

CASE REPORT

Beyond Boundaries: Breast Cancer Metastasizing to Colon—An Insight into a Rare yet Significant Clinical Scenario: A Case Series

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ABSTRACT

Background: Colorectal metastasis from primary breast cancer is rare and presents a challenge for diagnosis and treatment.

Aim: To report two cases of colorectal metastasis from a primary invasive lobular breast carcinoma (ILBC) with different presentations while discussing the mode of diagnosis, immunohistochemistry (IHC), course of treatment, and response.

Case descriptions:

Case 1: A 47-year-old female, with a known case of bilateral invasive lobular breast cancer, was diagnosed in 2015 and staged as pTx N3 M0. She underwent a bilateral nipple-sparing mastectomy and presented 8 years later with complaints of left-sided abdominal pain and altered bowel habits for 2 months. She underwent a colonoscopy, and an erythematous area was noted in the ascending colon, and narrowings were seen in the transverse and rectosigmoid junction. Histopathological findings were consistent with metastatic ILBC with the same IHC pattern.

Case 2: A 52-year-old woman presented in September 2019 with a 1-month history of constipation, generalized colicky abdominal pain, 7 kg weight loss, nausea, and anorexia. She underwent a colonoscopy, which revealed a malignant-appearing apple-core lesion at the proximal rectum with severe stenosis that could not be bypassed. A PET-CT showed suspicious breast lesions, and after further investigations and biopsies, she was diagnosed with primary invasive lobular carcinoma (ILC) of the breast with rectal metastasis.

Clinical significance: With the increasing incidence of both colorectal and breast cancer and the rarity of breast cancer metastasis to the gastrointestinal tract (GIT), this case series aims to highlight the growing incidence of lobular breast cancer metastasis to the colon and to shed light on the importance of further research in this area in terms of early detection and treatment to improve the prognosis of such patients.

Conclusion: This case series highlights the clinical presentations, diagnosis, histopathology, challenges, and trials of treatment in our patients. These findings show the importance of considering gastrointestinal (GI) involvement in breast cancer patients and the need for multidisciplinary approaches to achieve better outcomes. However, this is an area of need for more research and awareness to improve the understanding and management of GI metastases from breast cancer.

Keywords: Breast cancer, Case report, Colorectal cancer, Metastasis.

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BACKGROUND

Breast cancer is the most prevalent malignancy among women worldwide, accounting for 2.3 million cases in 2022.¹ It is characterized by its propensity to metastasize to distant organs, most frequently the brain, bone, liver, and lung.² However, metastasis of breast cancer to the gastrointestinal tract (GIT) is uncommon, reported in less than 5% of all breast cancer cases.^{3–5} Colorectal metastasis is considered a rare occurrence, seen in less than 1% of GIT metastasis.^{6,7} The manifestation of breast cancer in the GIT presents a challenge for diagnosis and treatment, considering its nonspecific clinical presentation and potential for misdiagnosis.

We report two cases of primary invasive lobular breast cancer, with one case presenting with colon metastasis a few years after surgical treatment of the breast tumor and the second case being diagnosed initially with rectal adenocarcinoma before finding the primary breast cancer.

CASE DESCRIPTIONS

Case 1

A 47-year-old Bahraini female, a known case of bilateral invasive lobular breast cancer diagnosed in 2015 and staged as pTx N3 M0.

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Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Both lesions were grade II, with axillary lymph node involvement seen only on the right side. Histopathological analysis and immunohistochemistry (IHC) showed the following: Estrogen receptor or estrogen receptor (ER) (positive), progesterone receptor

or progesterone receptor (PR) (positive), and human epidermal growth factor receptor 2 or HER-2 (negative).

She underwent bilateral nipple-sparing mastectomy with right axillary lymph node dissection and left sentinel lymph node biopsy with immediate reconstruction.

The patient received sequential FEC 100-Docetaxel chemotherapy and then was started on tamoxifen. She also underwent radiotherapy and had regular follow-ups. She finished her chemotherapy and radiotherapy sessions in 2016.

