



## Metastatic Breast Cancer First Presenting as a Primary Gastric Carcinoma

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### Abstract

Breast cancer is the most common cancer in women. Metastatic disease involvement of the stomach is usually a manifestation of advanced disease. Isolated metastatic involvement of the stomach from a primary breast lesion is rare. These lesions can mimic primary gastric carcinoma and can be hard to distinguish due to very similar clinical, endoscopic and histological features. The authors here describe a case of a 70-year-old woman who was admitted with anemia and weight loss. An oesophagogastroduodenoscopy identified a mass in the stomach and biopsies were consistent with upper gastrointestinal adenocarcinoma. However, a subsequent staging computational tomography showed a right breast lesion and immunostaining of the gastric biopsies were consistent with a breast metastasis. This is a rare case of metastatic breast cancer presenting with gastrointestinal tract symptoms and highlights the importance of considering breast cancer as the primary origin for any gastric malignancy.

**Keywords:** Breast carcinoma; Metastasis; Gastric neoplasm; Endoscopy; Linitis plastica

### Introduction

Breast cancer is the most common cancer in women and the second most common cause of cancer-related mortality [1]. Commonly, breast cancer metastasizes to bone, liver and lung. The gastrointestinal tract (GIT) however is a rare site for metastasis [2,3]. GIT metastasis from breast cancer usually manifests as a character of advanced stage disease. Moreover they are typically identified after a well-established diagnosis and treatment of the primary breast tumor [4]. The incidence of isolated GIT metastasis is very low. Furthermore, it is extremely rare to identify isolated GIT metastasis without a known or clinically evident primary breast cancer [4]. After a period of remission, breast cancer has been known to relapse to the GIT and can mimic that of a primary GIT malignancy in its initial presentation [5]. Breast metastasis to the GIT may fool the clinician in their oesophagogastroduodenoscopy (OGD), radiological, histological and immunohistochemical (IHC) appearance. As metastatic breast cancer is usually treated systemically rather than surgically, this stresses the importance of ensuring the diagnosis of a gastric lesion is entirely accurate [6]. Here, the authors describe a case whereby the initial presentation and investigations strongly suggested a diagnosis of a primary gastric carcinoma. However, further management revealed breast cancer primary with the gastric lesion being that of a metastasis. This is a rare case where, unlike other reports, the patient had no previous breast cancer history prior to presentation with their GIT symptoms. Atypically, the primary breast cancer and GIT metastasis presented synchronously.

### Case Presentation

#### Clinical findings

An independent and active 70-year-old woman presented to her General Practitioner (GP) with a 6 month history of dyspepsia and progressive unintentional weight loss of 6 kg. She was found to have a drop in hemoglobin from 10.0 g/dL to 8.3 g/dL (mean cell volume 100.7 fL).

She was referred for an urgent outpatient OGD which showed a non-bleeding infiltrative gastric neoplasm in the stomach gastric body. The lesion had thick folds and stiff texture (Figure 1). The gross morphology was reported as that of linitis plastica. Eight gastric biopsies were taken which confirmed a necrotic infiltrating adenocarcinoma of poorly differentiated invasive intestinal type (Figure 2). Focal glandular differentiation was appreciated with a few signet ring cells and staining for *Helicobacter pylori* was negative. An urgent outpatient staging computational tomography (CT) was organized. At this stage, the working diagnosis of both the gastroenterologist and histopathologist was one of a primary gastric adenocarcinoma and the patient was counseled with this differential.

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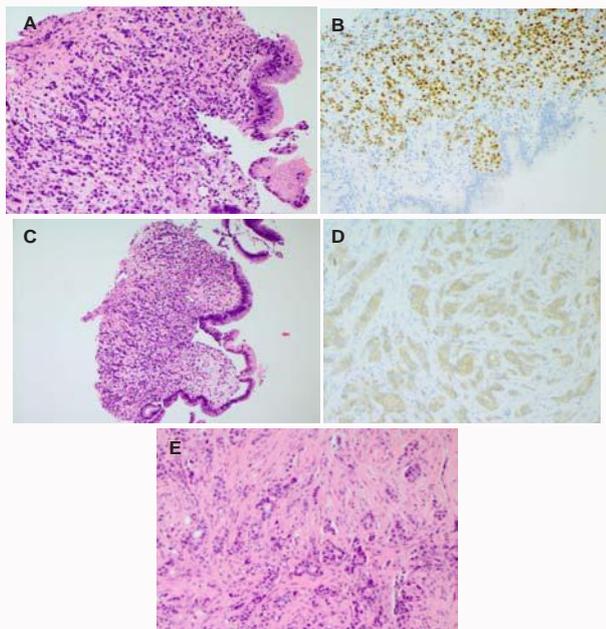
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**Figure 1:** Oesophagogastroduodenoscopy (OGD) view of the gastric body.

