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Case Report

Breast Cancer Metastasizing to the Lower Gastrointestinal Tract (the Small Bowel and Colon): A Case Presentation and Comprehensive Review of the Literature

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Abstract

Breast cancer metastases to the lower gastrointestinal tract (small bowel and colon) are rare, but there is a growing number of case reports in the literature. The overall incidence of this condition is not well established, and there might be underdiagnosis. The clinical presentation and endoscopic findings are often nonspecific and variable, potentially leading to misdiagnosis or underdiagnosis. Moreover, there are currently no guidelines for gastrointestinal surveillance of these patients. Given the potential diagnostic challenges, a high level of clinical suspicion is necessary. We present a clinical case to highlight subtle endoscopic findings of breast cancer metastasis to the colon, followed by a review summarizing the available literature on breast cancer metastases to the duodenum, jejunum, ileum, colon, rectum, and anus focusing on the clinical presentation, endoscopic features, imaging modalities, treatment, and outcome.

Introduction

Metastatic tumors in the gastrointestinal (GI) tract are rare, with an actual incidence unknown but potentially higher than presumed, possibly due to a lack of clinical suspicion. Moreover, the frequency of primary tumors metastasizing to the GI tract varies between surgical and autopsy specimens. In the study by Washington *et al*.,[1] melanoma, ovary, and bladder were the primary tumors most commonly found in surgical specimens, while lung, gynecological malignancies, and breast were prevalent in autopsy specimens.

Breast cancer remains the most common cancer in females and the second leading cause of cancer-related death in women. Approximately 12% of patients eventually develop metastases, most commonly in the bone, liver, lymph nodes, and lungs.[2] Nonetheless, virtually any organ can be affected.[3] Retrospective clinical studies estimate the frequency of breast cancer metastases to the GI tract to be around 0.3% to 2%.[2,4] However, the autopsy study by Asch *et al*. revealed a much higher incidence, up to 16.4%.[5] Furthermore, breast cancer accounts for approximately 13% to 21% of primary tumors metastasizing to the GI tract.[1]

We describe a case of a patient with a distant history of breast cancer who was diagnosed with isolated colon metastases of breast origin solely through endoscopy during an investigation for iron deficiency anemia. We also review the available literature on this case, which includes breast cancer metastases to the duodenum, jejunum, ileum, colon, rectum, and anus, focusing on clinical presentation, endoscopic features, imaging modalities, treatment, and outcomes.

Case report

A 65-year-old female with a medical history including diabetes, hypothyroidism, coronary artery disease, immune thrombocytopenic purpura treated with romiplostim, gastric bypass, and lobular breast cancer was under the care of the hematologist for management of immune thrombocytopenic purpura in 2013. The breast cancer was of the lobular type, with positive estrogen receptors (ER+) and negative human epidermal growth factor-2 (HER2), staged as T2 N0. In 1998, the patient underwent a left mastectomy and axillary lymph node dissection, followed by adjuvant therapy including cyclophosphamide, methotrexate, and 5-fluorouracil, followed by five years of tamoxifen therapy.

She presented with persistent fatigue and night sweats, denying fever or chills. Laboratory results showed a hemoglobin level of 11.2 g/dL and hematocrit of 35.7% (previously 12.3 g/dL and 37.1%, respectively). Iron studies revealed a total iron level of 60 mcg/dL, saturation of 15%, total iron-binding capacity of 404 mcg/