In late 2017, the patient had symptoms of lower abdominal pain, and a surveillance positron emission tomography/computed tomography (PET/CT) scan reported no evidence of local recurrence. However, it showed peritoneal thickening, ascitic fluid collection in the pelvis, and bulky bilateral adnexa with cystic changes. Further radiological assessment was done with an MRI of the abdomen, which showed diffuse enhancement of the peritoneum. The MRI of the pelvis showed bulky ovaries without a definite ovarian lesion. There was diffuse peritoneal thickening and enhancement with small amounts of free fluid. Therefore, she was suspected to have peritoneal metastasis from her original primary breast cancer and was scheduled for diagnostic laparoscopy in January 2018. During the procedure, omental, peritoneal, and iliac lymph node biopsies were performed. An intraoperative ovarian biopsy was sent for a frozen section, which turned out highly suggestive of malignancy. Subsequently, the patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy.

Histopathology analysis of the obtained biopsies reported metastatic invasive lobular breast carcinoma (ILBC). An ascitic fluid sample was also consistent with metastatic ILBC. Immunohistochemistry of the biopsies revealed the same receptor profile: ER (positive), PR (positive), HER-2 (negative), and Ki-67 was 20%. Her case was discussed in the National Tumor Board, and she was advised on CDK 4/6 inhibitors as further treatment.

The patient was started on fulvestrant and palbociclib. She had a good response until May 2022, when CT of the thorax, abdomen, and pelvis reported disease progression. The CT showed significant peritoneal congestion, with diffuse thickening of the peritoneal reflection and mesenteric folds and multiple enlarged mesenteric lymph nodes, suggesting progression of the peritoneal metastasis. In addition, focal segmental circumferential wall thickening involving the proximal part of the ascending colon was found, representing possible new large bowel metastasis. As per response evaluation criteria in solid tumors (RECIST) criteria, these findings were suggestive of progressive disease.

Restaging with FDG PET/CT also suggested residual or recurrent peritoneal involvement. Circumferential colonic wall thickening at the mid-part of the ascending colon was seen on the PET/CT, and she was referred for colonoscopic evaluation (Fig. 1). She underwent a gastro-colonoscopy, and biopsies were obtained from the stomach and right colon. The pathology findings were suggestive of metastatic lobular breast carcinoma, positive for ER and PR, and negative for HER2 (Figs 2 and 3). The patient was continued on the same regimen of fulvestrant and palbociclib, and a follow-up PET/CT in October 2022 showed a stationary course of the disease.

In May 2023, the patient presented with complaints of left-sided abdominal pain and altered bowel habits for 2 months. She underwent a colonoscopy, and an erythematous area was noted in the ascending colon, and narrowings were seen in the transverse and rectosigmoid junction. Histopathological findings of the suspicious areas were consistent with metastatic ILBC.

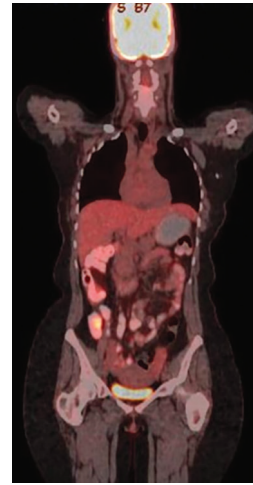


Fig. 1: Whole body F18-FDG PET/CT showing circumferential wall thickening of the ascending colon

