



Isolated Ileocecal Metastasis from Lobular Carcinoma of the Breast: A Case Report

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ABSTRACT

Invasive lobular carcinoma (ILC) is the second most common histologic subtype of invasive breast cancer, accounting for 5–15% of this type. Though its unique propensity to metastasize to the extra-hepatic gastrointestinal tract is well known, isolated colonic metastasis without disseminated or locoregional recurrence is rare. These isolated lesions may be amenable to curative treatment with a better prognosis. Here we present the diagnostic challenge faced while managing the case of a 62-year-old female who was treated for estrogen receptor-positive ILC of the breast 10-years previously, who presented with an ileocecal mass, which on biopsy revealed metastatic ILC. She was treated with laparoscopic hemicolectomy followed by hormonal therapy and remained asymptomatic at 18-months follow-up.

Keywords: Colonic breast metastasis; extrahepatic gastrointestinal metastasis; ileocecal metastasis; invasive lobular carcinoma; lobular carcinoma breast

Cite this article as: Radhakrishnan L, Mukherjee R, Singh BK, Maheswari Y, Dharmashaktu Y, Krishna A, et al. Isolated ileocecal metastasis from lobular carcinoma of the breast: a case report. Eur J Breast Health. [Epub Ahead of Print]

Key Points

- Isolated colonic metastases from invasive lobular carcinoma are rare and manifests with subtle clinico-radiological findings.
- A high index of suspicion and repeated deep biopsies are important for early diagnosis.
- A close follow-up is essential to monitor for the development of multifocal or disseminated disease.

Introduction

Invasive lobular carcinoma (ILC) is the second most common histologic subtype of breast cancer after invasive ductal carcinoma (1). Breast cancers tend to metastasize to the lung, bone, liver and brain, whereas ILC has a higher propensity to spread to the extra-hepatic gastrointestinal (GI) tract (2). Herein, we report the challenges faced during the diagnosis of a rare case of ILC which manifested as isolated colonic metastasis without locoregional symptoms, a decade after initial diagnosis.

Case Report

A 62-year-old female presented with on-and-off colicky abdominal pain with vomiting and abdominal distension for 3-months. In her past medical history she had been treated for ILC of the right breast (stage T2N3M0) 10-years earlier with modified radical mastectomy, adjuvant chemotherapy, radiotherapy to the chest wall and regional

lymph nodes followed by hormone therapy with Anastrozole for 5-years. She remained well in follow-up for 10-years until the onset of her present symptoms. There was no current clinical evidence of locoregional recurrence or distant metastasis and her screening mammogram of the opposite breast and abdominal examination were also normal.

On investigation, complete blood count and renal function tests were normal. Though ultrasonography of the abdomen revealed no abnormalities, contrast enhanced computed tomography showed mucosal thickening of the terminal ileum with an edematous serosal surface. Colonoscopy showed a bulky ileocecal junction but biopsy from the lesion was non-specific. She was managed conservatively but she remained symptomatic and presented with features of subacute intestinal obstruction. A repeat colonoscopy was done, which showed an edematous ileocecal junction with ulcerations and multiple deep biopsies were taken (Figure 1). Histopathological

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Received: 05.02.2025

Accepted: 08.06.2025

Epub: 08.07.2025



examination showed small intestinal mucosa infiltrated by dyscohesive monomorphic tumor cells scattered within the colonic mucosa with signet ring cell morphology, infiltrating into the submucosa. These cells were immunopositive for cytokeratin, mammaglobin and GATA-3 and exhibited loss of E-cadherin, compatible with metastasis from ILC. Further immunohistochemistry showed estrogen receptor positive (5/8), progesterone receptor and human epidermal growth factor receptor 2 negative disease, with a Ki-67 index of 7–8% (Figure 2). A whole-body PET CT also revealed mildly fluorodeoxyglucose (FDG)-avid, non-enhancing, irregular circumferential wall thickening of the terminal ileum and ileo-cecum with partial luminal narrowing, suggestive of malignancy. There were no other foci of FDG uptake in the body (Figure 3).



Figure 1. Colonoscopic image showing an oedematous ileocecal junction with superficial ulcerations

Diagnostic laparoscopy and curative resection of the isolated colonic metastasis of ILC was planned. Intraoperatively, there was no evidence of peritoneal deposits, liver metastasis or ascites and laparoscopic-assisted radical right hemicolectomy and ileo-transverse colon anastomosis was performed. The post-operative period was uneventful and the patient was discharged on post-operative day 3. Histopathology of the resected specimen showed an ulcero-proliferative and infiltrative tumor, involving the cecum and distal ileum, measuring 2.5x2.5x1.0 cm, showing features of lobular carcinoma with transmural involvement and focally involving the serosa with perineural invasion. Six out of 12 resected lymph nodes showed metastatic deposits, with the largest one measuring 8 mm.

