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# Breast Cancer Metastasis Masquerading as Primary Colon and Gastric Cancer: A Case Report

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Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
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**Conflict of interest:** None declared

**Patient:** Female, 68-year-old  
**Final Diagnosis:** Metastatic breast cancer  
**Symptoms:** Abdominal pain • constipation • vomiting  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Oncology

**Objective:** Unusual clinical course

**Background:** Breast cancer is the most common malignancy in women worldwide. Despite treatment, recurrence and metastasis are common. Lobular breast cancer most commonly metastasizes to the lungs, liver, lymph nodes, and sites in the brain. Metastasis to the gastrointestinal tract is rare, with few cases reported to date.

**Case Report:** This report describes a patient with late colon and gastric metastases from lobular breast cancer mimicking primary colon and gastric cancers.

**Conclusions:** Immunohistochemical methods can help differentiate metastatic breast disease to the gastrointestinal tract from primary gastrointestinal malignancy.

**MeSH Keywords:** Breast Neoplasms • Colonic Neoplasms • Neoplasm Metastasis • Stomach Neoplasms

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## Background

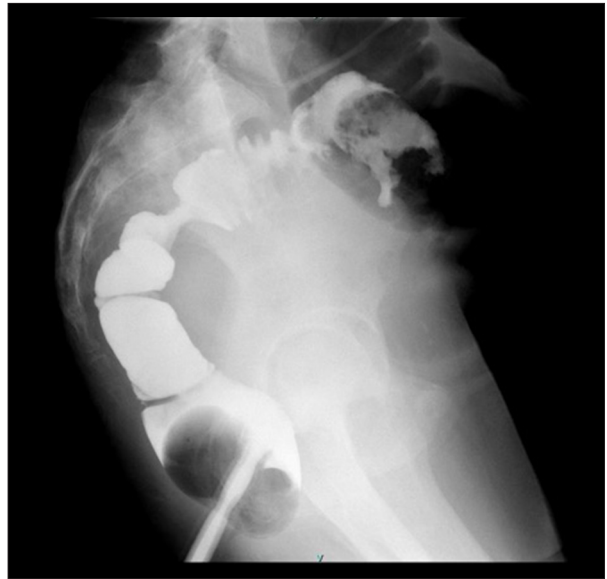
The objective herein is to describe a case of a woman with late gastrointestinal (GI) metastases from breast cancer, that mimicked primary colon and gastric cancer based on clinical presentation as well as imaging characteristics.

Breast cancer is the most common malignancy in women worldwide. It has been estimated that 1 in 8 women in the USA will develop invasive breast cancer throughout their lifetime [1]. Infiltrating lobular breast cancer (ILBC) represents 8% to 14% of all breast cancers [2]. Treatment typically consists of surgical resection followed by adjuvant chemo-radiotherapy along with systemic hormonal treatment [3]. Despite treatment, recurrence and metastasis are common. The most frequent sites for metastasis of ILBC include lungs, liver, lymph nodes, and brain [4]. However, the exact metastatic pattern of ILBC is not well known and atypical sites might be more common than expected. Primary GI tumors, non-Hodgkin's lymphoma, and ILBC metastasis share clinical and imaging characteristics, making it challenging to differentiate the precise type of malignancy. Immunohistochemical (IHC) markers are key in establishing a diagnosis, as these results will impact management options [5].