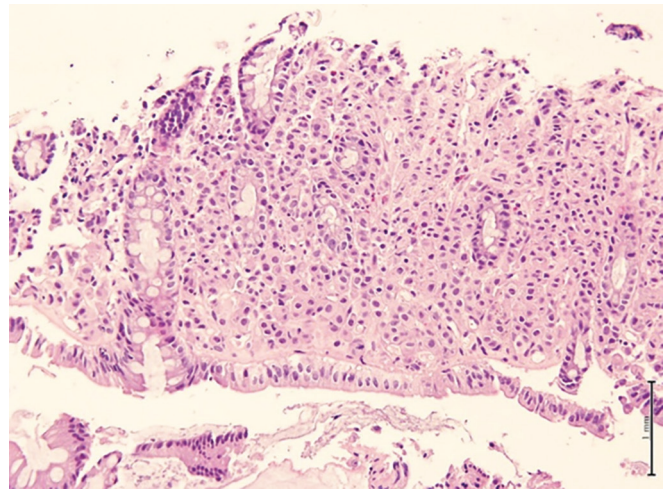


Fig. 2: Biopsy of the right colon showing sheets of neoplastic cells (invasive lobular carcinoma) infiltrating colonic mucosa

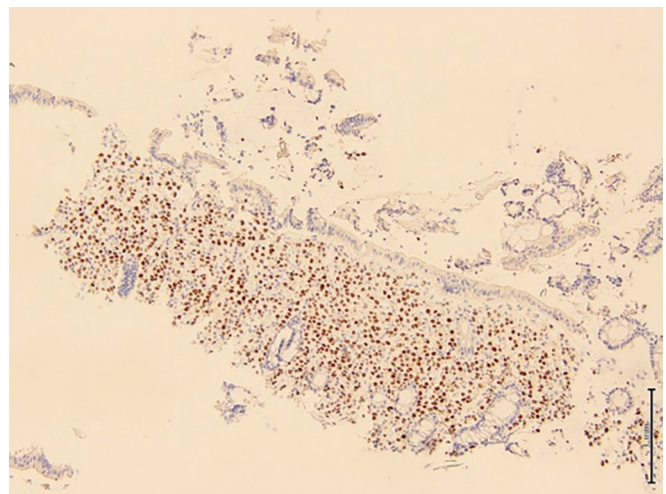


Fig. 3: Neoplastic cells positive for ER on immunohistochemistry

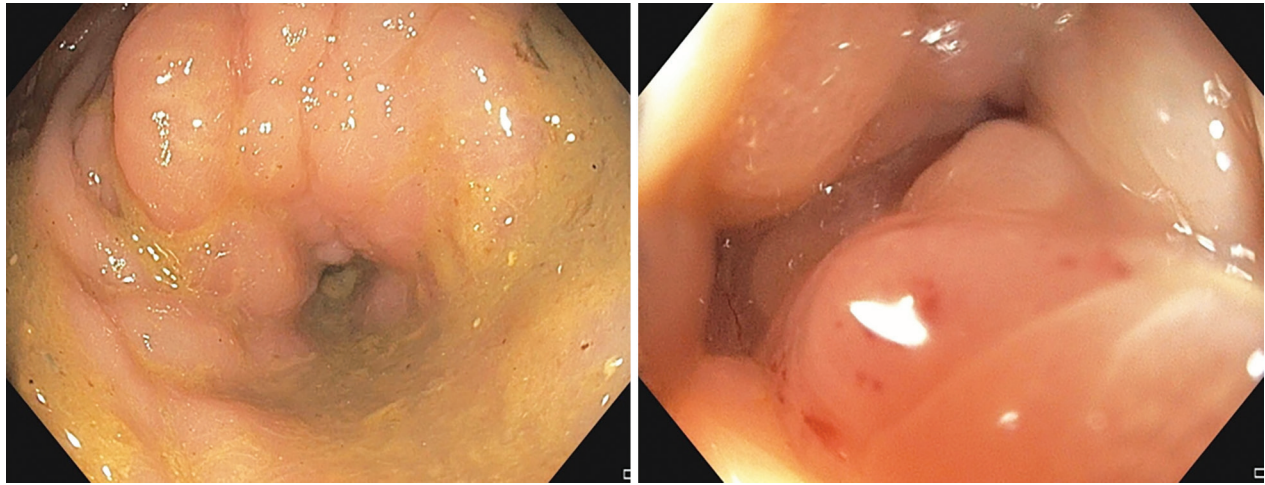


Fig. 4: Colonoscopy showing malignant appearing lesion with severe stenosis at the proximal rectum

Immunohistochemistry was as follows: Pan-CK (positive), ER (positive), and HER-2 (negative).

