

Case Report

Gastric metastasis from breast infiltrating ductal carcinoma: a case report

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Abstract: Gastric metastasis from breast carcinoma occurs rarely and generally derives from infiltrating lobular carcinoma (ILC) rather than infiltrating ductal carcinoma (IDC). Here, we reported a case of breast infiltrating ductal carcinoma metastasis to stomach in a 58-year-old woman, who experienced epigastric pain and abdominal distention for ten days. Gastric endoscopy was performed and revealed erosion lesions in gastric body and antrum with the initial biopsies suggestive of a low-differentiated adenocarcinoma. During the work-up procedure, a 16×13 mm nodule in the lower outer quadrant of the left breast and multiple enlarged lymph nodes in the left axilla were detected by positron emission tomography-computed tomography (PET-CT). Review of immunohistochemical analysis of the previous pathological sections from the gastric biopsies confirmed that the gastric tumor derived from breast infiltrating carcinoma. The patient received chemotherapy and hormonal therapy without surgery. To date, the patient has survived for 20 months.

Keywords: Breast carcinoma, gastric metastasis, infiltrating ductal carcinoma

Introduction

Breast carcinoma is the most prevalent female malignancy in China as well as in Western countries. The most commonly associated sites of breast carcinoma metastasis are the local and distant lymph nodes, brain, lung, liver and bones [1-3]. Gastric metastasis from breast carcinoma is rare and generally occurs several years and decades after the diagnosis of the primary lesion [2, 3]. Among the various types of breast cancer, infiltrating lobular carcinoma (ILC) has a more predilection to metastasize to the gastrointestinal tract, gynecological organs, and the peritoneum, whereas infiltrating ductal carcinoma (IDC) tends to spread to the lung, bone, and liver [3-5]. The most common type of gastric metastasis from breast carcinoma as seen on endoscopy is a diffuse linitis plastica-like infiltration [2]. To obtain an accurate diagnosis between gastric metastasis from breast cancer and primary gastric cancer is of great importance, as breast cancer metastasis to the stomach usually requires systemic therapies rather than surgery [6]. However, it may be very difficult to make this distinction only by endo-

scopic, radiological and histopathological features [7, 8]. In this paper, we present a peculiar case of breast infiltrating ductal carcinoma (IDC) metastasis to stomach, helping to improve knowledge about this uncommon breast cancer metastasis. The patient provided written informed consent and this study was approved by the ethics committee of First Affiliated Hospital of Zhejiang University, Hangzhou, China.

Case report

Patient data

A 58-year-old woman who presented with vague epigastric pain, abdominal distention for ten days was admitted to our department (First Affiliated Hospital of Zhejiang University, China) in November 2014. Due to obvious gastric discomfort, the patient received gastric endoscopy, and the result revealed erosive lesions in the gastric body and antrum. The initial pathological and immunohistochemical analysis indicated a low-differentiated adenocarcinoma with positive expression of cytokeratin (CK) 7

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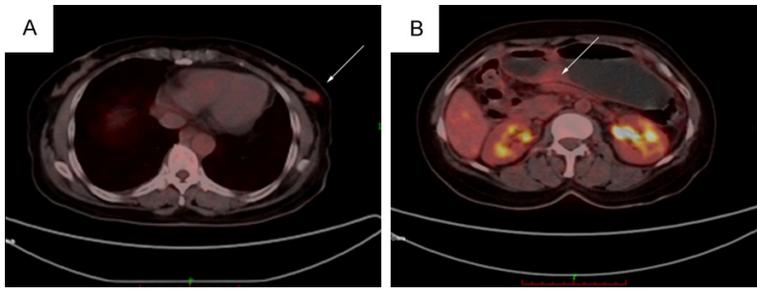


Figure 1. Positron emission-computed tomography (PET-CT) findings. PET-CT showed a 16×13 mm nodule in the lower outer quadrant of the left breast (A) and gastric wall thickening (B) with a significant 18F-fluorodeoxyglucose (FDG) uptake in December 2014.

