

## Peritoneal and gastric metastasis from invasive lobular breast carcinoma: a case report

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### 복막 및 위 전이를 동반한 진행성 소엽 유방암 1례 보고

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Peritoneal and gastrointestinal metastasis from breast cancer is very rare. We report here a rare case of metastatic peritoneal and gastric cancer from breast lobular carcinoma after modified radical mastectomy. A 65-year old woman presented with anorexia, nausea, vomiting and dyspepsia for several weeks at 44 months after surgery. Radiologic study showed peritoneal metastasis, and surgical histopathology reported peritoneal and omental metastatic carcinoma. Esophagogastroduodenoscopic (EGD) biopsy also confirmed metastatic carcinoma originated from breast primary.

**Key Words:** Breast neoplasms, Metastasis, Peritoneum, Stomach

Breast cancer is the most frequent malignant tumor among women and the second leading cause of cancer related death.<sup>1,2</sup> Metastasis mostly occurs at bone, lung, liver and brain in 20-30% of these patients.<sup>3</sup>

In rare cases, metastasis have been described in other sites including the gastrointestinal tract

(GIT).<sup>4</sup> Lobular carcinoma, accounting for only 10% of breast cancers, tends to metastasize to the GIT. Although the breast cancer uncommonly metastasize to GIT, it is very important to recognize the gastrointestinal symptoms for early diagnosis and accurate treatment.<sup>5</sup>

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**Received :** Jul. 9, 2013  
**Revised :** Jul. 9, 2013  
**Accepted :** Dec. 30, 2013

In this study, we want to discuss the clinical significance of breast cancer metastasis, presenting a rare case of peritoneal and gastric metastasis.

## CASE REPORT

In November 2007, a 65-year old woman who detected a mass in right breast presented to our outpatient clinic. A 3cm sized mass was identified in the upper outer quadrant on physical examination. Fine needle aspiration of the right breast mass was performed, and lobular carcinoma was confirmed. Baseline assessments, such as breast ultrasonography (USG), mammography, liver USG, bone scan and positron emission tomography (PET) scan, were performed. However, no other malignant lesion was identified. The patient underwent modified radical mastectomy; and histological pathology confirmed invasive lobular carcinoma. Immunohistochemical (IHC) staining showed positivity for estrogen receptor (ER), progesterone receptor (PR), p53 mutation and cathepsin D, but it presented negativity for human epidermal growth factor receptor-2 (HER-2) and E-cadherin. After surgery, the patient was treated with 4 cycles of doxorubicin and cyclophosphamide followed by 4 cycles of docetaxel chemotherapy. The patient received 28 cycles of ad-

juvant radiotherapy, and planned for 5 years of hormonal therapy. The hormonal therapy consisted of tamoxifen and letrozole for 2 and 3 years, respectively. Baseline assessments were performed every 6 months. No recurrent signs were detected for 4 years.

In July 2011, the patient visited outpatient clinic for ascites, right arm edema and dyspepsia. Assays for serum tumor markers showed elevated level of carcinoembryonic antigen (CEA) (84.58ng/ml, normal range: 0-5ng/ml) and cancer antigen (CA) 15-3 (40.66ng/ml, normal range: 0-35ng/ml), but the level of CA19-9 was within normal ranges. No apparent abnormalities were found on breast USG and bone scan. PET scan showed glucose hypermetabolism of abdominal cavity consistent with cancer peritonei (Fig. 1). Additional abdominal computed tomography (CT) showed evidence of cancer peritonei with ascites, omental smudge and cake. In addition, hydronephrotic change at the right kidney also reported (Fig. 2). Ascitic fluid study reported metastatic carcinoma from unknown origin. EGD and colonoscopy were performed to evaluate GIT, but no abnormalities were found except gastritis and colitis. The patient underwent laparotomy to find out the primary origin from GIT and gynecologic organs, but no primary lesion was found. After omentectomy and multiple peritoneal biopsies were done, histopathology reported metastatic lobular breast carcinoma with positivity for ER, CEA,

cytokeratin (CK) 7 and negativity for E-cadherin, PR, and CK20.