The most recent whole-body PET/CT done in January 2024 showed progression of the peritoneal and mesenteric metastasis and a newly developed mild bilateral pleural effusion with low-grade metabolic activity. Recently, The National Tumor Board has agreed on the next line of treatment for this patient, which is exemestane-everolimus. PIK3CA mutation analysis was also advised.

Case 2

A 52-year-old woman presented to the emergency department in September 2019 with a 1-month history of constipation, generalized colicky abdominal pain, 7 kg weight loss, nausea, and anorexia. Her medical history included a hysterectomy and repair of iatrogenic bladder injury in 2015. The initial physical examination was significant for generalized tenderness, predominantly in the lower abdomen. A digital rectal examination was performed in the emergency department, and the rectum was noted to be empty, and no masses were palpable. Her abdominal X-ray showed fecal loading, and she was started on laxatives. She continued to experience the same symptoms and was referred to the gastroenterology clinic 2 days later. She underwent a colonoscopy, which revealed a malignant appearing apple-core lesion at the proximal rectum with severe stenosis that could not be bypassed (Fig. 4). The lesion was located 10 cm from the anal verge, and multiple biopsies were taken. Histopathology showed a few signet ring cells with an IHC profile as follows: CK7 (strongly positive), CK20 (negative), CDX2 (negative) (Figs 5 and 6). The findings suggested an origin from the upper GIT, pancreaticobiliary, lung, or genital tract.

Further investigations were done to find the origin of the rectal mass. A CT scan of the chest, abdomen, and pelvis showed the same circumferential rectal lesion seen on colonoscopy. The lesion was 17.5 mm in maximal wall thickness and 7 cm in length, reaching the most caudal part of the sigmoid colon. Multiple small lymph nodes were noted in the mesorectum, right internal iliac, and right external iliac regions. Multiple focal lytic-sclerotic bone lesions were seen scattered all over the vertebral column, which were likely metastatic deposits. The MRI of the pelvis was performed for final confirmation, and the rectal mass was staged as T3 N2 M1.

Five days later, she underwent a PET scan, which revealed bilateral nodular breast lesions. Mammography and ultrasound

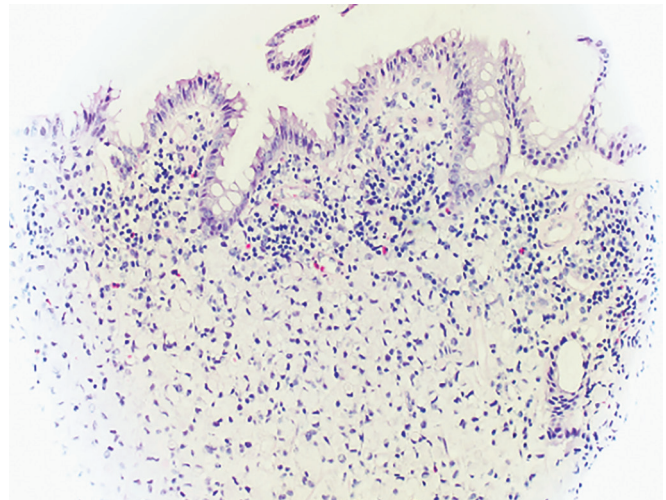


Fig. 5: H and E section of the rectal lesion showing the tumor cells infiltrating the lamina propria of the colonic mucosa in the form of sheets of discohesive cells