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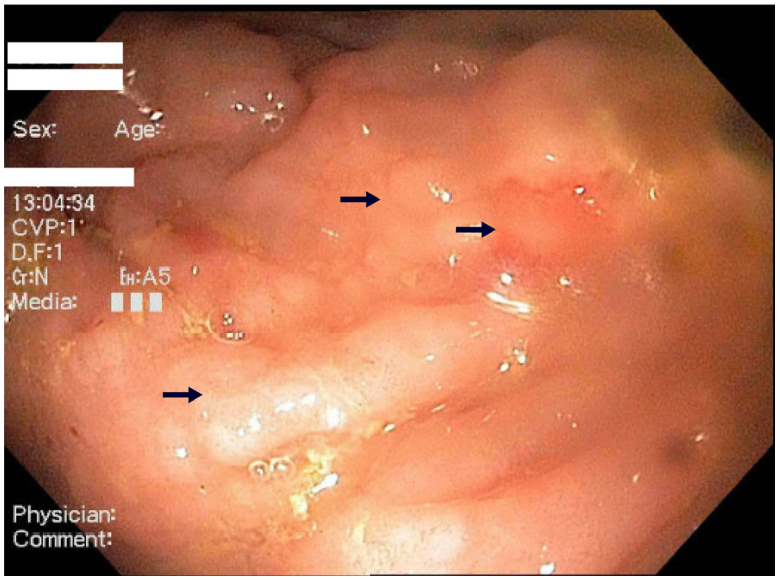

Fig. 1. Nodular colonic mucosa (arrows) on colonoscopy corresponds to the site of metastases.

dL, and ferritin level of 44 mcg/L. Stool analysis was positive for heme. She was referred to gastroenterology and underwent an esophagogastroduodenoscopy (EGD), which revealed erythema in the gastric pouch but normal postoperative anatomy. A colonoscopy revealed nodular, inflamed mucosa, and an ulcer in the ascending colon (Fig. 1), with nodular and inflamed mucosa extending to the hepatic flexure and part of the transverse colon.

Biopsy results from the stomach showed chronic active gastritis of the fundic mucosa and Helicobacter organisms. Pathologic examination of the cecal, hepatic flexure, and transverse colon mucosa showed extensive lamina propria infiltrates of metastatic adenocarcinoma with signet ring cell morphology and immunohistochemical features compatible with metastatic lobular breast carcinoma (Fig. 2a). The tumor cells in the lamina propria were strongly positive for cytokeratin 7 (CK7), carcinoembryonic antigen (CEA), and gross cystic disease fluid protein 15, as well as for mammaglobin and ER+ (Fig. 2b). The progesterone receptor (PR) was focally positive (Fig. 2c), while CK20 was negative. These colonic tumor cells exhibited a similar molecular subtype to the patient's previous lobular breast carcinoma cells.

Baseline tumor markers were obtained: CEA was 62.9 ng/ml, CA 15–3 141 U/ml, and CA 27.29 176 U/ml. A positron emission tomography (PET) scan demonstrated normal F-fluorodeoxyglucose (FDG) distribution without abnormal foci of increased metabolic activity that suggested residual, recurrent, or metastatic breast cancer. The left breast MRI revealed stable post-mastectomy changes with no suspicious masses or axillary adenopathy, while the MRI of the right breast was unremarkable. Treatment was initiated with fulvestrant and anastrozole for metastatic breast cancer, iron sucrose for anemia, and a 14-day course of lansoprazole, amoxicillin, and clarithromycin for *Helicobacter pylori*.

Unfortunately, in the following months, her disease progressed with metastases to the liver, severe ascites, and alteration of mental status. She was transferred to hospice care and died shortly after.

Literature review

In September 2022, the authors conducted a search of the PubMed database for articles on breast cancer metastases in the duodenum,