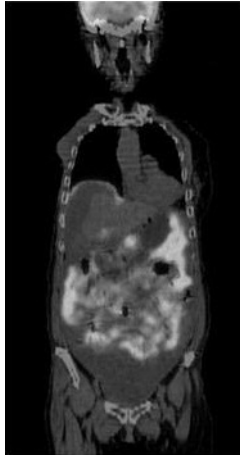


Fig. 1. PET scan showed glucose hypermetabolism of abdominal cavity consistent with cancer peritonei. PET: positive emission tomography.

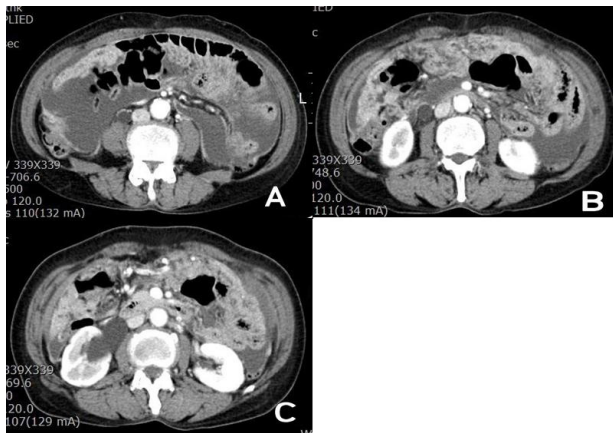


Fig. 2. (A, B) Abdominal CT scans showed ascites, peritoneal thickening, omental smudge and cakes consistent with cancer peritonei. (C) Hydronephrotic change at the right kidney also presented. CT: computed tomography.

After surgery, the patient was treated with 9 cycles of paclitaxel and gemcitabine regimen. The patient performed follow-up examinations every 3 cycles of chemotherapy. After chemotherapy was done, abdominal CT showed improving process with decreased ascites, and no interval change of the suspicious metastatic lesion in the right ureter (Fig. 3). After that, the patient was discharged, because she wanted to receive no more treatment. In May 2012, the patient admitted via emergency room for abdominal pain, nausea, vomiting and dyspepsia. In macroscopic findings of EGD, esophageal candidiasis and raised erosive gastric lesion were suggested (Fig. 4). However, histopathological examination of biopsy specimen from stomach revealed primary adenocarcinoma or metastatic carcinoma. IHC staining of the cells showed positivity for ER, CEA and CK7, and negativity for E-cadherin, PR and CK20, consistent with a diagnosis of metastatic invasive lobular breast carcinoma. The patient was so weak to administer anticancer therapy

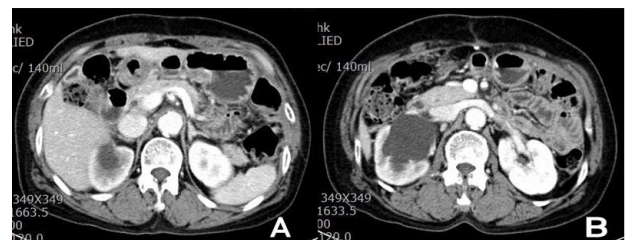


Fig. 3. (A) After 9 cycles of chemotherapy, abdominal CT scans showed improving process with decreased ascites. (B) There are also hydronephrosis and hydroureter at the right kidney and ureter. CT: computed tomography.

that conservative therapy was performed. After 15 days, the patient expired.

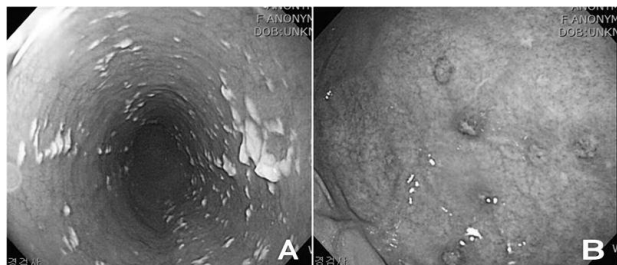


Fig. 4. EGD showed (A) esophageal candidiasis at the esophagus and (B) metastatic gastric carcinoma from breast at the body of stomach. EGD: esophagogastroduodenoscopy.