After discussion with the multidisciplinary team, the patient was started on Ribociclib and Anastrozole, with 3-monthly denosumab, calcium and vitamin D supplementation. She was switched to Palbociclib, due to a hypersensitivity skin reaction from Ribociclib, which she tolerated well. A repeat PET-CT scan was done in follow-up at 6-months and 1-year was normal. Informed consent was obtained from all individual participants included in the study.

Discussion and Conclusion

ILC has several unique characteristics, such as presentation with a vague ill-demarcated lump, a higher rate of multifocal or multicentric disease with a greater chance of involving the contralateral breast. ILC may be missed on screening mammograms due to subtle clinico-radiological features (3). During treatment, achieving a negative surgical margin is challenging, resulting in increased mastectomy rates and a propensity for late local recurrences (4). ILC typically metastasizes to the extra-hepatic GI tract, retroperitoneum, peritoneum and unusual sites, such as the genito-urinary system (5).

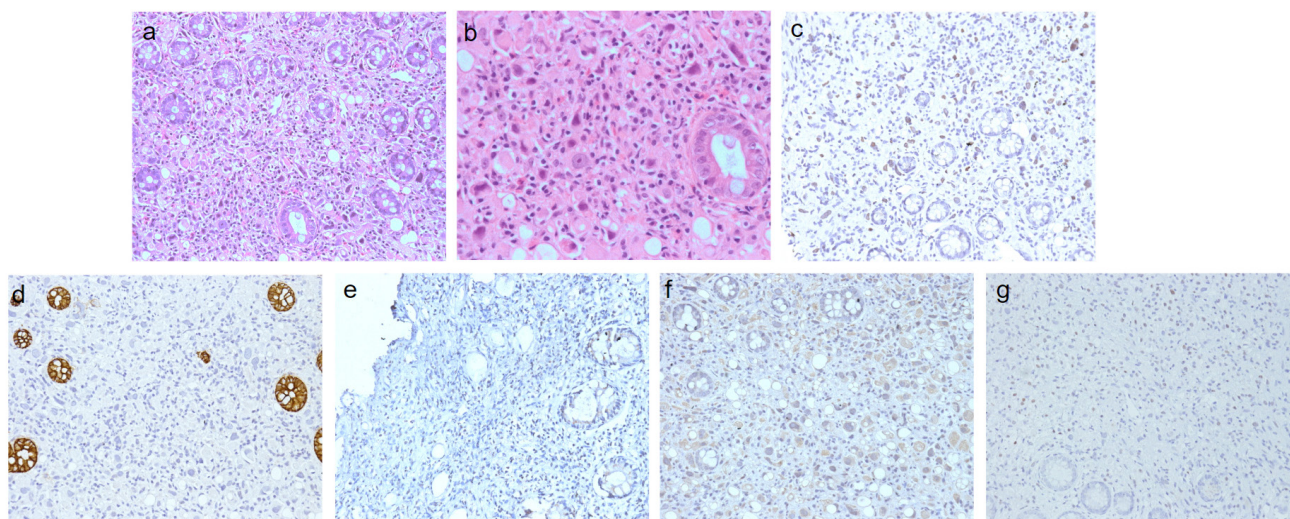


Figure 2. **a.** Section shows dyscohesive monomorphic tumor cells scattered within the colonic mucosa (H&E x200), **b.** Shows scattered tumor cells with vesicular nuclear chromatin, prominent nucleoli and moderate eosinophilic cytoplasm (H&E x400), **c.** Tumor cells showing nuclear immunopositivity immune-stain (GATA3 x200) **d.** Loss of immunoexpression in tumor cells (E-cadherin x200), **e.** Tumor cells show nuclear immunopositivity of moderate intensity (score 2) in 11-33% of tumor cells (score 3) (ER x200), **f.** Tumor cells are immune-negative (PR x200), **g.** Tumor cells are immune-negative (HER2/neu x200)

ER: Estrogen receptor; PR: Progesterone receptor; HER2: Human epidermal growth factor receptor 2; H&E: Hematoxylin and eosin

