

Received: 2019.04.27
Accepted: 2019.06.28
Published: 2019.11.11

Unusual Pattern of Invasive Lobular Carcinoma Metastasis: A Case Report

Authors' Contribution:
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, 58
Final Diagnosis: Metastasis of breast cancer to the sigmoid colon, appendix, and ovaries
Symptoms: Abdominal pain
Medication: —
Clinical Procedure: Abdominal laparotomy
Specialty: Surgery

Objective: Unusual clinical course
Background: Metastasis of breast cancer to the gastrointestinal (GI) tract is not common, however, invasive lobular carcinoma is more likely to metastasize to the GI tract than ductal carcinoma. The simultaneous metastasis of invasive lobular carcinoma to the GI tract and ovaries is an extremely uncommon presentation, which may mimic another rare entity that is peritoneal carcinomatosis secondary to breast cancer. Diagnosis of this entity is difficult as it can masquerade as a primary disease process instead of a secondary one. Treatment is even more difficult due to the sparsity of guidelines regarding this presentation.

Case Report: A 58-year-old female with a history of invasive lobular carcinoma of the left breast treated 5 years prior to presentation with GI symptoms. Workup revealed a stenosis of the sigmoid colon; however, colonoscopy and biopsy did not show signs of malignancy. The patient was initially diagnosed with diverticulitis and given appropriate treatment which mildly improved her symptoms but did not eradicate them. Continued symptoms and failed attempts at diagnosis prompted the decision to perform an exploratory laparotomy which revealed metastasis of invasive lobular carcinoma to the sigmoid colon, appendix, and ovaries.

Conclusions: GI metastasis of breast cancer is a difficult entity to diagnose and treat. Concomitant metastasis to the GI tract and genitourinary system is even more challenging to diagnose and treat. These variable metastasis presentations of breast cancer indicate a need for more specific modalities for follow-up of breast cancer patients especially those with the invasive lobular subtype which tends to metastasize to unusual distant sites and present years after diagnosis and treatment of the primary disease.

MeSH Keywords: Breast Neoplasms • Neoplasm Metastasis • Sigmoid Neoplasms

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/917237>

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Background

Breast cancer is the most common cancer in women. Ductal carcinoma is the most common type of breast cancer with invasive lobular breast cancer being the second most common at 8% to 14% of cases [1]. The metastatic patterns of invasive ductal carcinoma versus invasive lobular carcinoma differ significantly [2]. While the most common sites of metastasis are bone, lung, and liver; invasive lobular carcinoma has a propensity for unusual sites of metastasis such as the gastrointestinal (GI) tract, genitourinary system, and peritoneum. However, GI metastasis is still a rare entity. In a large series of 2604 cases of breast cancer, GI tract metastasis was found to occur in less than 1% of patients [3]. The most frequent site of GI metastasis of breast cancer is the stomach followed by the small bowel then the colon [4]. Another rare site of breast cancer metastasis is the peritoneum with prevalence ranging between 0.5% to 0.7% [5,6]. This report presents a unique case of invasive lobular carcinoma metastasis to the sigmoid colon, appendix, and ovaries 5 years after initial diagnosis and treatment of the primary breast cancer.

Case Report

A 58-year-old female patient presented in August 2004 with a 6-month history of altered bowel habits. The patient was experiencing an increase in frequency of stools to 5 to 6 times daily, that were of small quantities and normal appearance. Along with these symptoms, the patient also had crampy abdominal pain and bloating.

Her past medical history is significant for invasive lobular carcinoma in the left breast diagnosed in 1999 and treated with a total mastectomy, 9 cycles of chemoradiotherapy, and tamoxifen for 5 years. She had a follow-up positron emission tomography (PET) scan done in March 2003 which did not show any recurrence of the disease. The symptoms started in January 2004 and subsequently the patient had a colonoscopy done in June 2004 that showed severe sigmoid stenosis, however, biopsy did not show any evidence of malignancy. With the patient still experiencing symptoms, she underwent a CT scan of the abdomen which showed partial thickening of the sigmoid with pseudo-obstruction of the lumen and multiple cysts of the liver (Figures 1, 2). An initial diagnosis of diverticulitis was made, and the patient was started on antibiotics (ciprofloxacin and metronidazole) which improved her symptoms; however, she was still having bowel movements 3 times a day. As such, the patient underwent a barium enema (Figure 3) in July 2004 which showed irregular stenosis at the sigmoid level of around 6 cm.