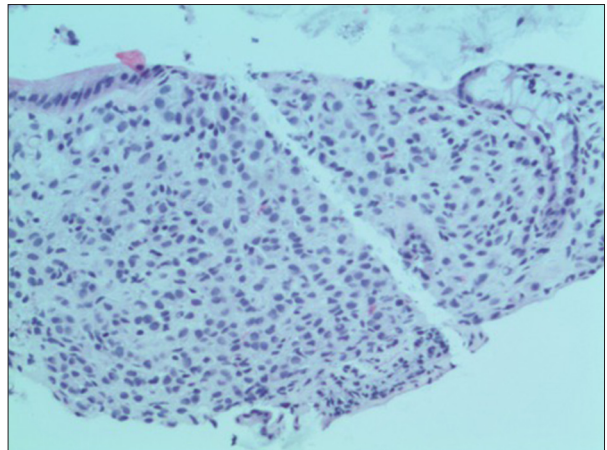
## Case Report

A 68-year-old female with a history of recurrent invasive lobular breast cancer, positive for estrogen receptor (ER) and progesterone receptor (PR), and negative for Her2/neu, who underwent bilateral mastectomy, followed by adjuvant chemo-radiotherapy and hormonal therapy, presented 27 years later with bone metastasis. She had been treated with anastrozole, letrozole, exemestane, and fulvestrant, and most recently, she was being treated with fulvestrant and palbociclib until year 30, when she presented with progressively worsening nausea, vomiting, abdominal pain, and refractory constipation. Physical examination revealed abdominal distension and tenderness. Laboratory results showed chronic anemia (hemoglobin, 9.8 g/dL) and mild elevation in liver function tests; etiology or significance of which was initially not known. Further evaluation by abdominal x-ray showed proximal large bowel obstruction, but no evidence of pneumoperitoneum. Subsequent gastrografin enema showed a focal, luminal narrowing "apple core" lesion in the sigmoid colon suggestive of primary colon cancer (Figure 1).

A computed tomography (CT) scan of the abdomen confirmed the large bowel obstruction, with a transition point within the distal sigmoid colon. Circumferential narrowing and mucosal thickening were observed at the transition point, thought to be due to an annular carcinoma. Surgical resection of the

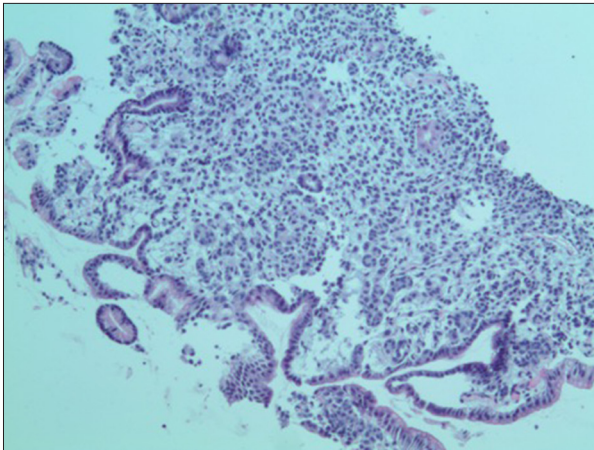


**Figure 1.** Gastrografin enema revealing limited and edema demonstrates opacification of the rectum and distal sigmoid with a short segment fixed moderate luminal narrowing near the rectosigmoid junction.

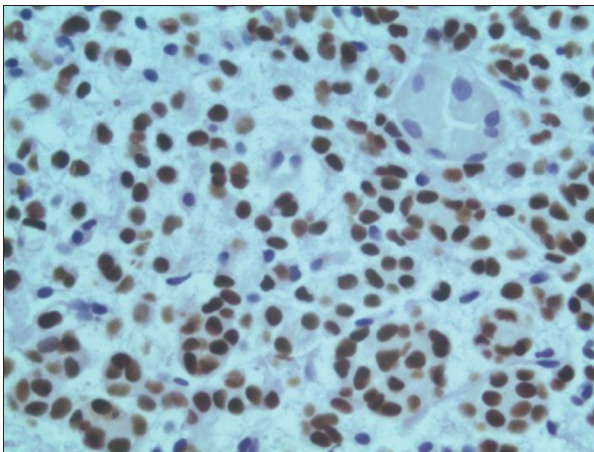


**Figure 2.** Colon biopsy of a stricture with mononuclear infiltrate in lamina propria, consistent with metastatic mammary carcinoma (200 $\times$ ).

obstructing mass was planned, as these findings were highly indicative of a primary GI malignancy. Because of her history of breast cancer, prior to the surgical resection, a colonoscopy with biopsy was performed. The biopsy showed diffuse infiltration and proliferation of neoplastic cells in a sheet-like arrangement within the lamina propria and submucosa consistent with a poorly differentiated adenocarcinoma (Figure 2). IHC staining of the biopsy sample was strongly positive for CK7, positive for ER and PR, and negative for Her2/neu, CK20, CDX2, and CA 19-9, supporting the diagnosis of metastatic breast cancer rather than primary colon cancer (Figure 3).