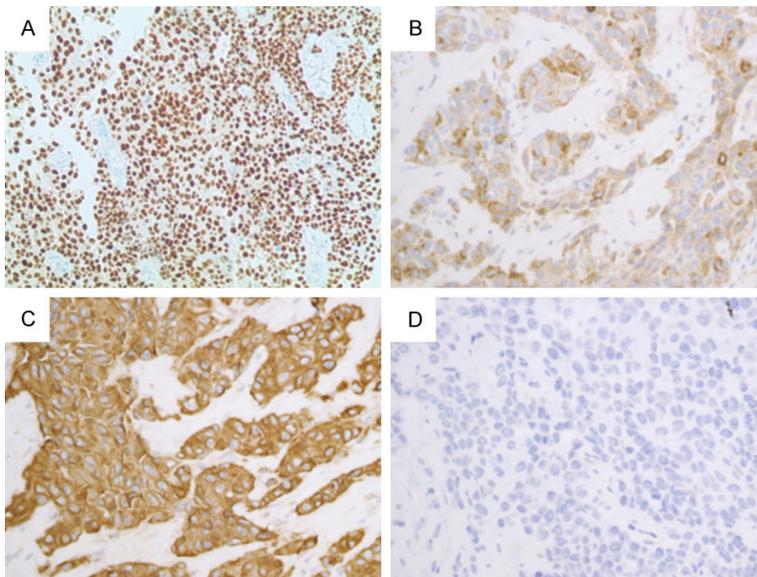


Figure 2. Immunohistochemistry (IHC) staining of breast specimen. IHC staining showed positive expression for (A) ER (magnification, ×100), (B) GCDFP-15 (magnification, ×400), (C) CK7 (magnification, ×400) and negative expression for (D) CK20 (magnification, ×400). ER, estrogen receptor; CK7, cytokeratin 7; CK20, cytokeratin 20; GCDFP-15, gross cystic disease fluid protein-15.

and negative expression of CD20, CD3 and human epithelial growth factor receptor type 2 (Her2). The abdominal computed tomography (CT) scan demonstrated gastric wall thickening, tumor involving serosal surface, multiple retroperitoneal lymph nodes and peritoneal metastases (cT4NxM1 stage IV). The initial diagnosis was mis-diagnosed as primary gastric cancer. Subsequently, PET-CT showed thickening in gastric wall, a 16×13 mm breast nodule in the lower outer quadrant of the left breast and multiple enlarged lymph nodes in the left axilla with a significant 18F-fluorodeoxyglucose (FDG) uptake (**Figure 1**). So, left breast tumor

biopsy was performed. The pathological and immunohistochemical analysis indicated an infiltrating ductal carcinoma with a result of positive expression of estrogen receptors (95%), progesterone receptors (65%), Her2 (2+), gross cystic disease fluid protein-15 (GCDFP-15), CK7 and negative expression of CK20 (**Figure 2**). Fluorescence in situ hybridization (FISH) showed Her2 was negative. In view of this special clinicopathological data, the previous gastric biopsy specimens were reappraised through immunohistochemical method and the result revealed positive expression for estrogen receptor (90%), GCDFP-15, CK7 and negative for CK20 and Her2 (**Figure 3**). This result was consistent with the findings of metastatic breast carcinoma. By comprehensive analysis of this patient's clinicopathological data, we confirmed the diagnosis of gastric metastasis from breast infiltrating ductal carcinoma (IDC).

Treatment procedures

After chemotherapy with 8 cycles of paclitaxel combined with epirubicin, the patient achieved partial response and the symptoms of abdominal discomfort was significantly relieved. Gastroscopy procedure exhibited that the lesions in the gastric body and antrum were significantly reduced. PET-CT revealed the breast nodule reduced and no aberrant FDG uptake of the gastric wall (**Figure 4**). The patient then received a single drug chemotherapy with capecitabine for four cycles until disease progression in September 2015. Subsequently, two cycles of paclitaxel combined with gemcitabine were administrated, demonstrating disease progress. Hence, chemotherapy was suspended and she received hormonal therapy with anastrozole. To date, the patient has sur-

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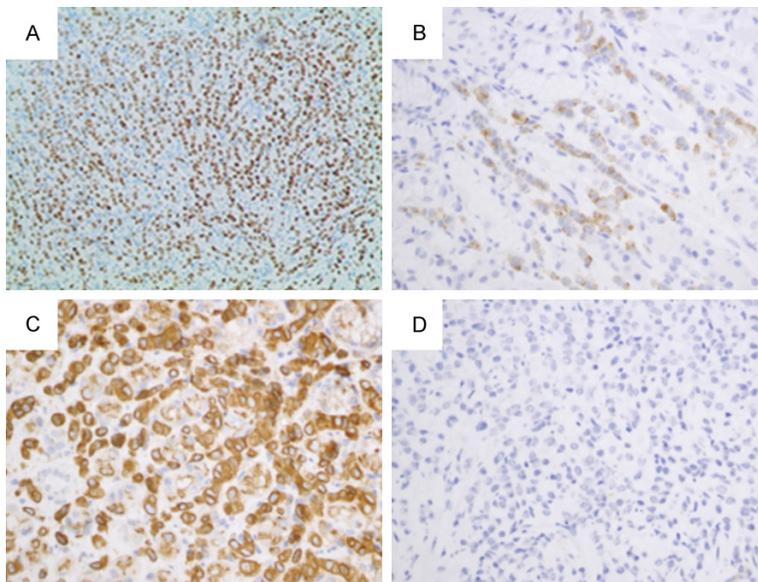


Figure 3. Review of immunohistochemical analysis of the previous pathological sections from the gastric lesions. IHC staining showed positive expression for (A) ER (magnification, $\times 100$), (B) GDCFP-15 (magnification, $\times 400$), (C) CK7 (magnification, $\times 400$), and negative expression for (D) CK20 (magnification, $\times 400$).