The patient presented in August 2004 previous workup. On physical examination, she had a soft non distended

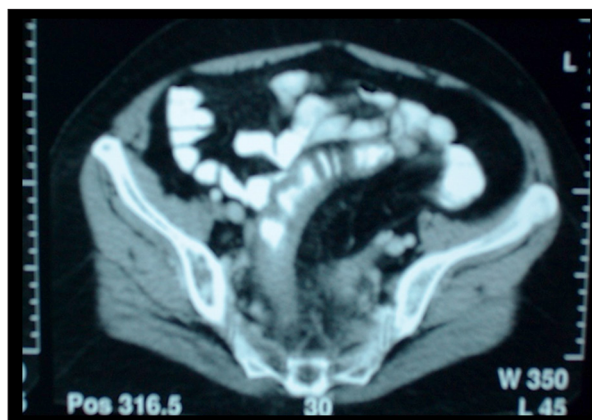


Figure 1. Abdominal-pelvic computed tomography scan with intravenous and oral contrast showing partial thickening of the sigmoid with pseudo-obstruction of the lumen. Possibly a sequela to diverticular disease, however neoplastic disease cannot be ruled out.

abdomen with slight left lower quadrant tenderness and no palpable masses. The computed tomography (CT) of the abdomen raised concerns of disseminated echinococcus infection, which is prevalent in our region (Figure 2), however, echinococcus tests were negative. With all the workup turning back negative, a decision was made to perform an exploratory laparotomy.

Laparotomy revealed an inflamed and stenotic sigmoid colon (Figure 4A, 4B), multinodular ovaries with irregular surfaces, and an indurated and enlarged appendix along with around 50 cc of fluid in the pouch of Douglas. The fluid was sent to cytology and it was positive for malignancy. The decision was made to perform an anterior resection, bilateral oophorectomy, and appendectomy.

Subsequent histopathology of the resected specimens showed metastasis of invasive lobular carcinoma with similar properties to the primary cancer the patient had being progesterone receptor positive and estrogen receptor weakly positive. To note, follow-up investigations did not reveal disease in the contralateral breast indicating metastasis after almost 5 years of treatment of the primary cancer.

Discussion

Metastasis of breast cancer to the GI tract is a rare phenomenon and there are not many large-scale studies regarding this pattern of disease spread. In the largest case series regarding this topic, Asch et al. reported the distribution of GI metastasis as follows: 25% metastasized to the esophagus, 25% to the stomach, 28% to the small bowel, 19% to the colon, and 4% to the rectum [7]. The timing of GI metastasis varies considerably,