**Figure 3.** Stomach biopsy with mononuclear infiltrate in lamina propria, consistent with metastatic mammary carcinoma (200×).



**Figure 4.** Immunoperoxidase stain for GATA-3 is positive in the tumor cells. GATA-3 – GATA binding protein-3.

The patient continued to be treated with palbociclib and fulvestrant, which was changed to everolimus and exemestane, and later to oral capecitabine due to the aggressiveness of the disease and the side effects of treatment. During year 32, following treatment with capecitabine, she developed epigastric pain. An upper GI endoscopy revealed a dominant lesion in the gastric body highly suspicious for gastric cancer. Histology was consistent with signet ring carcinoma, a rare variant of lobular carcinoma. IHC testing of the tumor cells were strongly positive for GATA-binding protein 3 (GATA-3), ER and PR, and negative for Her2/neu and CDX2, indicating that the stomach tumor was metastasis from breast cancer with signet ring phenotype (Figure 4).

The patient was treated with palliative paclitaxel and gemcitabine chemotherapy. She later developed septic shock with multiorgan failure and died shortly thereafter; 34 years after the initial diagnosis of lobular breast cancer.

## Discussion

Breast cancer is one of the most common malignancies in women. It is estimated to affect, on average, 1 in every 8 women [1,6,7]. Diligent cancer screening and improved treatment has resulted in overall improved survival. As a result, we are caring for many patients with advanced, disseminated metastatic disease. Despite treatment, more than half of the patients experience tumor recurrence or metastasis, some of which present even after 30 years of initial diagnosis. [1,8]. The prognosis for metastatic breast cancer remains poor overall, with most patients surviving only 1 to 2 years [1,3,9,10].

Breast cancer frequently metastasizes to the bones, lungs, central nervous system, and liver, whereas metastasis GI tract is rare, occurring only in 3.4% to 4.5% of patients [1,8]. Disparate breast cancer histological subtypes have a varying predilection with regards to site of metastasis, and therefore affect different organs. Invasive lobular carcinoma (ILC) tends to metastasize more frequently than other subtypes of breast cancer. ILC metastases affect the GI in up to 4.5% of cases, in comparison to 0.2% of invasive ductal carcinomas (IDC); the stomach being the most commonly affected site based on reports [11,12]. Montagna et al. analyzed lobular breast carcinoma patients with GI metastases. 80% of patients had presented with GI symptoms, 92% of which had stomach involvement [12].

Breast cancer metastasis to the GI can often present with nonspecific GI symptoms, such as abdominal pain, diarrhea, weight loss, bowel obstruction, anemia, and bleeding. It can often be challenging to differentiate breast cancer metastasis to GI from primary GI malignancies or other primary GI diseases such as inflammatory bowel disease [13].

Radiographic imaging is not particularly helpful, as oftentimes cancer involvement of the small intestine can be easily mistaken for Crohn's disease [8,13]. These factors lead to delay in appropriate referrals to consultants, use of invasive diagnostic modalities and hence delayed treatment.

As there is progression of disease, certain imaging features of the GI metastases include nodular or circumferential thickening with narrowing. This occurs secondary to tumor cell infiltration in the colonic wall which can subsequently lead to distinct strictures [8]. In contrast, primary GI malignancies frequently present as exophytic masses [14].

