A Case of Metastatic Small Intestine Tumor from Breast Cancer 19 Years after the Breast Operation

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Abstract
Breast cancer metastasis to the small intestine is relatively rare. Herein, we report a case of breast cancer metastasis to the small intestine that was found by preoperative small-bowel endoscopy 19 years postoperatively. The patient was a 65-year old female who underwent radical mastectomy for Stage III A (T3a, N1a, M0, ER(+), PgR(-), HER2 (+1)) left breast cancer in 1990. She developed epigastric pain in January 2009, and visited a local physician. CT scan revealed the presence of an abnormal chest shadow and the serum CA 15-3 level was elevated to 124 U/ml, so the patient was referred to our hospital. A close examination at the outpatient department was initially scheduled, but she was hospitalized with the diagnosis of ileus in late March. Enteroscopy revealed circumferential stenosis of the jejunum, approximately 50 cm from the Treitz ligament, and a biopsy indicated metastatic adenocarcinoma (ER(+), PgR(-), HER2 (+1)). Laparoscopic-assisted partial small bowel resection was performed based on the diagnosis of breast cancer metastasis to the small intestine. Furthermore, disseminated disease, approximately 10 mm in length, in the greater omentum was also isolated. A histopathological examination revealed that it was infiltrating lobular carcinoma.

Key words: breast cancer, intestinal metastasis, enteroscopy

Introduction
Distant metastasis in breast cancer can develop in any organs but the incidence of intestinal metastasis is rare. We report our case of small intestinal metastasis of breast cancer, which was diagnosed by enteroscopy 19 years after breast cancer surgery with the review of the literature.

Case Report
A 65-year old woman presented with the chief complaint of epigastric pain. She underwent radical...
mastectomy for cancer of the left breast (Stage IIIA, T3a, N1a, M0, ER(+), PgR(-), HER2 (1+)) in June 1990, and subsequently underwent postoperative adjuvant therapy (Tamoxifen (30mg/day) and tegafur and uracil (UFT) (600mg/day)) for 2 years. And she underwent appendectomy for treatment of acute appendicitis in 1980. She visited a local physician for epigastric pain, which had developed since January 2009. Because a CT scan revealed the presence of an abnormal chest shadow and CA15-3 tumor marker was elevated to 124 U/ml, she was referred to our hospital. She was supposed to undergo a close ex-

amination at the outpatient department, but she was admitted with the diagnosis of ileus, which could have been caused by constipation, and vomiting since the end of March.

Findings on admission were height of 154 cm, body weight of 45 kg, body temperature of 36.7°C, blood pressure of 145/70 mmHg, and pulse rate of 86 beats/min. Abdominal distention and tenderness were observed but rebound tenderness was not apparent. Laboratory testing revealed CA15-3 level was elevated at 309 U/ml, but no other abnormal findings were found. Abdominal X-ray revealed enlargement of the small intestine. Conservative treatment was initiated using intestinal intubation for the diagnosis of ileus. Intestinal imaging using an ileus tube revealed the presence of an almost circumferential stenosis of the jejunum approximately 50 to 60 cm from the Treitz ligament and dilation on the oral

![Fig. 2 CT scan revealed stenosis of the intestine and thickening of the intestinal wall.](image)

![Fig. 3 Intraoperative findings revealed stenosis of the intestine. On the oral side, the intestine was dilated (arrow).](image)

![Fig. 4 Intraoperative findings revealed a disseminated tumor of the omentum majus (arrow).](image)

![Fig. 5 Loupe image of the resected specimen revealed adenocarcinoma cell invading from the serosa to the mucosal layer. It was similar to the histological feature of breast cancer (H.E. × 12.5).](image)
side of the intestine. Intestinal imaging using an ileus tube suggested stenosis due to a tumor. After the ileus improved, enteroscopy was performed. Enteroscopy revealed circumferential stenosis in the jejunum, approximately 50 cm from the Treitz ligament, which completely prevented the passage of the enteroscope. Redness and edema were found in the mucous membrane (Fig. 1). Biopsy results indicated that it was metastatic adenocarcinoma. Chest-abdominal CT showed lung metastases because of the presence of nodular shadows at the left hilus and the right pulmonary lobe. Furthermore, wall thickening and stenosis at the jejunum, and dilation on the oral side of the intestine (Fig. 2). The laparoscopic assisted surgery was performed under the diagnosis of ileus induced by small intestinal metastasis of breast cancer, based on the above findings. A laparoscopic found an approximately 1.5 cm circumferential stenosis in the jejunum, approximately 50 cm from the Treitz ligament, and the presence of dilation on the oral side of the intestine (Fig. 3). A mesenteric lymph node close to the stenosis was swollen and a whitish mass with the maximum diameter of 10 mm was found in the omentum (Fig. 4). No other abnormal findings were observed. Partial small bowel resection and lumpectomy including the swollen lymph nodes were performed. The intraoperative rapid pathological examination demonstrated that the mass in the omentum was metastatic adenocarcinoma. Histopathological examination demonstrated a superficially elevated mass, 1.6 × 1.4 × 0.2 cm in size, was observed. The tumor was exposed on the serosal surfaces, but the cancer tissues were only slightly observed on the mucosal surfaces (Fig. 5). When compared histologically with the previously resected primary focus using H.E. staining, they were found to be similar. Therefore, it was diagnosed as metastatic lobular carcinoma of the breast. The results of immunostaining of the small intestine tumor were ER (+), PgR (+), HER2 (2+), Cytokeratin (CK) 7 (+) and 20 (-). Furthermore, the immunostaining results of the pri-
primary focus, which had been resected 19 years ago, were similar, i.e., ER (+), PgR (-), HER2 (2+), CK7 (+), and CK20 (-), which indicated that the primary focus and the small intestine tumor exhibited a similar staining profile (Fig. 6). Based on the above findings, it was diagnosed as small intestinal metastasis of breast cancer. The patient was discharged at day 14 because of a good postoperative course. The postoperative bone scintigraphy indicated systemic bone metastasis. Therefore, hormone treatment and chemotherapy are currently being planned.

