A Case of Synchronous Metastasis of Breast Cancer to Stomach and Colon

HIDEYA TAKEUCHI¹, SHOZI HIROSHIGE¹, YASUJI YOSHIKAWA², TETUSY AKUSUMOTO¹ and YOICHI MUTO¹

Departments of ¹Surgery and ²Pathology, National Hospital Organization Beppu Medical Center, Beppu, Japan

Abstract. A case of synchronous metastasis of breast cancer to the stomach and colon is reported. A 38-year-old woman with a history of bilateral breast cancer was admitted for endoscopic examination because of occult blood. Endoscopic examination showed elevated lesions on the mucosal surface of the stomach and cecum. Histopathological examination of the biopsy specimens obtained from both sites showed adenocarcinoma, comprised of tumor cells with structural and nuclear atypia, which were similar to those of the primary breast cancer cells. In immunohistochemical analysis, these tumor cells stained positive for ER. Therefore, we diagnosed a synchronous metastasis of breast cancer to the stomach and colon. Synchronous metastasis of breast cancer to the stomach and colon without liver metastasis or peritoneal dissemination is extremely rare, with only 4 reported cases existing in literature.

Breast cancer is the most common malignancy among women in Japan and in Western countries. The life-time risk for development of breast cancer in women is 5% (1). Common sites of breast cancer metastases include the lungs, liver, bones, and soft tissues. Metastatic disease in the gastrointestinal (GI) tract has been rarely reported (2). Borst and Ingold reported metastasis of breast cancer to the GI tract (MBGI) in only 17 of 2,604 cases (less than 1%) over an 18-year period (3). Other studies on MBGI are limited to autopsy cases (4, 5); thus, information on MBGI is scarce. We present a case of synchronous metastasis of breast cancer to the stomach and colon and discuss the clinicopathological characteristics of MBGI along with a review of the literature.

Case Report

A 38-year-old woman whose stool sample tested positive for occult blood during a medical check-up was admitted to the hospital for endoscopic examination. Three years ago, she had undergone left modified-mastectomy with axillary dissection for the treatment of lobular carcinoma (T2N1M0). Immunohistochemical analysis of the invasive lobular carcinoma after surgery (Figure 1) revealed positive staining for estrogen receptor (ER), but negative staining for progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2). The patient was sequentially administered four courses of epirubicin/cyclophosphamide (EC) therapy with 90 mg/m² epirubicin, 600 mg/m² cyclophosphamide, and 80 mg/m² paclitaxel. She also underwent radiation therapy to the chest wall and supraclavicular fossa, along with tamoxifen (20 mg/day) and luteinizing hormone-releasing hormone agonist (3.6 mg/month).

One year ago, she underwent right partial-mastectomy with sentinel lymph node biopsy for the treatment of lobular carcinoma (T1N0M0, ER+, PR-, HER2-), followed by four courses of docetaxel (70 mg/m²), and radiation therapy to the residual breast along with anastrozole (1 mg/day).

Endoscopic examination revealed elevated lesions on the mucosal surface of the stomach (Figure 2) and cecum (Figure 3). Histopathological examination of the biopsy specimens obtained from both sites showed adenocarcinoma, comprised of tumor cells with structural and nuclear atypia (Figure 4A and B). The histological characteristics of these tumor cells were similar to those of the primary breast cancer cells. In immunohistochemical analysis, these tumor cells stained positively for ER (Figure 4C) and negatively for PR and HER2. Computed-tomography (CT) and isotope bone scans both failed to demonstrate any other recurrence. Therefore, we diagnosed MBGI and administered capecitabine to the patient, who has subsequently remained completely asymptomatic without any distinct evidence of recurrence after 26 months of follow-up.
Discussion

The frequency of MBGI on autopsy is reported to be 2-8% (4, 5). Hoff et al. (6) reported that only 0.07% of 2,705 surgically-treated cases of breast cancer had clinical manifestations of MBGI. Similarly, McLemore et al. (7) reported that only 41 (0.34%) of 12,001 patients with metastatic breast cancer had pathologically confirmed MBGI, with a mean interval of 7 years since the diagnosis of the primary cancer. MBGI may occur many years after the primary breast cancer diagnosis; this interval is usually between 5 and 20 years, but may even rise to 30 years in some cases (8). The most frequent site of GI tract involvement is the stomach and small intestine, while co-lon and rectal metastases are very rare (9, 10). Co-existing metastases in other tissues are present in up to 90% of cases (11). Synchronous metastasis of breast cancer to the stomach and colon without liver metastasis or peritoneal dissemination is extremely rare, with only four reported cases (12-15).