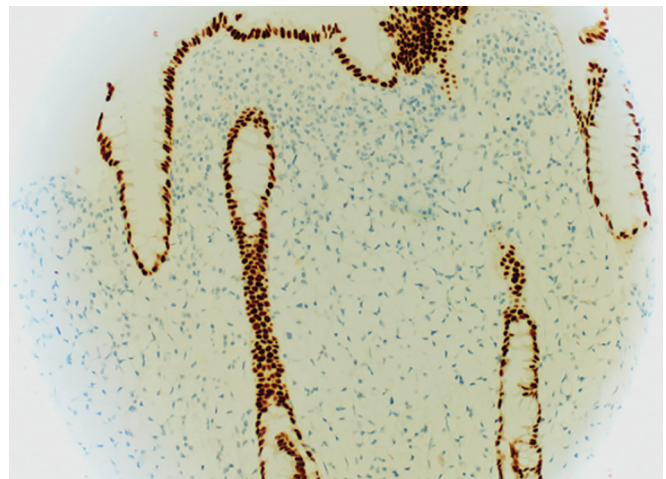


Fig. 6: Rectal biopsy showing negative immunohistochemistry for CDX2, ruling out an intestinal malignancy; an internal control with positive staining for the lining colonic cells is noted

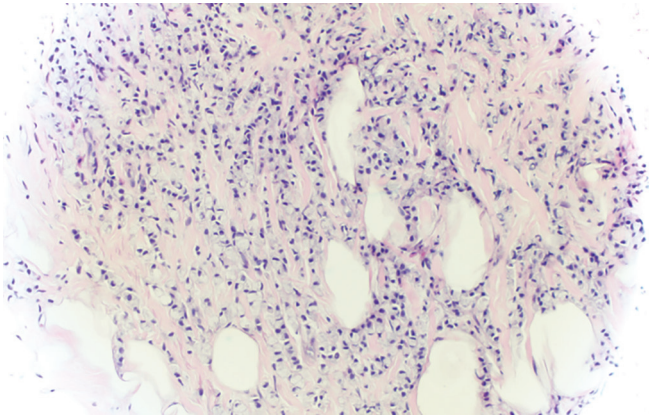


Fig. 7: Biopsy of the right breast lesion showing invasive lobular carcinoma of the breast, infiltrating the tissue in single cell cords, comprising medium-sized cells with an intracytoplasmic lumina

scanning of both breasts confirmed a lesion in the right upper outer quadrant. The lesion was nodular and 16 × 12 mm in size. It was hardly identified by ultrasound and induced posterior acoustic shadowing and a BIRADS IV score was assigned. No discrete masses were identified in the left breast. Bilateral axillary lymphadenopathy was also seen, and most of those lymph nodes showed preserved central fatty hilum.

Ultrasound-guided Tru-cut biopsy of the right breast lesion was done. The patient's histopathology report showed ILC of the signet ring cell variant (Fig. 7). Immunohistochemistry results were as follows: E-cadherin (positive in 30% of signet ring variant), CK7 (positive), CK20 (negative), ER (positive), PR (positive), Her2/neu (negative). The Ki-67 index was 1%.

These pathological results indicated a diagnosis of metastatic ILC and given a clinical stage of T1NxM1. The patient was started on palliative chemotherapy in October 2019 after a discussion at the National Tumor Board. While investigating the breast lesions, she also underwent a laparoscopic loop colostomy to relieve the symptoms of obstruction.

Although the histopathology reports suggested it, there was no final confirmation of the origin of the rectal mass until 2021. A colonoscopy was done to reassess the disease, which did not show an extension of the circumferential rectal mass or any new abnormalities. Biopsies were taken from the rectal mass, which showed colonic mucosa invaded by medium-sized singly dispersed cells with intracytoplasmic lumina. The colonic mucosa was unremarkable, with no evidence of surface ulceration or dysplasia. On IHC, the lesional cells were positive for CK7, ER, and PR, keeping with a breast primary of the invasive lobular signet-ring variant type (Fig. 8).

Since diagnosis, the patient has been on several palliative chemotherapy regimens. The longest progression-free survival (PFS) was 17 months while on Letrozole, Ribociclib, and Denosumab. She was later switched to fulvestrant-ribociclib and remained stable for 1 year.