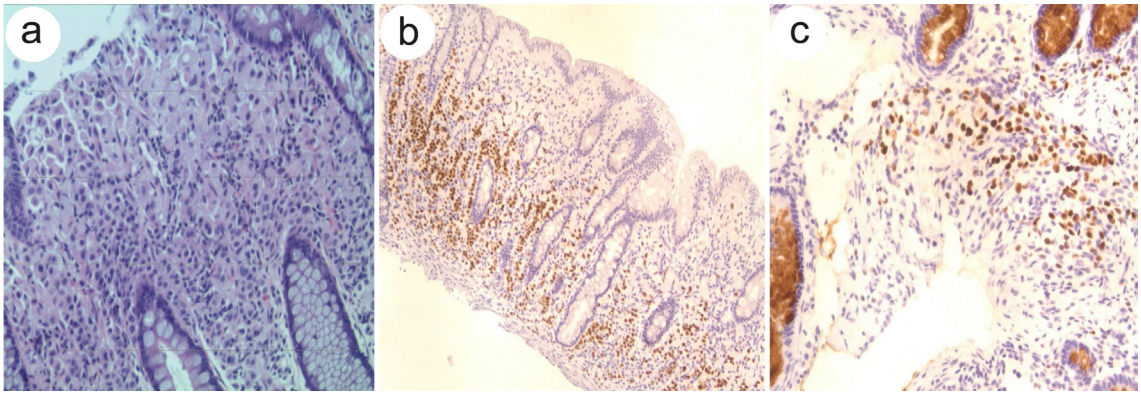

Fig. 2. Infiltrative adenocarcinoma involving mucosa and submucosa. (a) Hematoxylin and Eosin stain (original magnification 40×); (b) ER receptor positive on IHC (original magnification 40×); (c) PR receptor focally positive on IHC (original magnification 40×). ER, estrogen receptor; IHC, immunohistochemistry; PR, progesterone receptor.

Table 1. Location, endoscopic finding and clinical findings in breast cancer metastatic to small bowel and colon

	Small intestine (%)	Large intestine (%)
Location		
Duodenum	15 (45)	–
Jejunum	3 (9)	–
Ileum	12 (36)	–
Unspecified	3 (9)	–
Ileocecal	–	3 (4)
Ascending Colon	–	8 (11)
Hepatic flexure/Transverse Colon	–	9 (12)
Descending Colon	–	5 (7)
Sigmoid and Rectum	–	33 (43)
Anus	–	5 (7)
Multiple Colonic sites	–	13 (17)
Endoscopic finding		
Thickened duodenal papilla	4 (20)	–
Mucosal erythema	3 (15)	–
Ulcer	6 (30)	4 (7)
Mass	2 (10)	17 (30)
Duodenal stenosis	9 (45)	–
Mucosal erythema	–	11 (20)
Colonic lumen stenosis	–	28 (50)
Nodular thickening of the mucosa	–	8 (14)
Polyp	–	8 (14)
Imaging findings		
Abnormal CT findings	24 (86)	31 (60)
Abnormal PET findings	3 (11)	4 (8)
Abnormal MRCP/ERCP findings	3 (11)	–
Abnormal Xray findings	3 (11)	3 (6)
Abnormal MRI findings	–	9 (17)
Abnormal Barium study	–	8 (15)

CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging; PET, positron emission tomography.

jejunum, ileum, colon, rectum, and anus. All articles published until September 2022 were included. The following search terms were employed: "breast cancer metastasis duodenum", "breast cancer metastasis jejunum", "breast cancer metastasis ileum", "breast cancer metastasis colon", "breast cancer metastasis rectum", and "breast cancer metastasis anus". Articles written in English containing individual information regarding patient age, clinical presentation, diagnostics, and treatment modalities for breast cancer metastasizing to the small and large bowels were included. No autopsy studies were considered in this review. The references of each article were reviewed, and further articles meeting the inclusion criteria were retrieved.

From each study, two independent authors (TC, SAS) extracted the following variables: patient age, the interval between breast cancer diagnosis and GI metastasis diagnosis, histological type of breast cancer, the hormone receptor status of the primary tumor, the type of treatment of the primary tumor, the clinical presentation that led to the diagnosis of the metastatic lesions, misdiagnosis, the anatomical location of the metastatic lesions, the endoscopic findings, the use of additional imaging, the diagnostic modality that provided the confirmatory biopsies, the histological findings, hormonal status and specific markers of the GI metastases, the type of treatment for the metastatic lesions, the presence of other metastatic sites, and finally the outcome. All collected data were inserted into an MS Excel flow sheet. A descriptive analysis using the same software was performed, and a literature review was conducted.