The metastatic patterns of invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC) differ considerably. IDCs recur more commonly in lung, pleura, and bone, while ILCs metastasize more frequently to the bone marrow and peritoneum (16). Although the IDC subtype accounts for the majority of breast carcinomas (90%), the prevalence of ILC is higher in cases with MBGI (6, 7). The reason for the differences in metastatic patterns between ILC and IDC are poorly understood. One explanation could be the loss of expression of E-cadherin, a molecule responsible for cell-to-cell adhesion, in ILC (17).

Several factors can complicate the diagnosis and delay the treatment of MBGI. These include a potentially long disease-free interval, and diverse and non-specific symptoms at presentation, which often mimic the symptoms of other GI disorders (18). In the present case, the patient was asymptomatic and exhibited no abnormal findings except for the presence of occult blood during a medical check-up. Because of the variation in the endoscopic appearance of MBGI, endoscopic analysis may be insufficient to distinguish...
MBGI from primary GI tract cancer (4, 5). Endoscopy reveals only a few tumors in the gastric mucosa, because metastatic infiltration of the stomach is frequently limited to the submucosa or the seromuscular layer that cannot be accessed with the biopsy forceps. To overcome this shortcoming, deep and extensive biopsies should be performed at endoscopy (19). Even when adequate specimens for pathological examination are obtained, lobular carcinoma of the breast may exhibit a signet-ring morphology, a characteristic of primary gastric adenocarcinoma, and be mis-diagnosed as result (20). Taal et al. (12) reported that endoscopic biopsies from metastatic IDC are more likely to yield positive results (90%) than those from ILC (64%) (16). Comparison of mammary and GI tract specimens is mandatory for accurate histological diagnosis, and the standard method of analysis is immunohistochemistry (10). In the present case, the lesions of the stomach and colon were positive for ER and negative for PR and HER2, which matched the immunohistochemical findings of the primary breast carcinoma. This finding, along with the unique histological pattern of the disease, favored the diagnosis of metastatic lobular carcinoma.

More than half of all patients with MBGI have concurrent systemic metastasis to organs other than the GI tract (9), which suggests that MBGI occurs in the late stage of metastatic disease. Survival rates for MBGI are generally poor, with most patients surviving for less than two years (12). However, similar to this case, some other cases have shown long-term survival after chemotherapy and hormonal therapy (13). Appropriate systemic treatment for MBGI is the preferred therapeutic approach. The overall response rates to non-surgical treatment in breast cancer patients with gastric metastases and colon metastases are 32% and 53%, respectively (9). Systemic therapy for MBGI is a favorable prognostic factor for survival, while surgical intervention for stomach metastasis had no significant impact on survival (3). Therefore, surgery is generally reserved for palliation in cases of perforation, obstruction, and bleeding.

MBGI is rare, but is more common in cases of ILC than IDC. A high index of clinical suspicion should be maintained in patients with a history of breast carcinoma, particularly of ILC. Differentiation of MBGI and primary GI tract cancer is essential to ensure appropriate systemic treatment of breast cancer. If metastasis from the primary breast cancer is found in the GI tract, the other organs of the GI tract should be examined to identify any synchronous lesions, such as those observed in the present case. Physicians should be aware of these unusual metastatic patterns of breast cancer in order to improve treatment and prognosis.

References

Figure 4. Findings on histopathological examination of the biopsy specimens of the gastric (A) and cecal (B) lesions, showing adenocarcinoma comprising of tumor cells with nuclear and structural atypia (H&E staining, ×40). Findings on immunohistochemical analysis of the biopsy specimens from the stomach (C) (H&E staining, ×40). The specimen was positively stained for estrogen receptor.