Genetic testing for the PIK3CA gene mutation was positive. She was then started on Alpeliclib but was not able to continue the cycles due to uncontrolled hyperglycemia. The next line of treatment was everolimus-exemestane, but after 4 months, a follow-up PET/CT revealed disease progression. She was then started on capecitabine in September 2022. During the same period, she underwent two sessions of palliative radiotherapy for intractable rectal pain.

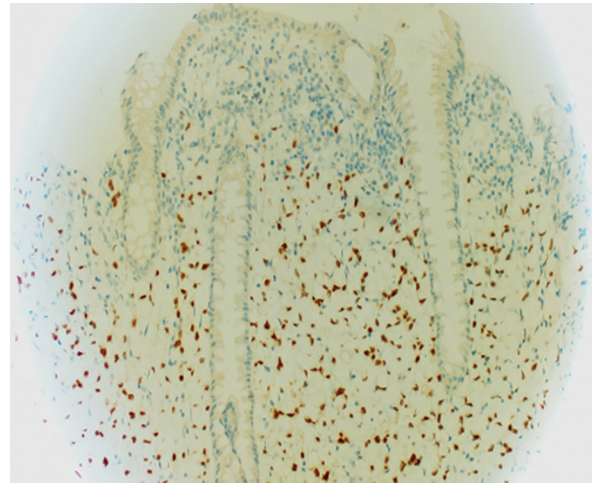


Fig. 8: Rectal biopsy showing tumor cells highlighted by positive nuclear staining for ER

Since starting capecitabine, follow-up scans showed partial disease regression and tumor markers continued to decrease. Her last colonoscopy revealed a rectal stricture at the site of the previously described rectal mass, which indicated regression of the tumor.

DISCUSSION

Breast cancer is the primary cancer found in women and a leading contributor to cancer-related deaths, while colorectal cancer ranks as the third most common cause of cancer mortality.¹ Histologically, subtypes of breast cancer exhibit specific tendencies for distant metastasis. Invasive ductal carcinoma (IDC) of the breast frequently spreads to the liver, lungs, and brain.⁸ Conversely, ILC follows a distinct pattern of metastasis, with a propensity to disseminate to the bones, gynecological organs, peritoneum, retroperitoneum, and the gastrointestinal tract.⁹ According to Otsuka et al., while the occurrence of breast cancer metastasizing to the GIT is uncommon, it is more frequently observed in ILC compared to IDC. Colonic metastasis, in particular, is a rare phenomenon.¹⁰ Another study found that the occurrence of metastases in the GIT outside of the liver, as reported in autopsy studies, shows variability in the literature, ranging from 6% to 18%. The stomach is the most frequently affected organ, followed by the colon and rectum. Gastric lesions appear to be slightly more prevalent compared to colorectal lesions, with incidences ranging from 6 to 18% and 8–12%, respectively.¹¹ According to Sastre-Garau, ILC is the second most prevalent form of invasive breast carcinoma, accounting for approximately 5–15% of cases. Patients diagnosed with ILC typically exhibit a slightly higher age compared to those with non-lobular invasive carcinoma, with a reported mean age of 57 years vs 64 years.¹²

In this case series, Patient 1, diagnosed at age 41 with bilateral ILC in 2015, developed pelvic peritoneal metastasis 3 years later, followed by gastric and colonic metastases identified seven years post-diagnosis. Conversely, Patient 2 presented at age 52 with symptoms of constipation, abdominal distention, and weight loss. A colonoscopy led to a diagnosis of Rectal Adenocarcinoma, and subsequent PET imaging revealed incidental breast lesions, resulting in a diagnosis of ILC of the Signet cell variant.