## DISCUSSION

Breast cancer commonly metastasize to nodes, skin, chest wall, bones, lungs, liver, and brain.<sup>6,7</sup> GIT metastasis of breast cancer is clinically considered to be very rare, but is found in about 4-35% of autopsy series.<sup>6,8</sup> It is well known that ductal carcinoma frequently metastasize to liver, lung and brain. However, lobular carcinoma has a greater tendency to relapse in GIT, gynecological organs and peritoneum.<sup>6</sup> Moreover, when the primary tumor is composed of ductal and lobular component, it is known that lobular component tends to metastasize to GIT.<sup>8</sup>

There are some previous studies with respect to survival outcomes of gastric and peritoneal

metastasis from breast cancer. Pectasides et al.<sup>6</sup> showed that the median time between primary breast cancer diagnosis and gastric metastasis was 41 months, and the median survival following the detection of gastric involvement was 11 months. Tuthill et al.<sup>9</sup> reported that the median duration between detection of metastatic disease and that of peritoneal spread was 19.2 months, and the overall median survival from time of early breast cancer diagnosis was 74 months. The median survival of patients with peritoneal disease measured 1.56 months, and it is worse than any other metastatic cancer from breast.

In patients with metastatic GIT cancer, every gastrointestinal symptom can be present, and it makes difficult to make the differential diagnosis from primary GIT tumors.<sup>3,7</sup> The most common pattern of metastatic gastric cancer is diffuse infiltration of the submucosa and muscularis propria (linitis plastica).<sup>7</sup> Because of this characteristic, the endoscopic evaluation may be normal in 50% of cases.<sup>6</sup> So, when the lesion is submucosal or seromuscular, combination with endoscopic ultrasound or deep biopsy should be needed.<sup>4,8</sup>

It has been suggested that ductal carcinomas tend to produce nodular stomach lesion, while lobular carcinomas have a tendency toward inducing more diffuse disease.<sup>8</sup> Additionally, lobular breast carcinoma often forms a signet ring morphology which may be hard to distinguish

it from a primary gastric carcinoma.<sup>6</sup> However, breast signet ring cell carcinoma (SRC) may show some morphological differences from GIT. Breast SRC presents “univacuolated lumen type” of signet ring cell, characterized by the presence of a round globule of syalomucin that imparts a “target” appearance to the cell or by the presence of a single sharply demarcated intracytoplasmic vacuole, with or without a central eosinophilic inclusions.<sup>1,6</sup>

Detailed IHC staining may be the only reliable method to differentiate between metastatic and primary gastric carcinoma. Metastatic breast carcinoma is usually positive for CK7, gross cystic disease fluid protein (GCDFP)-15, CEA, ER and PR, and negative for CK20.<sup>6</sup>

Although ER and PR can be present in a primary gastric carcinoma, a high level favors a breast cancer metastasis.<sup>4</sup> CK7 is registered in 90% of the breast carcinoma and expressed about 50-64% of primary gastric adenocarcinomas. CK20, in contrast, is particularly positive in gastric, colorectal, pancreatic and in transitional cell carcinomas, except breast carcinomas. GCDFP-15 is a sensitive marker for lobular breast carcinoma. It is a convenient addition in the diagnosis of metastatic carcinoma of suspected breast origin because it is not found in stomach cancers but in breast cancers. While GCDFP-15 is a useful marker to differentiate metastatic gastric cancer from primary one, it has unavoidable limitation of low

sensitivity. GCDPF has 90% of specificity for breast tissue, but a sensitivity is only 50%.<sup>1</sup> So, the positivity for CK7, GCDFP-15 and hormonal receptor with the negativity for CK20 and CA19-9 were of great value in differentiating an unsuspected lobular breast carcinoma from gastric carcinoma.<sup>6</sup>

E-cadherin can also be used to differentiate gastric metastasis from breast cancer. A previous study reported that the absence of E-cadherin staining was significantly related to metastatic breast carcinoma.<sup>10</sup> This report is consistent with our case. In this study, histopathology reported the negativity for E-cadherin.

The therapeutic recommendation for gastrointestinal metastasis from breast cancer is systemic treatment. Surgical resection is not routinely recommended. In case of emergency condition, the surgical palliation is only indicated in carefully selected patients.<sup>2,6</sup>

In conclusion, when the long-term gastrointestinal symptoms occur during the anticancer therapy, the possibility of GIT metastasis rather than anticancer treatment-related symptoms should be considered. In addition, the accurate therapy of primary lesion, and the analysis of biological characteristics using endoscopic biopsy may be needed for efficient diagnosis and treatment.

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