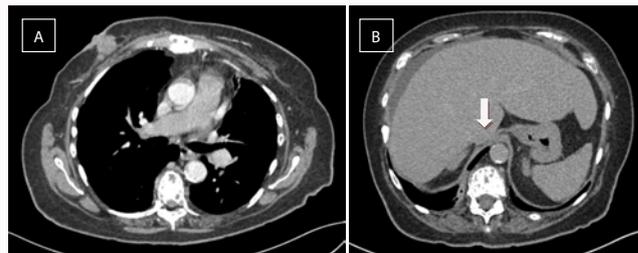


**Figure 2:** A) High power view of gastric biopsy showing tumour cells in the lamina propria with an 'Indian file' pattern. H & E. Magnification X200. B) ER immunostain showing strong positivity in tumour cells. Magnification X200. C) Low power view of gastric biopsy showing metastatic lobular carcinoma comprising of tumour cells in the lamina propria with an 'Indian file' pattern. H & E. Magnification X100. D) Infiltrating ductal carcinoma of breast. H & E. Magnification X200. E) E-cadherin immunostain showing diffuse membrane positivity confirming infiltrating ductal carcinoma of breast. Magnification X200.

Staging CT showed a spiculated mass in the right breast in the sub-areolar region measuring 2.3 cm (Figure 3). Abnormal lymphadenopathy was seen in the right axilla; the largest lymph node measuring 1.3 cm with smaller lymph nodes showing abnormal morphology. The wall of the stomach was thickened but had no dilatation (Figure 3, arrow).

IHC stains of the gastric body biopsies showed positivity for gross cystic disease fluid protein-15 (GCDFP-15), cytokeratin-19 (CK-19), human milk fat globule antigen-2 (HMFG-2), estrogen receptor (ER) and cytokeratin-7 (CK-7). The gastric lesion was negative for cytokeratin-20 (CK-20) and human milk fat globule antigen-1 (HMFG-1). IHC features revised the diagnosis to that of a metastasis from the breast rather than a gastric primary (Figure 2).

In the rapid access breast clinic, mammography and ultrasound showed a 19 mm × 21 mm mass with small axillary node. Core biopsies showed grade 2 (tubules 3, nuclei 2, mitoses 1) invasive non special type (NST) carcinoma, negative for HER2 gene but ER



**Figure 3:** CT scan of thorax and abdomen: (A) Mass seen in the right breast in the sub-areolar region measuring 2.3 cm. (B) Thickened stomach wall (arrow).

positive (Figure 2). The IHC profile was GCDFP-15, CK19, HMFG-2, ER, CK7 and E-cadherin positive but negative for CK20, HMFG-1 and CK14. Apart from the E-cadherin positivity in the breast biopsy, the IHC profile was identical to that of the neoplasm in the gastric biopsy.

She was commenced on palliative treatment of letrozole and dexamethasone and remains under oncology follow up, with good analgesic control.

## Discussion

Breast cancer is a leading cause of death in women aged 20-59 [7-9]. The incidence of isolated associated metastatic GIT disease is variable with post mortem studies approximating the incidence as 0.3% to 2% [6,10,11]. GIT metastasis from breast cancer usually manifests as a character of advanced stage disease, typically found after a diagnosis of the primary breast tumor. It is extremely rare to identify isolated GIT metastasis without a known or clinically evident primary breast cancer [4]. Here, the patient had no known personal or family history of breast cancer, with this being her first presentation of a malignant process. Rarely, case reports exist of a stomach lesion being the first presentation of metastatic breast cancer [12]. Synchronous presentation of breast cancer and metastatic GIT disease is rarely documented in the literature [4,13]. Ciulla et al. [12] describe a presentation of generic dyspeptic symptoms and weight loss. Routine histological and IHC analyses of OGD biopsies led to a diagnosis of a gastric carcinoma. The patient underwent a total gastrectomy following no evidence of metastatic disease on a CT scan. However, histological and IHC analyses of the resected gastric tissue revealed features in keeping with breast cancer metastasis. On confirming lobular carcinoma of the breast, the patient was started on postoperative hormone therapy, but died 10 months later [12]. Although all the clinical symptoms and preliminary investigations indicated a primary gastric carcinoma, warranting surgical treatment, further analysis of the gastric specimens to exclude breast pathology may have altered the treatment plan towards more systemic therapy.

