We report a case of small-bowel perforation due to metastatic carcinoma of the breast during chemotherapy. Partial resection of the small intestine and primary anastomosis were performed. Although the patient made a good recovery from panperitonitis, she died of the disease on the 55th postoperative day. Since perforation during chemotherapy results in an extremely poor prognosis, special caution during chemotherapy is needed for patients with possible gastrointestinal involvement with tumor.

Key words: breast neoplasms – intestinal perforation – antineoplastic agents – neoplasm metastasis

INTRODUCTION

Metastases of breast cancer frequently occur in the lungs, liver, adrenals and bone, but gastrointestinal involvement is rare (1,2). However, autopsy cases showed that 16% of patients with breast cancer have gastrointestinal metastases (3). The recent protocol of weekly docetaxel has been shown to be effective for such patients with metastatic breast cancer (4). However, effective chemotherapy may sometimes unmask gastrointestinal metastases, with the development of perforation or bleeding.

We report a case of small-bowel perforation due to metastatic carcinoma of the breast during chemotherapy and review the literature. Special caution during chemotherapy is needed for patients with possible gastrointestinal involvement with tumor.

CASE REPORT

A 46-year-old Japanese premenopausal woman underwent radical mastectomy with the diagnosis of left breast cancer, at the University of Tokyo affiliated hospital in August 1998. She received one cycle of preoperative chemotherapy with cyclophosphamide 500 mg, 5-fluorouracil 500 mg and pirarubicin 40 mg. TNM classification according to general rules of the Japanese Breast Cancer Society was T3N1M0, stage IIIA. Histopathology revealed double cancer consisting of scirrhous carcinoma and solid-tubular carcinoma. Histopathological grading could not be assessed because of the effect of preoperative chemotherapy. Metastasis was found in one of 32 lymph nodes. She received four cycles of postoperative chemotherapy with mitomycin C 4 mg, 5-fluorouracil 250 mg and pirarubicin 30 mg every 4 weeks. This regimen was chosen according to the drug sensitivity test. Although both estrogen and progesterone receptors were negative, she received tamoxifen. Tumor markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen 15-3 (CA15-3) were negative. She underwent video-assisted partial resection of the lung for metastasis in the left upper lobe, at the University of Tokyo Hospital in December 1999, at which time no other metastases were found. In January 2000, bone scintiscan detected multiple hot spots in the right scapula, bilateral femurs and left knee joint. Computed tomography (CT) also revealed multiple liver and lung metastases. Physical examination findings including abdominal signs and symptoms were not remarkable. Performance status was 2, height was 158 cm, weight was 58 kg, CEA level was normal and CA15-3 level was 26 (normal range, 0–21).

Chemotherapy with docetaxel hydrate at 40 mg i.v. once a week was started for palliation. On the night of the third course, she developed severe lower abdominal pain. Physical examination revealed tenderness and mild guarding of the lower abdomen. Laboratory data revealed a white blood cell count of $7100 \times 10^9/\text{L}$ and C reactive protein (CRP) of 3.5 mg/dl. Plain CT revealed free air and fluid retention around the liver (Fig. 1). She was clinically diagnosed as having panperitonitis due to gastrointestinal perforation and underwent emergency operation. Laparotomy revealed a 2 cm area of induration with an ulcerated free perforation in the middle of the small intestine and purulent peritonitis. Multiple meta-
tases to the liver and para-aortic lymph nodes were also noted. Partial resection of the small intestine and primary anastomosis were performed. The effect of chemotherapy on the bone, liver and lung metastases was difficult to evaluate, because thorough investigations such as enhanced CT or bone scintiscan could not be performed owing to the patient’s poor general condition at the time of salvage surgery.

The macroscopic appearance of the resected specimen is shown in Fig. 2. Microscopic examination was consistent with secondary involvement with the primary breast cancer (Fig. 3). Both estrogen and progesterone receptors were negative in the resected intestinal lesion. She made a good recovery from panperitonitis and returned to the Radiation Department for radiotherapy on the 25th postoperative day (POD). However, the CA15-3 level increased to 220 on the 51st POD and she died of cancer progression on the 55th POD.

DISCUSSION

Breast cancer metastases to the gastrointestinal tract are relatively rare. However, Cifuentes and Pickren (3) reported that metastases to the gastrointestinal tract were detected in 112 out of 707 autopsy cases (16%) with breast carcinoma. The small intestine was involved in 64 cases (9%), stomach in 69 cases (10%) and large intestine in 57 cases (8%). Metastases to the gastrointestinal tract may produce symptoms due to bleeding, obstruction or perforation, so that operative intervention is occasionally required.

Asch et al. (1) reported 18 cases that required operation due to gastrointestinal metastases of breast carcinoma. Cornu-Labat et al. (5) reported a case of small-bowel perforation due to metastatic breast cancer. In that case, the use of chemotherapy was not described. Seewaldt et al. (6) reported four cases of bowel perforation during paclitaxel therapy. They concluded that perforation was not the result of tumor lysis, because three patients had disease progression and the other one showed no evidence of carcinomatosis on surgical exploration.

In our case, microscopic examination showed the existence of tumor cells and necrotic cells around the perforated site. However, it was difficult to determine whether the perforation was due to drug toxicity or disease progression. Because we had no evidence that chemotherapy had any effect on the other metastatic lesions, disease progression could not be ruled out as a cause of the perforation. However, drug toxicity could not be ruled out either. The perforation occurred 21 days after first receiving docetaxel in our case and after 13–16 days in the previous four cases with paclitaxel (6). The similar interval between the start of chemotherapy and the occurrence of perforation suggests that our case was also docetaxel related. This makes us speculate that docetaxel might promote cytolysis of metastatic lesions, resulting in intestinal perforation.

Once perforation has occurred, surgery is the only option for salvage. However, the prognosis is very poor owing to the patient’s poor general condition and the poor prognosis of the original disease. Ferrara et al. (7) reported the morbidity of emergency operation in 21 patients with metastatic cancer receiving chemotherapy (15 cases of perforated viscus and six
of hemorrhage). Of these, 17 patients (81%) died in the immediate postoperative period. In our case, the patient made a good recovery from peritonitis and started food intake on the seventh POD. However, she died of progression of breast cancer on the 55th POD. Our experience, together with the data from Ferrara et al. (7), strongly suggests that perforation during chemotherapy results in an extremely poor prognosis. Autopsy studies indicate that the frequency of gastrointestinal metastases in advanced breast cancer is higher than anticipated. Effective chemotherapy may induce such critical peritonitis in these patients.

Therefore, we propose that in advanced breast cancer, involvement of the gastrointestinal tract should be carefully evaluated before chemotherapy and it should be noted that intestinal perforation may occur as one of the most serious complications of chemotherapy.

References