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When Breast Cancer Masquerades as Gastric Cancer : Gastric Metastasis from Invasive Lobular Carcinoma

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Abstract

Gastric metastasis from breast carcinoma is rare and poses a substantial diagnostic difficulty since it closely mimics primary diffuse-type gastric adenocarcinoma on histo-morphology. We report a 43-year-old premenopausal woman who presented with dysphagia, loss of appetite, loss of weight, melaena, and anaemia. Oesophago-gastroduodenal endoscopy revealed an ulcerated gastric lesion involving both greater and lesser curvatures, and biopsy showed poorly cohesive adenocarcinoma. Cross-sectional imaging demonstrated diffuse gastric wall thickening with bilateral ovarian masses, nodal deposits, peritoneal disease, bilateral multiple breast lesions, axillary lymph nodes and widespread skeletal metastases, a pattern strongly suggestive of advanced gastric malignancy, leading to an initial diagnosis of primary gastric cancer. She was commenced on FLOT (Fluorouracil, Leucovorin, Oxaliplatin, and Docetaxel) chemotherapy. Subsequent biopsy of a right breast lesion revealed oestrogen and progesterone receptor– positive, HER2-negative invasive lobular carcinoma. Further immunohistochemical studies confirmed the gastric lesion to be metastatic than a gastric primary. The diagnosis was revised to metastatic breast carcinoma, and treatment was changed to CDK4/6 inhibitor in combination with an aromatase inhibitor, resulting in significant clinical improvement. This case highlights the importance of a high index of suspicion of primary breast cancer in a female when imaging favors metastatic deposits along with clinicopathological and immunohistochemical correlation in evaluating poorly differentiated likely metastatic gastric carcinoma with deposits in the breast.

Keywords: Gastric metastasis; Immunohistochemistry; Metastatic Breast Carcinoma.

Introduction

Gastric involvement by metastatic breast carcinoma is an uncommon clinical entity and is frequently indistinguishable from primary gastric malignancy. Autopsy studies have reported gastrointestinal metastases in 6–18% of patients with metastatic breast cancer, with the stomach being the most involved gastrointestinal organ (Arrangoiz et al., 2011).

Among breast cancer subtypes, invasive lobular carcinoma (ILC) exhibits distinct biological behavior and a characteristic metastatic pattern, with a predilection for the gastrointestinal tract, peritoneum, ovaries, uterus, and leptomeninges (Arrangoiz et al., 2011; Kioleoglou et al., 2024). Gastric metastases from ILC often mimic primary diffuse-type gastric adenocarcinoma clinically, radiologically, endoscopically, and histologically. Patients commonly present with nonspecific gastrointestinal symptoms, and endoscopic biopsies may demonstrate poorly cohesive or signetring-like cells that are difficult to distinguish from primary gastric carcinoma (Doria et al., 2015; Khan et al., 2017). Owing to its diffuse infiltrative growth and lack of mass formation, both the primary ILC and metastatic deposits may be subtle, resulting in diagnostic delay. Failure to recognize this entity may lead to inappropriate chemotherapy or unnecessary surgical intervention (Arrangoiz et al., 2011; Woo et al., 2018).

We describe a case of metastatic invasive lobular breast carcinoma initially misdiagnosed and treated as primary gastric cancer, highlighting the diagnostic pitfalls and therapeutic implications.

Case Presentation

A 43-year-old premenopausal woman, mother of three, with a background of type 2 diabetes mellitus and hypertension, presented with a three-month history of progressive dysphagia, loss of appetite, significant weight loss, intermittent low-grade fever, melaena, and fatigue. She had no prior history of breast disease and no significant family history of malignancy. On general examination, she was pale, not icteric, with no palpable supraclavicular lymph nodes. A firm lump measuring 1x2 cm was noted in the right breast. Abdominal examination was unremarkable.

Oesophago-gastroduodenal endoscopy demonstrated a malignant-appearing ulcerated growth involving both the greater and lesser curvatures of the stomach. Histological examination of endoscopic biopsies revealed a poorly differentiated, poorly cohesive adenocarcinoma with signet-ring-like cells, leading to a diagnosis of primary gastric carcinoma (Figure 1).

