De Novo Metastatic Invasive Lobular Breast Cancer with Synchronous Gastric and Colonic Spread: a case report

Ahmad Antar (✉ a.antar@almoosahospital.com.sa)  
Almoosa Specialist Hospital

Ahmad AlHajjar  
Almoosa Specialist Hospital

Mahfood AlQatari  
Almoosa Specialist Hospital

Nadim El-Majzoub  
American University of Beirut Medical Center

Case Report

Keywords: de novo Metastatic Invasive Lobular Breast Cancer, Synchronous gastric and colonic metastases, immunohistochemistry

Posted Date: May 17th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1638501/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Gastrointestinal metastasis from invasive lobular breast cancer (ILC) is relatively rare. Simultaneous gastric and colonic metastases are extremely rare. Its presentation is typically vague; therefore, early recognition using clinical, radiological, endoscopic and histopathologic investigations is critical to distinguish it from primary gastric carcinoma. We report a 62-year-old woman who presented initially with atypical gastrointestinal symptoms and was diagnosed with de novo metastatic ILC with synchronous gastric and colonic involvement. She had excellent clinical response after 4 weeks of medical treatment. To our best knowledge, this is the first case of synchronous spread to stomach and colon as the first presentation of de novo metastatic breast cancer.

Introduction

Breast cancer is the most frequently diagnosed malignancy and the leading cause of cancer-related death in women worldwide. The most common histologic types of epithelial breast carcinoma are invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC), accounting for 80% and 8% of invasive lesions, respectively [1]. The most common sites of metastasis from breast cancer are bone, lung, liver, and brain. Metastasis to the gastrointestinal tract (GI) is not common; it varies from 2–18% and is more common in lobular breast carcinoma than ductal carcinoma [2]. The differentiation between primary GI cancer and GI metastasis from the breast based on clinical, radiological, endoscopic and histopathologic findings is challenging. Here, we report a rare case of metastatic invasive lobular breast cancer associated with de novo synchronous gastric and colonic spread.

Case History

A 62-year-old female known to have hypertension, presented for a 3-months history of abdominal pain, significant unintentional weight loss, nausea, and vomiting. She was referred from another hospital with a computed tomography scan (CT) of abdomen and pelvis showing two hepatic focal lesions (3x2.9 cm and 2.5x2.7 cm), in addition, to multiple extensive sclerotic and lytic bone lesions. On physical exam, she had an obvious left breast mass in the upper inner quadrant of about 4x3 cm, with nipple retraction and skin dimpling; she also had multiple palpable left axillary lymph nodes. CT scan chest revealed a left breast parenchyma (upper inner quadrant) irregular soft tissue mass lesion measuring about 3.5x2.9x3.6 cm associated with multiple enlarged left axillary lymph nodes largest measuring about 1.2x1.6 cm with loss of its fatty hilum (Fig. 1A, 1B). She underwent an ultrasound guided core biopsy from the left breast mass that showed invasive mammary carcinoma, lobular type, immunohistochemistry (IHC) for estrogen receptor (ER) and progesterone receptor were 100% positive and Human Epidermal Growth Factor Receptor 2 (HER2) was negative, and E-cadherin was negative (Fig. 2). Serum cancer antigen 15 – 3 was 364 U/mL (normal reference range less than 30 U/mL). MRI brain showed no evidence of metastasis. The patient was referred to the gastroenterologist for the unexplained persistent nausea and vomiting. A gastroscopy was performed and showed large thick erythematous gastric folds extending to the antrum, hard to palpation to a closed biopsy forceps (Fig. 3). A screening colonoscopy was performed at the
same time and revealed mild localized erythematous swollen/thick mucosa in the ascending colon (Fig. 4). Biopsies from gastric antrum, gastric body and ascending colon were consistent with metastatic mammary lobular/signet ring carcinoma. IHC staining of metastasized tumor cells were positive for GATA3 and ER while negative for CK20 (Fig. 5). The patient was started on Aromatase inhibitor (Letrozole) and CDK5/6 inhibitor (Ribociclib) and bone-modifying agent (Denosumab); she had significant clinical improvement after 4 weeks of treatment.