Similarly, metastases to the stomach might result in diffuse infiltration of the stomach wall, resulting in linitis plastica in 50% of the cases [15]. However, they can also present as a single mucosal lesion resembling primary gastric cancer. On endoscopy, mucosal involvement has been reported as flat, elevated, polypoid appearing lesions or as erosive ulcers with

visualization of enlarged mucosal folds [16,17]. Such similar imaging features may be easily mistaken for primary GI malignancies. In addition, when presence of intracellular mucin on biopsy specimens is identified, careful consideration is warranted, as it may resemble signet cell appearance, which can also mimic primary gastric malignancies [18]. Signet cell morphology might be found in metastatic lesions of invasive, primary lobular breast cancer, as is the case of our patient [19], as well as signet cell stomach cancer. The presence of >20% signet cells is required to confidently establish a diagnosis of gastric cancer [20].

In cases where metastases only involve the submucosa, biopsies obtained via endoscopy or colonoscopy might result in false negative results, and therefore multiple deep biopsies is recommended [21].

Due to above mentioned factors, the use of IHC staining has become an integral step in establishing the correct diagnosis. Breast cancer cells are often ER and PR positive, although 20% may be negative for ER. In contrast, 32% of gastric cancers were proven to be ER-positive, and 12% were PR positive [22].

Currently, multiple additional diagnostic markers are being utilized, such as gross cystic disease fluid protein-15 (GCDFP-15) and mammaglobin (MGB). GCDFP-15 has a specificity of 98% to 99%, and a sensitivity ranging from 50% to 74% [23]. In contrast, MGB has a specificity of 92% for detecting breast cancer, and a greater sensitivity than GCFDP-15 [24]. Most recently, GATA-3 has also been used. It is noted to be positive in 100% of lobular breast cancers and 96% of ductal breast cancers, compared to only 5% of gastric cancers [25]. CK7 and CK20 are also useful in differentiating among breast, colon and gastric cancers due to their varied expression. Most breast cancers are positive for CK7 and negative for CK20, whereas most GI cancers are negative for CK7 and positive for CK20.

Immune markers are also helpful in distinguishing breast cancer metastases from primary GI cancers [26]. For instance, most breast cancer adenocarcinoma cells are positive for Mucin 1 (MUC1) and negative for Mucin 2 (MUC2), whereas most GI cancer adenocarcinoma cells are negative for MUC1 and positive for MUC2 [27].

Establishing the correct diagnosis as early possible is vital; as treatment for primary GI malignancy and breast cancer metastasis to the GI tract vary significantly and carry a different prognosis. The treatment of choice for localized primary GI cancer is surgical resection, while metastatic breast cancer is treated with systemic chemotherapy and/or hormonal therapy. There is a lack of consensus regarding the standard of care for GI metastases from breast cancer; however, primary resection of metastases has not been shown to improve survival but may be used as a palliative tool to aid with symptom control [7].

In this case, the patient presented with bowel obstruction. Initial impression was concerning for primary colon cancer, however, with the help of IHC, the correct diagnosis of metastatic breast cancer was established. In this setting, the initial plan for primary surgical resection was aborted, and instead treatment with palbociclib and fulvestrant was promptly initiated. Several months later, she presented to the hospital with nonspecific epigastric pain and was found to have a gastric lesion suspicious for primary gastric cancer. Biopsy was consistent with signet cell morphology, and again, with the aid of IHC, appropriate diagnosis was achieved.

## Conclusions

Findings in our patient demonstrated how breast cancer metastases to the GI tract can mimic primary GI cancers, especially when the former lesions appear many years after initial cancer diagnosis and treatment. The clinical, radiographic, and histologic findings pose a diagnostic challenge. Fortunately, a detailed IHC profile can aid in establishing a diagnosis, which can profoundly affect patient management and prognosis. New GI symptoms in patients with a prior history of breast cancer should be thoroughly investigated. In particular, the likelihood of metastases should be evaluated as breast cancer can be clinically and morphologically very heterogeneous.

Breast cancer patients should have close follow-up throughout their lifetime, as recurrence and metastatic lesions can present ambiguously even decades later.

## Conflict of interest

None.



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