Classic ILCs are predominantly influenced by hormonal regulation. Approximately 95% of cases exhibit the expression of ER, while PR expression is observed in 60–70% of cases.¹³ Both patients

tested positive for ER and PR but negative for HER-2 in the breast. With regards to the colorectal biopsies, patient 1 tested positive for ER, and negative for PR and HER2. Conversely, patient 2 had a rectal biopsy taken which tested strongly positive for CK7, ER, and PR and negative for HER2. Signet cell carcinoma is “a rare subtype of ILC defined by the presence of signet-ring cells.”¹⁴ These types of tumors show a propensity for involvement of the GIT and tend to present in women of older age, it is also associated with a worse prognosis.^{15,16}

Detecting breast cancer based on gastrointestinal (GI) metastases is challenging due to the nonspecific nature of the associated clinical manifestations. Symptoms such as abdominal pain, diarrhea, nausea, and occasionally asymptomatic presentations are not specific to breast cancer, making it rare for the disease to be identified solely based on these symptoms.^{17,18} Another reason clinicians face challenges in diagnosing colonic metastasis of ILC is due to the macroscopic appearance of the intestinal tract, which can resemble inflammatory bowel disease like Crohn's disease.¹⁹ Considering these challenges, clinicians must differentiate GI metastasis from other GI conditions, this distinction ensures a prompt diagnosis of GI metastasis. Recent studies have revealed that the median time between the initial diagnosis of primary breast cancer and the subsequent diagnosis of GI metastases is approximately 6 years.²⁰ In the cases discussed, the interval between the diagnosis of ILC and the detection of GI metastasis differed. For example, the period from the initial diagnosis with bilateral ILC to the diagnosis of gastric and colonic metastasis was 7 years in case I. On the other hand, in the case of patient 2, the primary breast tumor was found incidentally weeks after the rectal cancer was detected.

The patients discussed both underwent a series of whole body F18-FDG PET-CT scans, and it was found that patient 1 had circumferential colonic wall thickening at mid-part of the ascending colon, while patient 2 had circumferential rectal and sigmoid wall thickening. These observations align with the findings of Matsuda et al. which state that colonic metastases from breast cancer are characterized by diffuse thickening of the intestinal wall, along with ulcerated or nodular lesions.²¹ Endoscopic findings frequently resemble those seen in primary colon cancer or inflammatory bowel disease.²²

The treatment of metastatic breast cancer involves a combination of surgery, radiation, and systemic therapy. While local tumors are typically addressed first with surgery and radiation, with optional systemic therapy, a multifocal disease process is often managed primarily with systemic therapy. Systemic hormonal or chemotherapy, either alone or in conjunction with surgery, has shown positive responses in patients with GI metastases of breast cancer. In cases presenting with acute or subacute symptoms, surgery is necessary for palliative purposes and may also be employed to obtain an accurate diagnosis.²⁰ The patients discussed in this report received different types of medical therapy, including hormonal therapy given that they both tested positive for hormonal receptors. Neither one of the patients underwent therapeutic surgical measures. However, patient 2 underwent a diverting loop ileostomy as a palliative measure for the bowel obstruction caused by the rectal mass. As well as palliative radiotherapy to the metastatic deposits. Patient 1 was recently started on a combination treatment of exemestane and everolimus. On the other hand, patient 2 is currently on palliative medical therapy and is receiving capecitabine.

Based on the literature, the prognosis for patients with GI metastases is generally unfavorable, as survival rates are typically low, with only a small number of patients surviving beyond

2 years.²³ However, both patients in this case have surpassed the estimated survival rate associated with GI metastases. Patient 1 is alive, having survived for 7 years since her initial diagnosis, as well as patient 2, who has surpassed 4 years since her initial diagnosis of colorectal metastasis from ILC.

CONCLUSION

In conclusion, this case report highlights the clinical presentations, challenges, and treatment associated with GI metastases from breast cancer, specifically in ILC. Although the diagnosis can be difficult due to nonspecific symptoms, the reported cases demonstrate that early detection and appropriate management can lead to long-term survival despite the typically poor prognosis. These findings highlight the importance of considering GI involvement in breast cancer patients, and the need for multidisciplinary approaches to achieve better outcomes. Further research and awareness in this area are crucial for improving the understanding and management of GI metastases from breast cancer.

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