



## De Novo Metastatic Breast Carcinoma with Gastrointestinal (GI) Symptoms

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### Keywords

Breast carcinoma; Metastasis; Gastrointestinal symptoms; Immunohistochemistry

### Introduction

Breast cancer is the most common cancer among women [1]. The majority of metastatic breast cancer cases are due to the recurrence of primary breast cancer, which has been previously treated. *De novo* metastatic breast cancers include 3% to 6% of all breast cancers in high-income countries [2]. Common sites of breast cancer metastasis include lungs, liver, bones, soft tissue, brain, and adrenal glands [3]. The upper gastrointestinal tract is an infrequent site for metastatic cancers. Cancers of the breast, lung, kidney and malignant melanoma are among the most common origins of such metastasis [4]. However, the occurrence in autopsy series varied from 8% to 35% [5]. Among GI metastases from the breast, lobular types (ILC) are more prevalent [5]. Reports on this subject in the literature are poor and mostly limited to case reports. Since metastases to GI from breast cancer are uncommon and rare, the main problem is to recognize them in patients affected by breast cancer and with GI symptoms, like nausea and vomiting, diarrhea, and abdominal pain. These symptoms may delay the definite diagnosis and treatment of GI involvement by breast cancer.

This paper represents a case of metastatic breast cancer with an initial presentation of GI symptoms. After a biopsy from the stomach and small bowel and doing an Immunohistochemistry (IHC) test and systematic staging evaluation, the breast was the origin of the GI malignancy.

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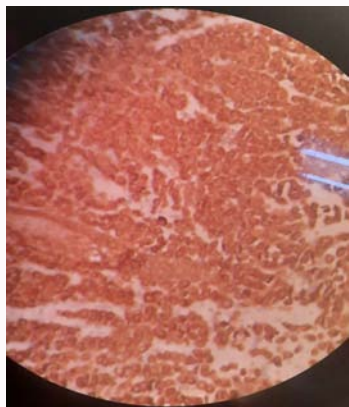
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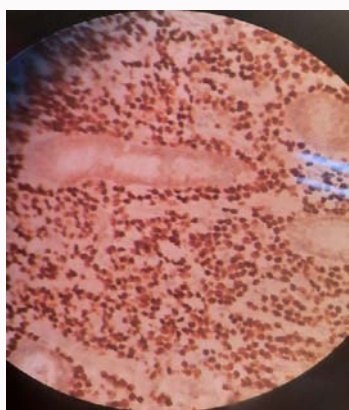
### Case Presentation

A 70-year-old female came to the oncology clinic with a pathology report and accompanying IHC result which showed a metastatic upper GI malignancy, most probably breast origin. She had a history of abdominal surgery because of the obstructive symptoms five months ago. At that time, she had abdominal pain, nausea, vomiting, and no defecation that had developed four days before surgery. Abdominal pain X-ray showed multiple air-fluid levels and CBC revealed leukocytosis. She was referred to the operation room with the final diagnosis of small bowel obstruction. Surgery was done and luminal construction of the small bowel at the level of the jejunum was responsible for the obstructive symptoms. The pathology report suggested a malignant round cell tumor of the small intestine involving the full thickness of the luminal wall and causing intraluminal constriction. At that time Immunohistochemistry (IHC) result was done and it was as follow: Ki67 20%, CK AE1/AE3(+), CD45(-), CD3(-), CD20(-), CD43(-), CD56(-), CD30(-), CD5(-), PAX5(-), and cyclin D1(-). The patient came back to the hospital with symptoms of dyspepsia especially nausea and vomiting after five months. Upper gastrointestinal endoscopy and colonoscopy were done and a large ulcer with hypertrophic gastritis in the antral region of the stomach and duodenum and also a large size sliding hiatal hernia were detected. The microscopic diagnosis of the ulcer and complementary IHC result revealed a malignant tumor which marker expressed as follows: GATA-3 (+), ER (50% positive), CK7 (+), GATA-3 (+), ER (20% positive). Colonoscopy showed only several diverticula in the sigmoid region. The final diagnosis of the pathology report confirmed GI metastasis from breast origin.