Duodenum, jejunum, and ileum

After reviewing the literature, we included 33 studies, all of which consisted of individual case reports, thus totaling 33 patients. The locations of metastases were distributed as follows: duodenum (n = 15, 45%), jejunum (n = 3, 9%), ileum (n = 12, 36%), and unspecified sites within the small intestine (n = 3, 9%) (Table 1).

Table 2. Age, pathologic type, initial treatment and median time to diagnosis for breast cancer metatstatic to small bowel and colon

	Small intestine (%)	Large intestine (%)
Median age (years)	57	65
Breast cancer type		
Lobular carcinoma	14 (45)	47 (64)
Ductal carcinoma	12 (39)	20 (27)
Phyllodes tumor	4 (13)	–
Mixed lobular and ductal carcinoma	–	3 (4)
Initial treatment of breast cancer		
Surgery	27 (87)	55 (86)
Chemotherapy	18 (58)	34 (53)
Hormonal therapy	14 (45)	38 (59)
Radiotherapy	12 (39)	28 (44)
Median time between diagnosis of primary breast cancer and GI metastases (years)	2.5	5

GI, gastrointestinal.

The median age was 57 years (range: 31–82). The median interval between the diagnosis of breast cancer and the diagnosis of metastasis in the small bowel was 2.5 years (Table 2). Four patients were discovered to have small bowel metastases prior to the diagnosis of primary breast cancer. Only one patient experienced a misdiagnosis, initially labeled as lymphoma.

Information regarding the primary breast cancer type was available in 31 cases: lobular type in 14 (45%) patients, ductal type in 12 (39%) patients, and phyllodes type in four (13%) patients. Data on the hormonal status of the primary tumor were available in 23 patients, revealing positive estrogen receptors in 18 (78%) patients and negative in five (22%) patients. PRs were positive in 14 (61%) patients and negative in eight (35%). HER2s were positive in four (17%) patients and negative in 14 (61%) patients (Table 3). The type of treatment for the primary tumor was reported in 31 patients: surgery (mastectomy or lumpectomy) in 27 (87%) patients, chemotherapy in 18 (58%), hormonal therapy in 14 (45%), and radiotherapy in 12 (39%).

Data on the clinical presentation prompting further evaluation and leading to the diagnosis of GI metastases were available in 30

Table 3. Hormonal status and immunohistochemistry in breast cancer metastatic to small bowel and colon

	Small intestine (%)	Large intestine (%)
Hormonal receptors of primary breast tumor		
ER+	18 (78)	42 (86)
ER−	5 (22)	3 (6)
PR+	14 (61)	26 (53)
PR−	8 (35)	10 (20)
HER2+	4 (17)	7 (14)
HER2−	14 (61)	26 (53)
Hormonal receptors and markers of gastrointestinal metastases		
ER+	15 (65)	47 (80)
ER−	7 (30)	8 (14)
PR+	5 (22)	22 (37)
PR−	13 (57)	19 (32)
HER2+	4 (17)	4 (7)
HER2−	6 (26)	23 (39)
CK7	9 (39)	27 (46)
CK7−	–	2 (3)
CK20−	6 (26)	24 (41)

+ positive; − negative; CK, cytokeratin; ER, estrogen receptor; HER2, human epidermal growth factor 2; PR, progesterone receptor;

Table 4. Clinical presentation of breast cancer metastatic to small bowel and colon

	Small intestine (%)	Large intestine (%)
Symptoms		
GI bleed	4 (13)	14 (19)
Abdominal fullness	6 (20)	–
Weight loss/Anorexia	7 (23)	11 (15)
Jaundice	5 (17)	–
Nausea/Vomiting	19 (63)	7 (10)
Abdominal pain	18 (60)	32 (44)
Asymptomatic	–	8 (11)
Fatigue/Weakness	–	4 (5)
Change in bowel habits	–	13(18)
Diarrhea	–	9 (12)
Tenesmus	–	11 (15)
Constipation	–	23 (32)

GI, gastrointestinal.

patients: nausea and/or vomiting in 19 (63%) patients, abdominal pain in 18 (60%), weight loss/anorexia in seven (23%), and jaundice in five (17%) patients (Table 4).