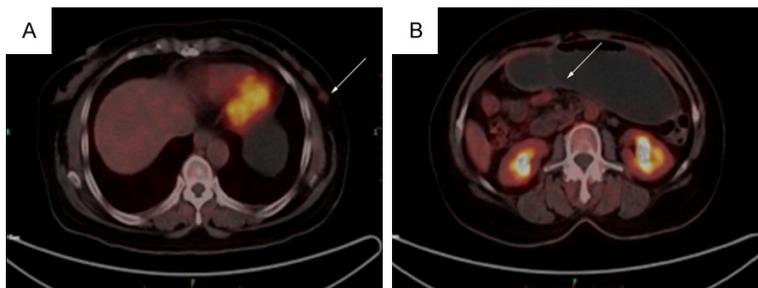


Figure 4. PET-CT findings after 8 cycles of first-line treatment. PET-CT revealed reduction of the left breast nodule (A) and no aberrant FDG uptake of the gastric wall (B) in June 2015.

vived for 20 months and has been receiving hormonal therapy.

Discussion

Gastric metastasis is relatively rare in patients with metastatic breast carcinoma and the incidence of gastric metastasis from breast carcinoma varies between 2 and 18% based on the investigation of long-time follow up and post mortem series [2, 7, 9]. Occurrence of gastric metastasis as the first symptom of breast carcinoma before presentation of the primary breast lesion is rarer, similar to the present case. Metastatic pathways of breast carcinoma

to the stomach are probably via hematogenous dissemination and lymphatic spread [2, 9, 10]. Firstly, breast carcinoma cells can be transferred through vessels directly into the stomach or involve the stomach via lymphatic ducts into vessels and finally metastasis to the stomach. Secondly, tumor cells can reach the stomach via lymphatic communicating branches between the internal mammary lymphatic duct and thoracic duct. In our case, given the patient's multiple enlarged lymph nodes in the left axilla, we speculated that the second approach may give rise to gastric metastasis. Previous studies have reported that the most common histological type of gastric metastasis from breast carcinoma is ILC rather than IDC. This finding was confirmed by Almuarak et al. who reported 35 cases of gastric metastasis from breast cancer, 97% of which were ILC, and only one patient was IDC [11]. According to Taal et al.'s study, ILC is the prime source of metastasis to stomach at the rate of 83% (20 of 24 cases), with the others being from IDC [2]. The reasons for different metastatic

patterns between ILC and IDC are still unclear. The loss of expression of E-cadherin, a cell-cell adhesion molecule in ILC, which is not observed in IDC, may account for this difference [12].

It is difficult to obtain an accurate diagnosis of gastric metastasis from breast carcinoma only depending on clinical, endoscopic, radiological and histopathological features [2, 3, 10]. Symptoms related to gastrointestinal manifestations often lack specificity such as nausea, vomiting, epigastric pain and anorexia, which also may result from primary gastric cancer, liver metastasis, drug-related gastric lesions or electrolytic disorders [2, 13]. CT scan of gastric

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metastasis from breast cancer generally presents gastric wall thickening, similar to primary gastric cancer [4]. Although endoscopic diagnosis is indispensable to be a part of the diagnostic examinations, it also may be disturbed by diffuse infiltration resembling benign hypertrophic gastritis or primary gastric carcinoma [2, 3, 10, 11]. According to Taal's study, there are three patterns of endoscopic features in metastatic gastric carcinoma: localized tumor presentation with ulceration or a polyp (18%); diffuse infiltration with linitis plastica (57%); and external compression (25%) [2]. The endoscopic features of IDC and ILC often showed various findings. In IDC, common endoscopic features were discrete nodules [14]. In ILC, endoscopic features often showed linitis plastica with diffuse infiltration under mucosa, which can present resembling primary gastric cancer or benign-appearing lesions such as gastritis, erosion or polyp [13]. As gastric tumor cells often spread in deep mucosal layer, endoscopic biopsies might be about 30% tumor negative [2]. Of note, deep and extensive endoscopic biopsies should be recommended to avoid the misdiagnosis.