Discussion
The incidence of small intestinal metastasis of malignant tumor is rare, and has been reported as approximately 1% in the Western countries\(^6\). According to a report by Cifuentes et al.\(^6\), 16% of 707 breast cancer autopsy cases had gastrointestinal tract involvement, and small intestinal metastasis cases comprised only 9%. When we searched for related articles between 1983 and 2008 in Japan using “breast cancer” and/or “small intestinal metastasis” as keywords, only 18 reports were obtained. This article refers to these 18 reports, in addition to our current case.

The age of the patients ranged between 41 and 80 years old (mean age: 58.9 years old). The major clinical symptoms were abdominal pain, nausea, and vomiting due to the intestinal obstruction. Among these patients, 6 (31.6%) were suspected to be due to breast cancer metastasis during the preoperative diagnosis and 2 (10.5%) received a definitive diagnosis, including 1 patient who was diagnosed by peritoneal fluid cytology and the 1 patient who was our case. Furthermore, 3 patients also developed small intestinal perforation and were diagnosed with peritonitis. The duration between the breast cancer surgery and the development of gastrointestinal symptoms was 10 to 228 months (mean: 66.5 months) and was relatively long, except for 2 patients who developed synchronously. In particular, our case took 228 months to develop gastrointestinal symptoms (19 years), which was the longest duration. As for tumor markers, CEA increased in 10 out of 17 patients (58.8%) and CA15-3 was elevated in 5 out of 8 patients (62.5%). Ushio et al.\(^6\) categorized metastatic small intestinal tumors into disseminated and vascular tumors, based on the imaging findings, and reported that the disseminated metastasis rarely formed a deep ulcer or high protrusion while the vascular tumors became submucosal tumors or ulcers. Most of the cases described in this article had circumferential stenosis and did not exhibit any characteristic findings. The CT revealed hypertrophy and stenosis of the intestinal walls. Enteroscopy was performed only in our case, and identified edema and redness in the mucous membrane but showed that the morphology was relatively well-maintained so that it might be consistent with serosal infiltration. Enteroscopy, which is becoming widely used in the medical field, may be useful, considering that pathophysiologic diagnosis is essential to successfully perform a definitive preoperative diagnosis. Metastases of the primary cancer into regions other than the small bowel were observed in all of the patients, who experienced surgical treatment. Radical operation was performed successfully in only 5 of 18 patients (27.8%). The disease stages when the breast cancer surgeries were performed included Stage I in 2 patients, Stage II in 2 patients, Stage IIIB in 2 patients, Stage IIIA in 5 patients, Stage IIIB in 4 patients, and Stage IV in 2 patients. The percentage of patients with Stage III was 52.8%; accounting for more than half of the patients. In terms of the histology of breast cancer, scirrhous carcinoma was the most common and was seen in 6 of 19 patients (31.6%), followed by solid-tubular carcinoma in 4 patients, invasive lobular carcinoma in 4 patients, and spindle cell carcinoma and medullary carcinoma in 1 patient each. Furthermore, these previous reports indicated that 3 patients had infiltrating ductal carcinoma, but the details were unknown. In general, the incidence of infiltrating lobular carcinoma with intestinal metastasis was higher\(^6\), but the incidence was the second highest following that of scirrhous carcinoma, which was found in this study. Intestinal metastasis types are hematogenous, lymphatic, and disseminated metastasis, but according to the literature, the metastasis experienced by 5 of 8 patients (62.5%) was disseminated and 3 patients (37.5%) had hematogenous metastasis. Disseminated metastasis may be caused by lesions of hematogenous or lymphatic metastasis to abdominal organs, which was also suggested by Nishi et al.\(^4\), but it would be difficult to prove. Currently, in order to diagnose whether a lesion is primary or metastatic, the similarity of the histology to that of the primary tumor and/or the findings of
immunostaining, such as ER and PgR, are used. Our case used CK7 and CK20, in addition to such immunostaining, and compared the immunostaining with the primary tumor. The immunostaining results indicated that both the primary breast cancer and the small intestinal tumor exhibited CK7(+) and CK20(-) and that the pattern was characteristic of breast cancer⁰. Furthermore, in consideration of a report that the primary lesions of the jejunum and ileum were 100% positive for CK20⁰ the small intestinal tumor was determined to be a metastasis of the breast cancer that had developed 19 years ago. The therapies, including chemotherapy, hormone therapy, and radiotherapy, were applied to 11 of 15 patients (73.3%) reported in this study, who underwent postoperative therapy. But in general, the prognosis of patients in whom small intestinal metastasis was found was poor, and 13 out of 21 patients described previously in the literature (61.9%) were deceased within 1 year; they also had metastases to other organs, so that the small intestinal metastasis might have been one part of multiple systemic metastases.

Some patients who survive for long periods after breast cancer surgery exhibit intestinal metastases. Postoperative hormone therapy and bisphosphonate medication for metastasis into the bone were applied to her after the operation, who has remained stable in pathological condition and at the present day, 12 months after the operation, continues to visit our hospital for follow-up. Therefore, close examination, including a GI series and endoscopy, should be provided as part of the diagnostic procedures to patients who present with any gastrointestinal symptoms.

References


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