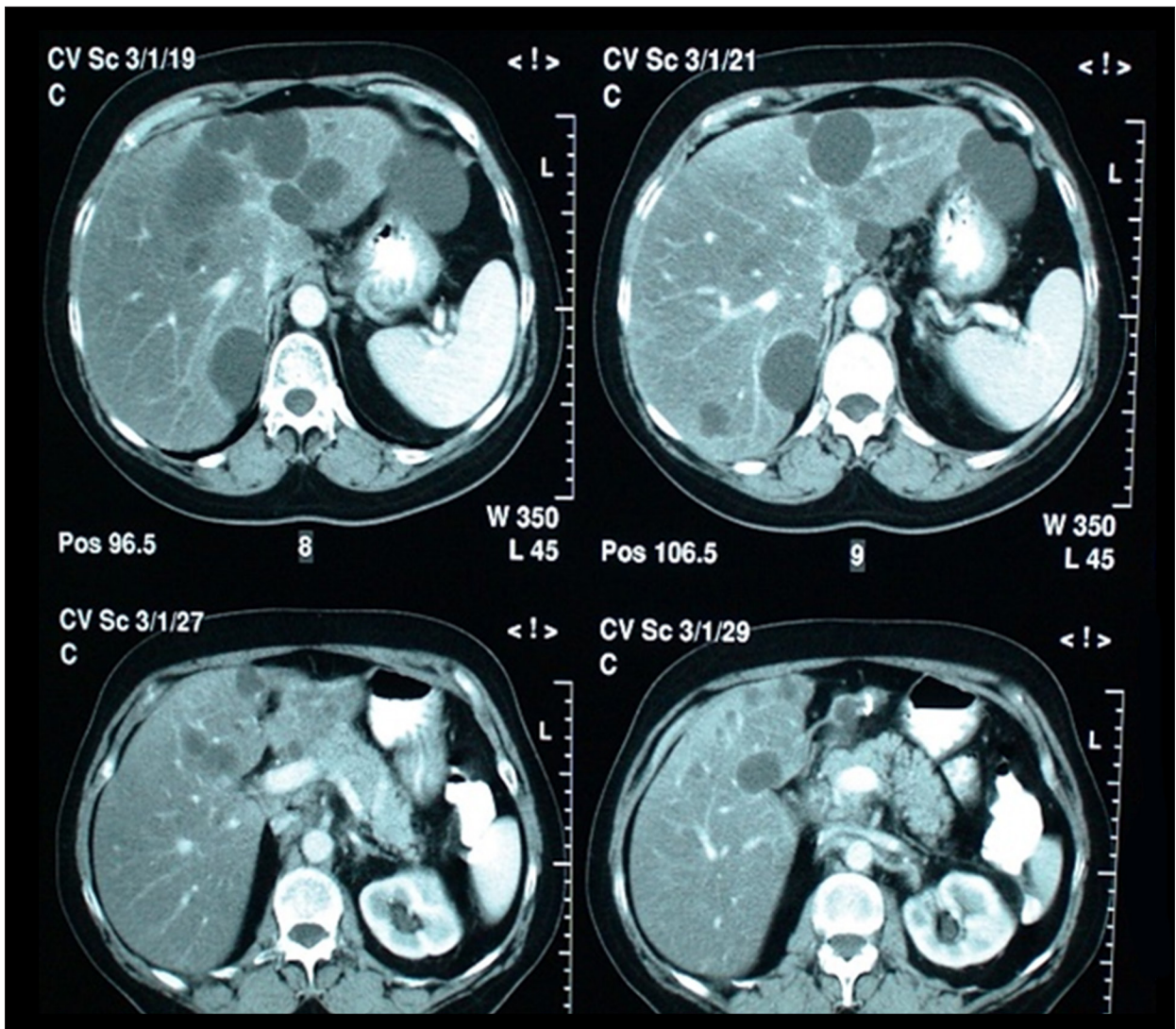


Figure 2. Abdominal-pelvic computed tomography scan with oral and intravenous contrast showing multiple liver cysts.



Figure 3. Barium enema showing irregular stenosis at the sigmoid level (6 cm) with no anomalies in the rectum.

with some reports of simultaneous presentations, and others stating a 26-year interval between initial diagnosis of breast cancer and GI metastasis presentation [8]. On the other hand, metastasis to the genitourinary system is more common than to the GI tract, with 36% of cases metastasizing to the ovaries, and 43% to the uterus [9]. Furthermore, breast carcinoma was found to be the origin or ovarian metastasis in almost 50% of cases [10]. Our patient was found to have simultaneous metastasis to the GI tract and ovaries, a clinical scenario that was only described in 3 reports to the best of our knowledge [1]. We were not able to find a case describing metastasis of invasive lobular carcinoma to the appendix making this case even more unique. Another possible differential diagnosis for our patient was peritoneal carcinomatosis secondary to breast cancer which is a rare entity as well. Peritoneal carcinomatosis secondary to breast cancer has been described in the literature with a prevalence of 0.5% to 0.7% [5,6].

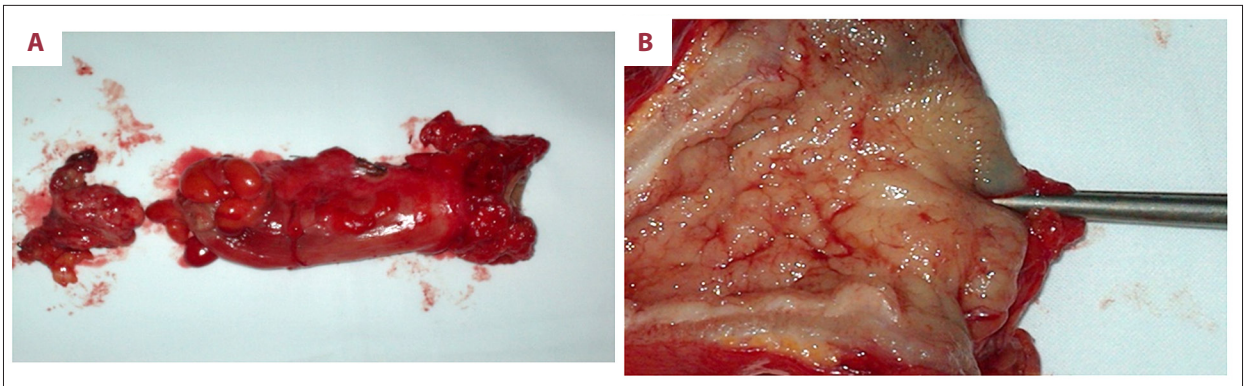


Figure 4. (A) Resected sigmoid colon. (B) Tumor specimens in sigmoid.