A total of 20 patients underwent EGD, revealing main findings such as lumen stenosis (n = 9, 45%), ulcer (n = 6, 30%), thickening of the duodenal papilla (n = 4, 20%), mucosal erythema (n = 3, 15%), and mass formation (n = 2, 10%). Twenty-four patients had an abnormal computed tomography (CT) scan, with findings including thickening of the bowel wall (n = 11), mass formation (n = 3), signs consistent with small bowel obstruction (n = 3), intussusception (n = 2), and pneumoperitoneum (n = 2) (Table 1).

The procedures providing tissue acquisition for confirmatory diagnosis were surgery in 18 (55%) patients, EGD or colonoscopy in 13 (39%) patients, and endoscopic retrograde cholangiopancreatography (ERCP) in two (6%) patients. Signet-ring cells were observed in two patients. Additionally, information regarding hormone receptors and other tumor markers in metastatic lesions was available in 23 patients, showing ER+ in 15 (65%) patients, ER- in seven (30%), PR+ in five (22%), PR- in 13 (57%), HER2+ in four (17%), HER2- in six (26%). Moreover, nine (39%) patients had tumors with CK7+ immunostaining, and six (26%) had lesions with CK20+ immunostaining (Table 3).

Twenty-nine patients had details about the presence or absence of additional metastases, revealing no other organ involvement in 11 (38%) cases, one additional site of metastases in seven (24%) cases, and two or more sites in 12 (41%) patients.

The overall treatment modalities for metastatic tumors in the small bowel included surgery (n = 26, 84%), chemotherapy (n = 14, 45%), and hormonal therapy (n = 13, 42%) (Table 5). When analyzing cases by tumor location in the small bowel, similar treatment patterns were observed, except for the three cases with jejunal involvement, where chemotherapy was not part of the treatment.

Finally, from a total of 15 patients with available outcome data, seven (47%) passed away within one year, one (7%) passed away at two years, and seven (47%) were alive after one year of follow-up (Table 5).

Table 5. Treatment and outcomes in breast cancer metastatic to small bowel and colon

	Small intestine (%)	Large intestine (%)
Treatment of metastases		
Surgical	26 (84)	40 (60)
Chemotherapy	14 (45)	36 (54)
Hormonal Therapy	13 (42)	27 (40)
Radiotherapy	0 (0)	9 (13)
Outcome		
Alive within 1 year of diagnosis	4 (27)	14 (47)
Alive after 1 year of diagnosis	7 (47)	14 (47)
Death with 1 year of diagnosis	7 (47)	9 (30)
Death within 1–5 years of diagnosis	1 (7)	5 (17)
Death after 10 years of diagnosis	–	2 (7)

Colon, rectum, and anus

A total of 77 studies individually characterizing and describing patients with colon metastases from breast cancer were included. The total number of patients, including ours, was 78. The median age was 65 years (range: 38–88). The median time interval between the diagnosis of breast cancer and colon/rectum/anal metastasis was five years (Table 2). In four cases, colonic metastases were discovered prior to the diagnosis of primary breast cancer.

The type of breast cancer was described in 70 patients, with 47 patients having a lobular type (64%) and 20 (27%) having a ductal type. Additionally, three patients had both lobular and ductal types. The hormone status of the primary breast cancer was described in 49 patients. ER were positive in 42 (86%) patients, and PR were positive in 26 (53%) patients. Twenty-three (47%) patients were positive for both ER and PR. HER2s were reportedly negative in 26 (53%) patients and positive in seven (14%) patients (Table 3). The type of treatment for the primary breast cancer was available for 64 patients. Surgery (total or partial mastectomy) was performed in 55 (86%) patients, 34 (53%) patients received chemotherapy, 38 (59%) patients received hormonal therapy, and 28 (44%) patients received radiotherapy. Out of 64 patients, 11 (17%) received all four modalities.