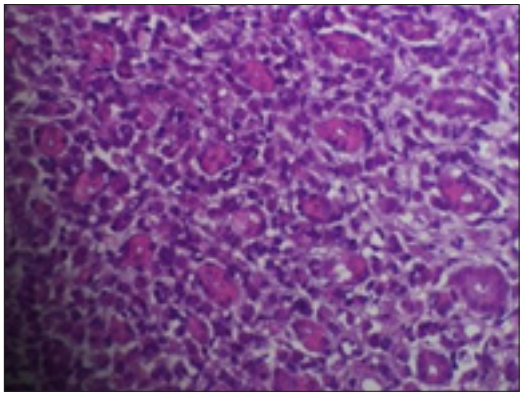

Figure 1: Singly scattered malignant cells in gastric lesion (Hematoxylin and Eosin stain)

A staging contrast-enhanced computed tomography of the chest, abdomen, and pelvis demonstrated diffuse gastric wall thickening with perigastric and coeliac lymphadenopathy. There was bilateral ovarian enlargement with solid components suggestive of Kruckenberg tumors together with mesenteric and omental nodularity, mild to moderate ascites, and diffuse sclerotic skeletal metastases. Additional findings included multiple pulmonary nodules with bilateral pleural effusions, bilateral axillary lymphadenopathy, and small bilateral breast lesions, more prominent in the right breast, which were initially interpreted as metastatic deposits in the context of disseminated disease. There was no evidence of hepatic metastasis. Overall, the imaging findings favored advanced primary gastric carcinoma with widespread metastatic involvement.

Though the multiple nodules in the breasts favoured metastatic deposits rather than a primary breast cancer, a biopsy of the breast lesion was performed before the initiation of FLOT (Fluorouracil, Leucovorin, Oxaliplatin, and Docetaxel) chemotherapy for gastric cancer. The tolerance to chemotherapy was poor, with no clinical improvement. Subsequently, histology of the breast lesion revealed a poorly differentiated carcinoma (Figure 2). Immunohistochemical analysis showed strong estrogen and progesterone receptor positivity with HER2 negativity, findings consistent with invasive lobular carcinoma of the breast (Figure 3). Further immunohistochemical analysis of the gastric biopsy demonstrated oestrogen and progesterone receptor positivity (Figure 4), consistent with the immunophenotype of breast lesion, and favouring a diagnosis of metastatic breast carcinoma over a synchronous primary gastric carcinoma.

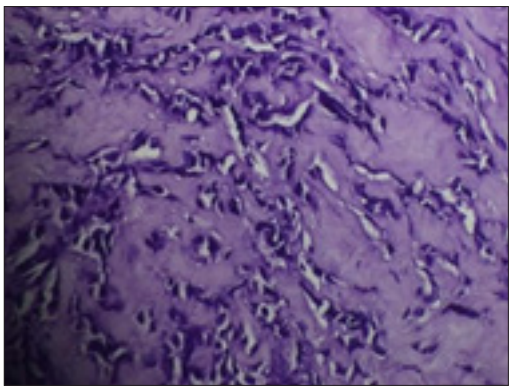

Figure 2: Cords of malignant cells in breast lesion (Hematoxylin and Eosin stain)

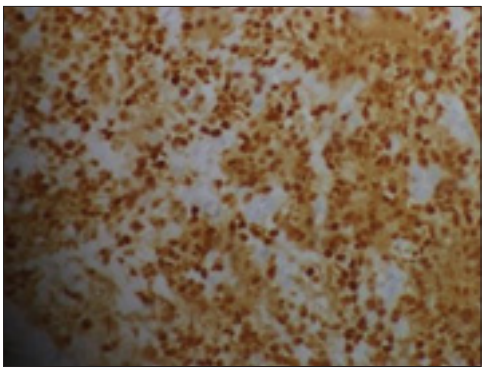

Figure 3: Positive oestrogen receptor (ER) IHC in breast lesion

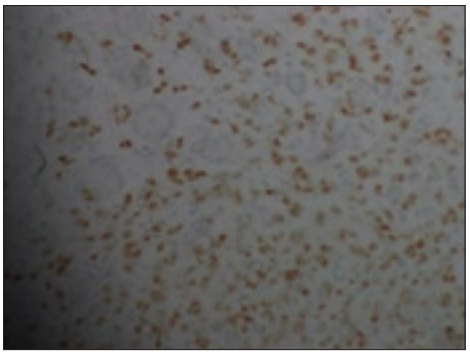

Figure 4: Positive oestrogen receptor (ER) IHC in gastric lesion

Following revision of the diagnosis, FLOT chemotherapy was discontinued after the 2nd cycle, and systemic therapy was changed to Palbociclib, a CDK4/6 inhibitor in combination with an aromatase inhibitor- Anastrozole. Initiation of appropriate therapy led to marked clinical improvement. At her most recent follow-up, eight months after commencement of Palbociclib, she was clinically stable, was fully ambulatory, independent in activities of daily living, and had resumed her full-time work. The CT scan done to assess response revealed a significant therapeutic response, with complete resolution of the previously documented gastric wall thickening and ascites, with no radiological evidence of residual gastric metastasis. Diffuse bony metastases remained present but without new visceral involvement.