**Discussion**

Breast cancer is the second commonest primary tumor responsible for gastrointestinal metastases after malignant melanoma [3]. Single gastric or colon metastasis from breast cancer have been previously described [4–6], but metastasis in both locations at the same time is extremely rare and only reported in a few case reports [8, 9], but to our knowledge, this is the first case of synchronous spread to stomach and colon as the first presentation of de novo metastatic breast cancer. The incidence of extrahepatic gastrointestinal tract metastasis in autopsy studies has been recognized in 4–18%, with the most affected organ being the stomach, followed by the colon and then rectum [10, 11]. GI metastasis has seen reported more frequently with ILC than IDC of the breast. In a study published by Mayo clinic [12], ILC accounts for 61% of breast cancer with GI metastasis. In another study, 83% of the primary breast cancers were confirmed as ILC [2]. The diagnosis of gastrointestinal metastasis secondary to breast cancer can be difficult and requires a high index of clinical suspicion. The clinical presentation is usually inexpressive and can vary from asymptomatic to non-specific symptoms, such as anorexia, weight loss, abdominal pain, nausea, vomiting and diarrhea [4, 13]. It could also be more severe causing GI bleeding, intestinal obstruction or perforation [14, 15]. In the present case, the main symptoms were nausea, vomiting and abdominal pain resulting from gastric involvement. CT scan and ultrasound abdomen can easily miss the gastric and colonic involvement like in our case or can show features like the primary carcinoma such as marked thickness of the gastric or bowel wall [2]. The endoscopic pattern of gastric metastasis is usually confounded with primary gastric cancer. It generally presents with diffuse gastric wall infiltration, which resembles linitis plastica and mostly spreads to the seromuscular and submucosal layers, whereas it is rarely accompanied by separated nodules [16, 17]. Furthermore, endoscopic biopsy may present as normal in 50% of the cases and this is attributed to the submucosal distribution of the tumor [18]. Colonic metastasis could also imitate primary colon malignancy and may acquire a similar pattern of linitis plastic or Crohn's disease and may uncommonly present as an obstructing mass or polyp [7, 19]. In our case the colonic involvement could be easily missed because of the subtle nonspecific changes that were noted at the involved segment of the colon but the initiative to take biopsies for this nonspecific suspicious abnormality in this patient was the presence of her known primary breast cancer and this is what led to the detection of this rare simultaneous upper and lower GI breast cancer metastasis. Therefore, it's very important to keep in mind the possibility of GI breast cancer metastasis, to look carefully for any mucosal abnormality that could be subtle and non-specific and to have a low threshold to take biopsies from any abnormal mucosal changes in similar patients.
The final diagnosis of GI metastatic tumor from breast cancer requires an accurate histological examination including a thorough disease-specific immunohistochemical analysis. IHC for estrogen receptor is the most influential and sensitive marker used to differentiate metastatic breast cancer [20]. In addition, IHC staining of GATA3 is highly specific and sensitive for breast cancer. Other IHC such as mammaglobin and gross cystic disease fluid protein-15 (GCDFP-15) are also breast specific, but less sensitive than GATA3 [20, 21]. In our patient GATA3 and ER stains were positive both in gastric and colonic metastatic lesions.

The prognosis of metastatic breast cancer to the GI tract is dismal. One retrospective study of 73 patients reported a median overall survival of 28 months [12]. Treatment mainly consists of systemic medical therapy with chemotherapy, endocrine therapy or/and targeted therapy based on the hormonal receptor and HER2 status of the tumor, the patient performance status, and the extension of disease. Gastrectomy does not have an impact on survival, and surgical palliation is only reserved for those with obstruction or mass effect [12]. We started our patient on hormonal therapy (Aromatase inhibitor) and CDK4/6 inhibitor (Ribociclib) and bone health therapy (denosumab). She had excellent long-lasting response to treatment after 10 months follow up.

**Conclusion**

To our knowledge, this is the first reported case of a patient with concurrent gastric and colonic metastasis as first presentation of invasive lobular carcinoma of the breast. GI metastasis due to breast cancer has a typically vague presentation, and it's difficult to distinguish it from primary gastric or colonic carcinoma. We emphasize on the early recognition of these cases and the performance of necessary investigations, including CT imaging, endoscopy and pathological/IHC examinations to make an accurate diagnosis. Systemic treatment based on tumor biomarkers is likely to be palliative and could benefit the survival of patients.

**Methods**

Written informed patient consent was obtained for publication of the information contained in this case report.

**Declarations**

**Data Availability:**

No datasets were generated or analyzed during the current study.

**Competing Interests:**

This case report is original and has not been submitted to any other journal. All authors on this paper do not have any conflicts of interest to disclose.
Authors’ Contribution:

AA, AAH, MAQ, and NEM contributed to data collection, interpretation, literature searching, manuscript drafting, and critical review of the manuscript. All authors approved the final manuscript draft.

Financial support or competing interests:

The authors disclose no conflicts of interest.

References


Figures

Figure 1

CT scan chest shows left breast irregular mass (A) with left axillary lymph node metastasis (B).
Figure 2

Images of H&E stain show infiltration of breast tissue by invasive lobular carcinoma. The tumor cells are round, poorly cohesive and showing a single-file growth pattern. Signet ring cells are present and characterized by the presence of a prominent intracytoplasmic mucin droplet with an enlarged eccentric nucleus.

Figure 3
Endoscopic view of the gastric cavity of our patient: The yellow arrow is pointed in the direction of the Pylorus. We can clearly see very thick gastric folds extending into the antrum.

**Figure 4**

Endoscopic view of her ascending colon: The black arrows delineate an irregular thick colonic mucosa that does not show the normal mucosal vascular pattern which is clearly visible in the adjacent healthy mucosa.

![Figure 4](image)

**Figure 5**

Image of H&E stain shows infiltration of gastric mucosa by signet ring cell carcinoma (A). The tumor cells are positive for GATA3 (B), and ER (C) and negative for CK20 (D).