The clinical presentation that led to the diagnosis of colonic metastases was characterized in 73 patients. Thirty-two (44%) patients had abdominal pain/discomfort, 11 (15%) reported weight loss, seven (10%) experienced nausea and/or vomiting, and four (5%) complained of fatigue. Twenty-three (32%) patients experienced constipation, nine (12%) patients reported diarrhea, and 13 (18%) experienced some form of change in bowel habits. In addition, tenesmus was disclosed in 11 (15%) patients. Furthermore, 14 (19%) cases presented with GI bleeding, described as hematochezia, bright red blood per rectum, or blood in stools (Table 4).

Most studies reported the site of metastases as the colon (n = 76). The rectum/sigmoid was the most common location (n = 33, 43%). Thirteen (17%) patients had involvement of multiple sites in the colon. The transverse colon/hepatic flexure was involved in nine (12%) cases, the ascending colon in eight (11%), the descending colon in five (7%), the anus in five (7%), and the cecum in three (4%) cases.

Colonoscopy results were available in 56 patients, revealing luminal stenosis (most common with n = 28, 50%), followed by a mass (n = 17, 35%), mucosal erythema (n = 11, 20%), nodular thickening of the mucosa (n = 8, 14%), polyp(s) (n = 8, 14%), and an ulcer (n = 4, 7%) (Table 1). Thirty-five patients underwent CT scan imaging, with abnormal findings in 31. The most common CT scan finding was the thickening of the colonic wall at the site of metastasis. All patients who underwent MRI had abnormal findings at the site of metastasis (n = 9) (Table 1).

In seven patients with a colonoscopy, their first biopsy showed no evidence of malignancy. The procedure providing tissue acquisition for confirmatory diagnosis was colonoscopy in 51 (68%) patients and surgery in 24 (32%). Histologically, the hormonal status of the metastatic lesions was reported in 59 patients. Although all cases reported ER and PR expression, the identification of cytokeratins (CK) was described in only 29 patients. Forty-seven patients with colonic metastasis were ER+, and eight patients were ER-; 22 patients were PR+ while 19 were PR-; four patients were HER2+, and 23 patients were HER2-. Finally, on immunohistochemical staining, 27 patients were CK7+, and two patients were CK7- (Table 3). Moreover, in 12 cases, the metastatic adenocarcinoma in the GI tract exhibited signet-ring cell features. Misdiagnosis occurred in only three patients; two were initially diagnosed with primary colon cancer, and one with anal cancer.

The presence of additional metastases was stated in 58 patients. Twenty-three (40%) had no additional metastasis, 15 (26%) had one additional site of metastasis, and 21 (36%) had two or more sites of metastasis.

A total of 67 cases had information on the treatment of metastatic lesions in the colon. Partial colon resection was performed in 40 (60%) patients, chemotherapy in 36 (54%) patients, hormonal therapy in 27 (40%) patients, and radiotherapy in nine (13%) patients (Table 5). Two patients underwent all four treatment modalities, 13 patients were exclusively treated with chemotherapy, and eight patients only received a combination of chemotherapy and hormonal therapy.

From the available follow-up of 30 patients, 14 (47%) were alive after one year of follow-up, nine (30%) passed away within one year, five (17%) passed away between one and five years after the diagnosis of GI metastases, and two (7%) patients passed away between five and 10 years after the diagnosis (Table 5).