The presentation of GI metastasis from breast cancer is variable and unspecific. Most commonly, the presentation is similar to that of a primary GI malignancy, with abdominal pain, early satiety, melena, and obstructive symptoms being frequent [2,11,12]. A common finding of GI metastasis from breast cancer is stenosis, with multiple reports presenting this finding [8,9,13,14]. Approach to the patient with a history of breast cancer and new onset of GI symptoms suspicious of malignancy is the same as that with any patient without a history of breast cancer and includes endoscopic and radiological evaluation. This approach can be misleading, as the diagnosis might not be achieved if the medical history of the patient is not taken into account. These patients might be misdiagnosed with a primary GI tumor or even not diagnosed with malignancy at all, as many reports have mentioned an inaccurate initial diagnosis [8,9,12,14,15]. In a case series of 12 001 patients, McLemore et al. found that 21% of patients presented with metastatic disease masquerading as an alternate disease process with the most common initial diagnosis being disseminated ovarian cancer [2]. Furthermore, 11% of the patients in this case series were not diagnosed with GI metastasis from breast carcinoma until an exploratory laparotomy was performed, as was the case with our patient. With our patient's unusual presentation, the diagnosis of secondary peritoneal carcinomatosis was not considered, as there were no typical signs and symptoms of the disease such as abdominal distention or ascites.

Radiologically, CT scan might reveal evidence of a disease process, however, it fails to provide insight as to the primary location of the disease. In cases of metastasis from breast cancer, imaging might reveal what seems to be primary GI or genitourinary disease process [1]. PET-CT is not recommended for diagnosis of a primary cancer and is best used as a staging and follow-up to treatment modality [9,14]. As for endoscopic evaluation, it is also a non-specific modality for diagnosis of breast cancer metastasis as it can have high rates of false negatives [8,14]. This observation can be explained by the nature of metastatic invasion of the GI tract which starts

in the serosa and moves in towards the mucosa, as such superficial biopsies will not show evidence of disease. However, this does not negate the importance of endoscopy to rule out a primary GI cancer [1,13].

Definitive diagnosis of breast cancer metastasis to the GI tract or genitourinary system can only be made with histopathology. Sample from distant sites will often show features similar to that of the primary breast cancer which is most commonly an infiltrative lobular carcinoma (ILC).

These features include typical arrangement of cells in an "Indian file" pattern, along with immunohistochemistry specific to ILC including progesterone receptor and estrogen receptor expression, and to a lesser extent human epidermal growth factor receptor 2 (HER2) overexpression [1,4,8,9,13–15]. In addition to these properties, ILC features mutation in E-cadherin a cell-to-cell adhesion protein which can explain the propensity of ILC to metastasis to unusual distant sites [4]. All these features make it important to inform the pathologist of patients' history of breast cancer with an emphasis of the subtype in order to determine whether the disease process at hand is a primary one or secondary due to breast cancer metastasis.

Treatment of patients presenting with multiple metastasis of breast cancer is difficult, especially if the sites of metastasis are unusual, such as the combination of sigmoid, appendiceal, and ovarian metastasis in our patient. For these patients, there is no consensus on the method of treatment, as there have not yet been any large-scale studies that compare the efficacy of different managements [1,8,12,13]. Surgical debulking followed by systemic chemotherapy has been described in the treatment of metastatic breast cancer involving more than 1 organ [1,14], however, as with any treatment it should be tailored to the patient and their projected performance status along with quality of life considerations. Prognosis is poor in patients with multiple metastasis sites, as their presentation is often late in the course of the disease. The average survival time in these patients has been described to be about 1 year,

with a partial response to treatment occurring in 50% of patients [16]. Surgical debulking is also a treatment modality for peritoneal carcinomatosis along with hyperthermic intraperitoneal chemotherapy (HIPEC), however, there are no guidelines for the treatment of peritoneal carcinomatosis secondary to breast cancer. A few studies have been published describing the use of cytoreductive surgery and HIPEC in patients with secondary peritoneal carcinomatosis due to breast cancer as well as other primary diseases [17,18]. Combination of cytoreductive surgery and HIPEC in these patients showed improvement in morbidity and mortality [17–19]. However, these studies are small scale ones, and there is no large-scale research due to the rare nature of peritoneal carcinomatosis secondary to breast cancer. It would be interesting to study the role of HIPEC in patients with GI and/or genitourinary metastasis secondary to breast cancer as is the case of our patient.

Conclusions

Metastasis of breast cancer to the GI tract and genitourinary system simultaneously is a rare entity, one which is challenging

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Conflicts of interest

None.