Discussion

This case illustrates a recognized but frequently overlooked diagnostic pitfall: metastatic invasive lobular carcinoma of the breast masquerading as primary gastric cancer. In this patient, the combination of dominant gastrointestinal symptoms, diffuse gastric wall thickening, bilateral ovarian masses, peritoneal involvement, multiple bilateral breast lesions and a poorly cohesive gastric adenocarcinoma created a compelling but misleading picture of advanced primary gastric malignancy (Doria et al., 2015; Woo et al., 2018; Zhang et al., 2021). However, this constellation of findings is also well described in metastatic ILC (Arrangoiz et al., 2011; Kioleoglou et al., 2024; Xu et al., 2017).

The distinct biological behavior of ILC provides a mechanistic explanation for this presentation. Loss of E-cadherin expression in ILC results in reduced intercellular adhesion, allowing tumour cells to infiltrate tissues diffusely rather than forming discrete masses (Kioleoglou et al., 2024).

Consequently, primary breast lesions may be small or clinically occult, while metastatic disease is extensive. In the stomach, metastatic ILC infiltrates the mucosa and submucosa in a diffuse pattern, often producing signet-ring-like cells that closely resemble diffuse-type gastric adenocarcinoma on routine histology (Doria et al., 2015; Zhang et al., 2021).

Radiological and endoscopic findings are similarly nonspecific. Gastric metastases from a breast carcinoma may present as linitis-plastica-like thickening, ulcerative lesions, polypoid masses, or even normal mucosa, making distinction from primary gastric malignancy difficult (Doria et al., 2015; Woo et al., 2018). These overlapping features commonly lead to anchoring bias and delayed consideration of alternative primary sites, particularly in patients without a known history of breast cancer.

Immunohistochemistry is therefore pivotal in resolving this diagnostic dilemma. Most gastric metastases from breast carcinoma are oestrogen and progesterone receptor positive and HER2 negative (Kioleoglou et al., 2024; Xu et al., 2017). Although hormone receptor expression may occasionally be observed in primary gastric adenocarcinoma, interpretation of immunohistochemical findings within the appropriate clinicopathological and radiological context strongly favours a breast origin (Kioleoglou et al., 2024; Li et al., 2022; Woo et al., 2018). In this patient, recognition of the hormone receptor profile in gastric histology prompted revision of the diagnosis and initiation of appropriate systemic therapy.

An important differential consideration in cases where diffuse-type gastric carcinoma and invasive lobular breast carcinoma coexist is Hereditary Diffuse Gastric Cancer (HDGC) syndrome, an autosomal dominant cancer syndrome associated with germline CDH1 mutations. Patients with HDGC may develop synchronous or metachronous diffuse gastric carcinoma and lobular breast carcinoma, which can confound the distinction between metastatic disease and multiple primary malignancies. In the present case, concordant hormone receptor positivity in both the gastric and breast biopsies supported metastatic breast carcinoma rather than synchronous primary tumors (Blair et al., 2020).

Correct identification of tumour origin has major therapeutic implications. Metastatic breast carcinoma with receptor positivity and Her-2 negativity involving the gastrointestinal tract is best managed with systemic therapy, particularly endocrine therapy combined with kinase inhibitor, rather than conventional chemotherapy or surgery (Kioleoglou et al., 2024; Xu et al., 2017). In the present case, discontinuation of inappropriate chemotherapy and initiation of endocrinebased combination therapy resulted in clinical stabilization.

High index of suspicion and appropriate immunohistochemical evaluation should be considered in female patients presenting with poorly differentiated gastric adenocarcinoma, and particularly in a female with clinical and radiological findings suggestive of breast metastasis. Early identification of a breast primary using targeted immunohistochemistry can help avoid unnecessary staging laparoscopic procedures, reduce the risk of adverse clinical outcomes and inappropriate chemotherapy-related toxicity, and prevent unnecessary use of limited healthcare resources.

Conclusion

Metastatic invasive lobular carcinoma of the breast should be considered in the differential diagnosis of poorly differentiated or signet-ring gastric adenocarcinoma in women, even when the breast lesions favour metastasis than a primary. It is vital to have a suspicion index for other diagnoses, particularly when a patient is not responding well to a particular treatment. To prevent incorrect diagnosis and guarantee proper treatment, early application of immunohistochemistry and cautious clinicopathological correlation are crucial.

Patient Consent

Informed written consent was obtained from the patient for the publication of this case report.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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