Discussion

Secondary tumors of the small bowel, colon, and rectum are rare, and no studies provide their overall incidence.[6] The main mechanisms of metastatic spread include lymphatic permeation, dissemination through the peritoneal fluid, and hematogenous spread.[7] Aside from breast cancer, primary tumors of the lung, ovary, prostate, kidney, and skin (melanoma) can metastasize to the lower GI tract.[6] In the autopsy study by Antler *et al*., which included 423 patients with lung cancer, 6% were found to have metastases to the small bowel and colon.[8] However, clinical studies show a much lower incidence (< 2%).[9] Maelle *et al*.[10] observed a frequency of 0.8% of renal cell cancer metastasizing to the duodenum. In the study by Caramella *et al*., the authors reviewed 467 cases of metastases to the small intestine (including the duodenum), in which melanoma accounted for 25–33% of metastases.[7] In addition, from 265 cases of metastases to the colon and rectum, prostate and ovarian cancer were the most common causes.

Very few studies analyzed the frequency of breast cancer metastases to the small bowel, colon, and rectum. For example, the study by Montagna *et al*. included 2,588 patients diagnosed with lobular breast cancer and found 40 (1.55%) patients with metastases in the GI tract. Among these, only 5% had colon metastasis.[11] Similarly, autopsy studies showed an incidence of breast cancer metastasizing to the colon of around 8% and the rectum of 2%. This could be related to multiple factors, including a lack of GI symptoms or nonspecific symptoms that would not prompt an endoscopic evaluation and subtle changes in the GI mucosa that may be difficult to identify at the time of endoscopy. Furthermore, the lesions may not be FDG avid on the PET scan, as was the case with our patient.

A review by di Micco *et al*.[3] included 1,224 patients with breast cancer metastasis. Of these, 11 (0.9%) had duodenal metastases, 24 (2%) had metastases in the small bowel, and 59 (4.8%) had metastases to the colon and rectum.

Borst and Ingold identified a significant difference in the metastatic patterns between lobular and ductal breast carcinoma.[2] In their study, the rate of metastasis to the GI tract was higher in the lobular group (4.5% vs. 0.2%). We also noted a higher number of metastases originating from lobular carcinoma in both the small intestine and the colon and rectum. However, in three cases involving the small intestine, the primary tumor was of the phyllodes type, a type not observed in the colon and rectum. The increased tendency for invasive lobular carcinoma to metastasize to the GI

tract may be related to the loss of E-Cadherin function, which reduces cellular adhesion and increases the likelihood of metastasis. Unlike ductal carcinoma, the loss of function of this receptor is considered one of the hallmarks of invasive lobular carcinoma and may be present in up to 90% of cases. Additionally, both breast and colonic tissue have hormone receptors for estrogen and progesterone. While lobular carcinoma can commonly express these receptors, it is possible that they may find a receptive environment in the colon. Even though most patients are found to have GI metastases after the diagnosis of breast cancer, a significant number of patients presented with GI symptoms without a prior diagnosis of breast cancer (18% and 16% in the small bowel and colon and rectal/anal groups, respectively). Furthermore, some patients underwent screening mammograms shortly before the diagnosis of metastases, which did not reveal any evidence of disease.[12,13]

The clinical presentation is nonspecific. Abdominal pain was widespread in both groups; however, it is more frequent in patients with small bowel involvement than in those with colon and rectum/anus disease. The latter group mainly presents with changes in bowel habits, typically expressed as constipation. Gastrointestinal bleeding is also more common in this group. However, some patients may be completely asymptomatic.[14–18] Conversely, nausea/vomiting and weight loss are more frequent in patients with small bowel involvement. Additionally, due to duodenal anatomy, jaundice is a unique sign in patients with duodenal disease.[19–23] The more acute symptoms observed in patients with small bowel involvement, such as nausea/vomiting, abdominal pain, and weight loss, may prompt endoscopic or surgical evaluation sooner than those with large bowel involvement, whose primary symptom is often a change in bowel habits. This might explain the difference in the median time for diagnosis with an earlier diagnosis observed in the small bowel group.