Median interval between breast cancer diagnosis and GIT metastatic involvement usually varies from a few months to many years [14,15]. A review of the literature identifies multiple cases of patients with a previous well-established history of breast cancer who subsequently present with a GIT metastasis [5,16,17]. Nazareno et al. [5] describe 6 cases of GIT breast metastasis following treated breast cancer with a wide range of remission periods (2-20 years). The common "disease-free" period interval between initial breast cancer presentation and subsequent GIT involvement can make diagnosis of metastatic breast cancer disease a challenge.

As with a primary gastric carcinoma, symptoms of a gastric breast metastasis are variable and may be non-specific. Symptoms can include dyspepsia, anorexia, epigastric pain and early satiety [9,18]. The patient described here presented to her GP with a number of 'red flag' signs and symptoms (age >55, weight loss, anemia and new dyspepsia) that warranted an urgent OGD to investigate a possible upper GIT malignancy. Thus the difference in clinical presentation of GIT breast cancer metastasis and primary gastric carcinoma may be indistinguishable.

The typical endoscopic appearance of breast cancer GIT metastasis resembles linitis plastica [19]. As in our case, the stomach usually appears diffusely thickened as a result of infiltration of the submucosa and muscularis propria [14]. The presence of signet rings cells were visualized in the gastric biopsies supported the histological evidence of a primary adenocarcinoma. It has been shown that lobular carcinoma of the breast may produce a signet ring morphology which can mimic other primary tumors, including GIT neoplasms, making them histologically indistinguishable [15]. It is thus important to be aware of this overlap in cytomorphological features [16,20]. Furthermore, it has been noted that endoscopic biopsies may be false-negative for malignancy, partly due to the inability to access the tumor cells, localized only in the deeper tissue layers [6,21].

It is well established that IHC is of great importance when attempting to accurately define the exact tumor type. In previous cases of metastatic breast cancer to the GIT, IHC has been the only method for making a clear diagnosis [16]. It is worth noting that the accuracy with the use of GCDFP-15 marker in IHC is variable. In terms of sensitivity and specificity this is 55% to 76% and 95% to 100%, respectively [22,23]. As with our case, metastatic breast carcinomas usually show positivity for GCDFP-15, CK-7, ER and negativity for CK-20, which are the common markers used for diagnosis [24,25]. Breast cancer can also be positive for progesterone (PR) receptors [18], though this has been shown not to be pathognomonic [26]. CK-20 is particularly positive in GIT carcinomas [27].

Histology in our case was consistent with a metastatic lobular breast carcinoma. The incidence of invasive lobular breast carcinoma (ILC) is less common than that of invasive ductal carcinomas (IDC). However its incidence is increasing, and in addition, ILC has a higher incidence of metastasizing to the GIT than IDC [28]. Therefore, in future, this unusual presentation of breast metastatic disease to the GIT may be more frequently recognized.

Prognosis is strongly associated with the presence of hormonal receptors, tumor grade and size, the evidence of lymph node involvement and demonstration of metastatic disease [18]. As with other breast metastatic sites, gastric lesions are responsive to systemic therapy (chemotherapy and/or hormonal therapy), thus negating the need for surgery. However, primary gastric neoplasms may be treated directly with surgery. This adds weight to ensuring the diagnosis of a lesion is entirely accurate to ensure the most appropriate management. It is argued that surgery may have a therapeutic role in patients with isolated metastasis [29], however this should be reserved for tumors causing obstructive symptoms, emergencies or palliation and seldom has an impact on improving prognosis [15,19].

Our rare case is of interest for two reasons, both of which have salient points. Unlike many other published cases with an established breast cancer diagnosis, here the GIT symptoms preceded the presentation of breast cancer. Furthermore, the diagnosis of metastatic gastric disease was made synchronously to that of the

primary breast cancer, without the usual time interval often observed between the two presentations. This reinforces the consideration of metastatic breast cancer as a differential in patients with GIT lesions, which in turn would have a significant impact on the patient's subsequent management.

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