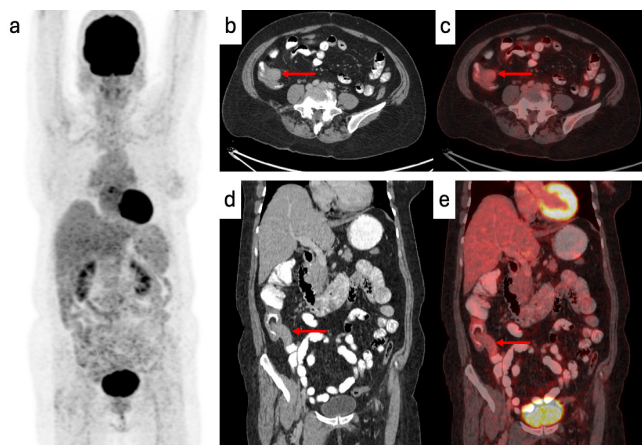


Figure 3. This is the maximum intensity projection image **a.** of F-18 FDG PET/CECT of the patient with invasive lobular carcinoma of right breast. Axial CECT, PET/CECT images **b, c.** & coronal CECT, PET/CECT **d, e.** images show mildly FDG avid non enhancing irregular circumferential wall thickening involving the terminal ileum and ileocecum with partial luminal narrowing (red solid arrow)

CECT: Contrast enhanced computed tomography; FDG: fluorodeoxyglucose; PET: Positron emission tomography

Loss of E-cadherin molecules by lobular breast cancer cells leads to dedifferentiated, non-cohesive tumor cells resulting in diffuse infiltration and a pattern of spread different from invasive ductal carcinoma (6, 7). While most of these metastases are multifocal or disseminated and associated with locoregional recurrence, isolated bowel metastasis is rare. Usually, breast carcinoma spreads to the abdomen by subdiaphragmatic lymphatics resulting in disseminated peritoneal involvement, whereas isolated GI involvement, as in this case, may be explained by hematogenous spread and seeding of tumor cells in the GI tract.

Initial ILC deposits in the intestine are difficult to detect by both endoscopy or radiography because of its appearance as smooth bowel wall thickening that can mimic peristalsis. Colorectal linitis plastica is the term used for diffuse infiltration of all the layers of the colon by ILC, similar to that of the stomach, where a concentric ring or the “target sign” is seen on cross-sectional imaging. FDG avidity of these tumor cells is also comparable to normal tissues, and so can be easily overlooked. It is imperative to take deep and repeated biopsies in these scenarios as the deposits are primarily submucosal and more superficial biopsies remain normal in around half of the patients, as in our case (8).

Most of the cases of ILC with GI metastasis reported to date either had multifocal GI involvement or were associated with locoregional recurrence and distant metastasis (9-13). Switzer et al. (9) described the largest case series of 21 patients and the most frequent sites of involvement were stomach (52%), peritoneum (38%), omentum (19%), esophagus (10%), duodenum (5%), jejunum (5%), transverse colon (5%), and pancreas (5%) with multiple GI site involvement seen in six (28.6%) patients. Presence of isolated colonic metastasis after a decade of initial diagnosis, in the absence of other metastatic sites confirmed thorough metastatic evaluation, thus enabling curative treatment is unique to our case.

Management options for isolated ILC metastasis include complete resection with adequate margins and regional lymph nodal basins.

However, attempts at complete resection should always be preceded by a thorough work-up to rule out evidence of multifocal or disseminated disease. Adjuvant treatment with aromatase inhibitors and CDK4/6 inhibitors or Fulvestrant may delay disease progression. However, given the limited literature in this regard, long-term outcomes and prognosis of such patients are yet to be elucidated and close follow-up is required (14, 15).

Isolated colonic metastases from ILC are rare and manifest subtle clinico-radiological findings. A high index of suspicion and repeated deep biopsies are important for early diagnosis as this may facilitate complete surgical resection which, along with adjuvant therapy, may lead to favourable outcomes. A close follow-up is essential to monitor for the development of multifocal or disseminated disease.

Ethics

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: L.R., R.M., B.K.S., Y.M., Y.D., A.K., V.S.; Concept: L.R., B.K.S., A.K., V.S.; Design: L.R., R.M., B.K.S., A.K., V.S.; Data Collection or Processing: L.R., R.M., B.K.S., Y.M., Y.D., A.K., V.S.; Analysis or Interpretation: L.R., R.M., B.K.S., Y.M., Y.D., A.K., V.S.; Literature Search: L.R., R.M., B.K.S., Y.M., Y.D., A.K., V.S.; Writing: L.R., R.M., B.K.S., Y.M., Y.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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