As noted with breast cancer metastases to the esophagus and stomach, diagnosis is challenging and might require several diagnostic tools. In some patients, imaging serves as the initial step, typically a CT scan, which can identify lesions in the GI tract. However, in a few cases, it fails to show any evidence of disease.[17,24–26] Moreover, as observed in our case and others, a PET scan may not reveal any increased FDG uptake.[26] A barium enema can also serve as the first step in patients with distal colon, sigmoid colon, and/or rectal disease, as it can identify stenotic lesions and masses.[27–30] However, biopsy with histological assessment remains the gold standard.

A meticulous endoscopic examination is recommended, especially in the rectum and sigmoid colon, as these are the most frequently affected areas. Endoscopic findings are nonspecific, ranging from mucosal erythema or a polyp to large ulcers and an obvious malignant mass.[15,31–38] However, luminal stenosis is the most common finding in both the small and large intestines.[34,35,37–44]

Biopsies can be obtained by different methods, with endoscopy and surgery being the most commonly used. However, the use of more advanced tissue acquisition methods, such as endoscopic mucosal resection and endoscopic ultrasound-guided Trucut biopsy, has become popular, and depending on the type of lesion, their use should be encouraged to decrease false-negative results. This is particularly relevant due to the significant number of reported false-negative biopsies on the initial colonoscopies of patients with metastases to the large intestine.[27,30,41,42,44–46]

The histological appearance is usually that of a poorly differentiated adenocarcinoma, and, similarly to our case, a significant number have signet ring cell features, which can easily lead to a misdiagnosis of a primary GI cancer.[13,42,43,47–53] For these reasons, immunohistochemistry is essential to detect hormone receptors and other markers, including cytokeratin 7, which is associated with breast cancer, whereas cytokeratin 20 is more often associated with primary GI tumors.[54] Moreover, breast-specific immunocytochemical stains such as GATA3 , gross cystic disease fluid protein 15, mammaglobin, and SOX10 can be used to establish the correct diagnosis, especially in hormone-negative tumors.[55]

Surgery, along with chemotherapy and/or hormonal therapy, is the mainstay of treatment. Unfortunately, the individual case reports did not provide a follow-up period large enough to draw conclusions regarding the type of treatment and overall survival. There was no significant difference in the type of treatment received by patients who passed away within one year in each group. However, in both groups, patients with more than two affected sites with metastases still underwent surgery at a rate not significantly different from patients without additional metastases. Nonetheless, among the patients who passed away within one year in both groups, only two patients (one in each group) had no additional site of metastasis. Hence, the disease stage and progression are likely more critical factors in the overall prognosis than the treatment type.

Conclusion

While breast cancer metastasizing to the GI tract is relatively uncommon, its true incidence is probably higher than expected. Hence, it is crucial to have a high degree of suspicion during colonoscopy and/or EGD procedures in patients with a history of breast cancer, even in the absence of GI-related symptoms. Misdiagnosis can occur due to unfamiliarity with the disease and its nonspecific clinical presentation. Consequently, GI symptoms accompanied by weight loss in patients with a history of breast cancer should prompt further investigation, even if endoscopic results appear normal. Additionally, the use of immunohistochemical staining of biopsy specimens is essential for accurate diagnosis, as histological findings are often nonspecific, potentially leading to misdiagnosis of a primary GI carcinoma.

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Conflict of interest

The authors do not have any conflicts of interest to declare.

Author contributions

Conception (TDC, MD), literature search (TDC, SAS), drafting of manuscript (TDC, SAS), revision of manuscript (TDC, MD), critical revision of the manuscript (MD), and study supervision (MD). All authors have made a significant contribution to this study and have approved the final manuscript.

Ethical statement

The study was performed in accordance with the ethical standards of the institutions to which we are affiliated and with the Decla-

ration of Helsinki (as revised in 2013). Informed consent for the publication was obtained from the patient and her family.

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