival time in appropriately selected patients, and selection criteria have been widely published. Similar data for patients with hepatic metastases from primary sites other than the colon and rectum are lacking (9). However, recently some authors have reported that hepatic resection of metachronous metastases from gynecologic carcinomas

including ovarian serous cystadenocarcinoma could be performed safely and might help prolong survival in carefully selected patients (4, 10).

Ovarian epithelial cancers spread primarily by exfoliation of cells into the peritoneal cavity, by lymphatic dissemination, and by hematogenous spread. The most common and earliest mode of dissemination of ovarian cancer is through the exfoliation of cells that implant along the surfaces of the peritoneal cavity. Therefore, metastases are typically seen on the posterior cul-de-sac, paracolic gutter, right hemidiaphragm, liver capsule, and the peritoneal surfaces of the intestines and their mesenteries, and the omentum. Hematogenous dissemination at the time of diagnosis is uncommon and liver metastases from epithelial ovarian cancers are less frequent than other ovarian cancers, for example, stromal tumors, sarcomas, and germ cell tumors (11). Total of 224 cases of variable hepatic resection were performed for metastatic tumor from March 1986 to May 2000 in our hospital. Among them 77 cases were metastatic liver neoplasms from non-colorectal primary tumors (34.8%). There were only 2 cases of hepatic resection for metastases from ovarian cancer (0.9% of the total number of hepatic resections for metastatic tumors). Various chemotherapeutic agents have been found to be active against ovarian serous cystadenocarcinoma. This additional therapy is indicated for patients in which the disease is more poorly differentiated or in whom there are malignant cells either in the ascitic fluid or in peritoneal washings (1). Single-agent cisplatin or cisplatin-based combination therapy is the most effective regimen. Recently, paclitaxel (Taxol), a microtubule stabilizer, was found to have significant activity in many cancers, and reported to be the drug of choice in the treatment of patients with cancer of the ovary and Fallopian tube that are resistant to conventional chemotherapy (12). Oliverio et al. reported the efficacy of paclitaxel in the second-line treatment of refractory and relapsed ovarian cancer patients. They concluded that this therapy is an acceptable treatment with a good safety profile, and can be safely administered at a dosage of 175 mg/m² (13). For patients treated initially with platinum therapy, paclitaxel has therapeutic responses occurring in 20-36% of patients (1). Our patient had already received 6 cycles of chemotherapy with cisplatin and alkyloxan after the first operation for ovarian cancer. Although all resection margins were negative for malignancy, the pathologic diagnosis of the tumor was poorly-differentiated adenocarcinoma with areas of necrosis and lymphovascular invasion and the tumor extended to the soft tissue of the Glisson's capsule. So we performed adjuvant chemotherapy with paclitaxel after hepatic resection.

In summary we report a rare case in which hepatic resection was done for metastatic liver neoplasm from serous cystadenocarcinoma of the ovary. The patient should be carefully followed-up with physical examinations, serial blood cell counts, blood chemistry, imaging studies, and the eval-

uation of tumor marker levels.

REFERENCES

1. Berek JS, Adashi EY, Hillard PA. *Ovarian cancer*. In Novak ER, eds. *Novak's Gynecology*. 12th ed. Baltimore: Williams & Wilkins, 1996; 1155-92.
2. Leifer DM, Chan TW. *Liver metastases from ovarian cystadenocarcinoma masquerading on CT as lobar fatty infiltration*. *J Comput Assist Tomogr* 1993; 17: 816-8.
3. Scott JR, Saia PJ, Hammond CB, Spellacy WN. *Disease of the ovary and fallopian tube*. In Danforth DN, Saia PJ, eds. *Danforth's Obstetrics and Gynecology* 8th ed. Baltimore; Lippincott, Williams & Wilkins, 1999; 892-901.
4. Chi DS, Fong Y, Venkatraman ES, Barakat RR. *Hepatic resection for metastatic gynecologic carcinomas*. *Gynecol Oncol* 1997; 66: 45-51.
5. Lygidakis NJ, Pearl A. *Metastatic liver disease-a review*. *Hepato-gastroenterology* 1997; 44: 1484-7.
6. Schwartz SI, Shires GT, Spencer FC. *Metastatic neoplasms in liver*. In Schwatz SI eds. *Principles of Surgery* 6th ed. NewYork: McGraw-Hill, 1994: 1339-40.
7. Tang Y, Yamashita Y, Ogata I, Namimoto T, Abe Y, Urata J, Takahashi M. *Metastatic liver tumor from cystic ovarian carcinomas: CT and MRI appearance*. *Radiat Med* 1999; 17: 265-70.
8. Cobourn CS, Makowka L, Langer B, Taylor BR, Falk RE. *Examination of patient selection and outcome for hepatic resection for metastatic disease*. *Surg Gynecol Obstet* 1987; 165: 239-46.
9. Wolf RF, Goodnight JE, Krag DE, Schneider PD. *Result of resection and proposed guidelines for patient selection in instances of noncolorectal hepatic metastases*. *Surg Gynecol Obstet* 1991; 173: 454-60.
10. Harrison LE, Brennan MF, Newman E, Fortner JG, Picardo A, Blumgart LH, Fong Y. *Hepatic resection for noncolorectal, nonneuroendocrine metastases: a fifteen-year experience with ninety-six patients*. *Surgery* 1997; 121: 625-32.
11. Rose PG, Piver MS, Tsukada Y, Lau TS. *Metastatic patterns in histologic variants of ovarian cancer. An autopsy study* *Cancer* 1989; 64: 1508-13.
12. Cai S, Tang J, Fan J. *A clinical report of refractory carcinoma of ovary and fallopian tube treated with taxol*. *Zhonghua Zhong Liu Za Zhi (Chinese J Oncol)* 1995; 17: 135-8.
13. Oliverio G, Canuti D, Tononi A, Scarpellini M, Danzini I, Galli I, Ravaioli A. *Paclitaxel efficacy and tolerability in second-line treatment of refractory and relapsed ovarian cancer patients*. *J Chemotherapy* 1999; 11: 301-5.