In physical examination signs of discharge, skin or nipple retraction, and Peau d'orange were not observed. Likewise, there were no signs of axillary lymph node swelling or tenderness. Ultrasonography of breasts and both axillary areas reported a microlobulated & hypochoic nodule



**Figure 1:** Cytokeratin was positive in cytoplasm of tumoral cells.



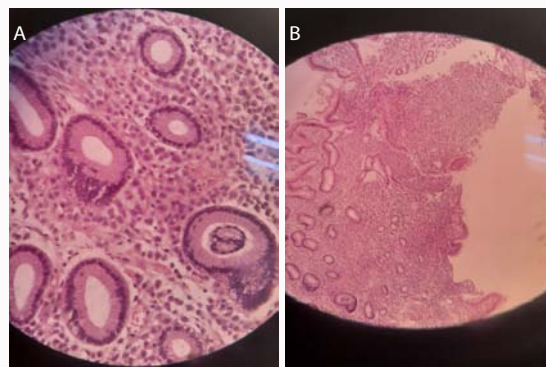
**Figure 2:** GATA as marker of breast origin was positive in nuclei of tumoral cell.

with the dimensions of 5.5 mm × 5.2 mm in the 2 o'clock position in the left breast. It also reported infiltrated and hypertrophied lymph nodes in the left axilla (BIRADS-4c).

Mammography reported an asymmetry in the left UOQ and two benign calcified foci in the left breast. Core Needle Biopsy (CNB) of the left breast 2 o'clock mass and a biopsy of left axillary lymph nodes were taken and the pathology and their IHC results were suggestive of Invasive Lobular Carcinoma (ILC) of the left breast and a positive infiltrative axillary node according to positive CK7 staining, and MBC (GATA-3 (+), ER (20% positive), PR (negative), HER-2 (negative, 1+), and Ki67 27%). Results of tumor markers measurement detected increased levels of CA 15-3 (71), LDH (331), and C.E.A (1.04 ng/mL). We did an F-FDG PET/CT scan and it revealed mildly FDG avid gastric antrum wall thickening and soft tissue lesion in left breast UOQ which was indicative of malignancy. Several faintly FDG avid left axillary & subpectoral lymph nodes were suspicious of metastasis. There was no bone FDG avid significant lesion. After confirming the diagnosis of *de novo* metastatic invasive breast carcinoma with initial presentation of gastrointestinal symptoms, the patient received six cycles of a combination chemotherapy regimen including Cyclophosphamide and docetaxel with G-CSF support every 3 weeks. Then after the ending of intravenous chemotherapy an aromatase inhibitor - letrozole started.

## Discussion

The most common sites of breast cancer metastasis are the



**Figure 3:** Gastric biopsy shows single epithelioid cell reminiscent of signet cell infiltrating lamina propria. A) H&E (×400) B) H&E (×100).

skeletal bone, lungs, liver, brain, stomach, peritoneum, colon, retroperitoneum and small bowel all have been reported as potential sites of metastatic involvement [5]. Metastatic spread to the stomach may occur many years after the initial treatment for breast cancer. It may prove very difficult to distinguish from primary gastric cancer on clinical, endoscopic, radiological, and histopathological features. However, it is important to make this distinction in the beginning because there are so different treatment schedules for the management of both cancers [6].

Metastatic Breast cancer patients with extramammary symptoms have been reported in the literature, but symptoms of *de novo* metastatic breast cancer with invasion to the gastrointestinal tract is a rare phenomenon [5]. Breast cancer can spread anywhere but symptoms of skeletal pain, cough, and dyspnea with bone or lung involvement and occasionally neurologic deficits such as headache, blurred vision, nausea, vomiting following brain metastasis or jaundice, and elevated liver enzymes with liver metastasis are the prominent signs and symptoms.

According to the Mayo Clinic data, among 12,000 cases of metastatic breast cancer, 73 cases had GI metastasis. Invasive Lobular Carcinoma (ILC) is more likely to have distant metastases such as GI metastasis, rather than invasive ductal carcinoma [5]. Metastasis to the stomach causes polyps and mucosal erosions, but metastasis to the intestine can cause intestinal stenosis due to occult clinical symptoms. Our case was a *de novo* metastatic breast cancer with symptoms of small bowel obstruction and dyspepsia in the beginning. It was difficult to distinguish between a primary GI malignancy from a *de novo* metastatic GI tumor by a conventional biopsy. In addition, imaging, and clinical findings didn't help directly.

Although Immunohistochemistry (IHC) was so helpful, it was not diagnostic because nobody was suspicious of the breast origin in the beginning. Probably the most predictive markers in breast cancer are Estrogen Receptor (ER), and Progesterone Receptor (PR), HER-2 is a prognostic and predictive marker in breast cancer, and also GATA3 and CK7. As we knew some cases of primary gastric malignancy are positive for PR and ER markers, and on the other hand some cases of metastatic breast carcinoma, are ER and PR negative and HER-2 negative.

Diagnosis of a *de novo* metastatic breast carcinoma with GI symptoms is a challenging issue and it is needed to be aware of occasional aberrant symptoms and signs of common cancer.

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