Comprehensive immunohistochemical analysis may be the only optimal method to differentiate between gastric metastasis from breast carcinoma and primary gastric cancer. According to previous medical literature, metastatic breast carcinoma usually has positive expression for CK7, GCDFP-15, ER and progesterone receptor (PR), and negative expression for CK20 [6, 13]. However, it was demonstrated that up to 28% of primary gastric cancer may be ER positive, with a focal weak-to-moderate staining intensity [15, 16]. In our case, ER staining was strong and diffuse with ER (+++90%). When the primary breast carcinoma is negative for ER and PR, ER or PR expression is useless for diagnosing gastric metastasis from breast carcinoma [17]. CK20 and CK7 expression are also important markers. Generally, CK20 is positive in gastric, colorectal, pancreatic, and transitional cell carcinoma, while it is not usually observed in any kind of breast carcinoma [18]. In contrast, CK7 is expressed positively in 90% of breast carcinoma and also present in 50-64% of primary gastric adenocarcinoma [18, 19]. Furthermore, GCDFP-15 is confirmed to be of mammary origin that can be detected in breast cyst fluid and in the plasma of patients with

breast cancer [20, 21]. Wick MR et al. reported that the rates of specificity and sensitivity for GCDFP-15 were 95% and 74% to correctly identify metastatic carcinoma of the breast [20].

In our case, gastric endoscopy revealed erosive lesions with pathology of a low-differentiated adenocarcinoma. Subsequently, immunohistochemical analysis of pathological sections was reappraised for the accurate diagnosis. As the results were as follows: CK7 (+); CK20 (-); GCDFP15 (+); ER and PR (+); Her2 (-); and mammaglobin (+). So, pathologists easily diagnosed the specimens obtained from breast carcinoma.

To our knowledge, metastatic breast cancer has been deemed incurable, and the main goals of treatment are prolongation of survival and palliation of symptoms. The therapeutic recommendation for metastatic breast cancer is typically a systemic treatment (chemotherapy, biological therapy, hormonal therapy or combination of these) rather than loco-regional treatment (surgery, radiation therapy) [2, 7, 10, 11, 22]. A randomized controlled trial in India, comprising of 716 patients with metastatic breast cancer at initial diagnosis, suggested that loco-regional treatment of the primary tumor did not affect overall survival and this procedure should not be recommended for routine practice [22]. Likewise, surgical intervention of gastric tumor secondary from breast carcinoma should be reserved for palliation or certain cases of solitary resectable metastatic lesions [2, 3, 7]. In McLemore et al.'s series, palliative surgery (resection, GI bypass, and debulking of metastatic disease) for obstructive symptoms or mass effect failed to prolong overall survival [3]. Median overall survival of patients with gastric metastasis from breast carcinoma is 28 months, which is consistent with that of all females with secondary tumor from breast carcinoma, ranging from 24 to 36 months [3].

In accordance with other sites of metastatic breast carcinoma, gastric metastasis from breast cancer should be treated with a systemic treatment (chemotherapy, biological therapy, hormonal therapy or combination of these), which is based on symptoms, age, performance status, disease severity and previous systemic treatments. These therapies can lead to the median survival time ranging between 10

and 28 months [2, 3, 6]. Taal et al.'s series reported that the median survival was almost 2 years, and 22 percent of the patients survived for more than 2 years [2, 8].

Chemotherapy is routinely used as the first treatment option for women who experience multiple metastases or symptomatic visceral disease secondary to breast carcinoma [23]. The most effective anti-tumor drugs include the anthracyclines and the taxanes, followed by alkylating agents, antimetabolites, vinca alkaloids [24]. Trastuzumab (a monoclonal antibody to Her2/neu receptor) should be initiated as biological therapy for patients with Her2-positive breast carcinoma. Hormonal therapy is only given to the patient whose cancer positively expresses hormone receptors (estrogen or progesterone receptors). According to previous treatment modalities for metastatic breast cancer, the patient discussed in our case was treated with multi-line chemotherapy (Paclitaxel combined with epirubicin, capecitabine, paclitaxel combined with gemcitabine) and hormonal therapy (anastrozole). The patient avoided unnecessary surgery and has survived for 20 months until now.

This case is unlike the majority of previous reported cases for several reasons. First, the primary breast carcinoma was an IDC, which was recognized less possibility of metastasizing to stomach, compared with an ILC. Second, the breast lesion in this case was discovered after the diagnosis of secondary gastric tumor. Third, despite the patient's chief complaints that only revolved around gastric discomforts, the misdiagnosis was avoided, because a thorough examination was performed. Finally, the patient only received a systemic treatment (chemotherapy, hormonal therapy) without surgery.

Our goal in this case report is to increase the awareness of clinicians and pathologists about the possibility of gastric metastasis originating from breast IDC, although a rare occurrence. It is an inevitable choice to have a comprehensive histopathological and immunohistochemical analysis of the gastric biopsies to make an accurate diagnosis [7, 10, 13]. Appropriate systemic treatment (chemotherapy, biological therapy, hormonal therapy or combination of these) for gastric metastasis from breast carcinoma is the preferred choice.

Disclosure of conflict of interest

None.

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