Annals of Medicine and Surgery 78 (2022) 103841

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Case Report

# Rectal metastasis originating from breast cancer: A rare case report

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ARTICLE INFO

*Keywords:*
Breast cancer
Rectal metastasis
Rectal cancer

ABSTRACT

*Introduction:* Gastrointestinal tract involvement in breast cancer is rarely encountered clinically. Data about this condition is limited and mostly from case reports.
*Case presentation:* We report a case of rectal metastasis originating from breast cancer, which presents after a long-term latency of initial diagnosis. The patient had a history of diagnosis and treatment of stage II triple-negative breast cancer with mastectomy and adjuvant chemotherapy and radiotherapy. She showed no signs of recurrence up to eleven years, then presented with hematochezia and mild constipation. A rectal lesion was found on colonoscopy, which raise the initial suspicion of primary rectal cancer, but surprisingly, immunohistochemistry staining of the rectal specimen confirmed the origin of breast cancer.
*Clinical discussion:* Breast cancer with rectal metastasis is very rare. Immunohistochemistry combined with medical history is essential for definitive diagnosis in this situation. Mammaglobin and GCDFP-15, CDX2, CK20, and CK7 help differentiate the origin from the breast or the rectum.
*Conclusion:* Though breast cancer metastasizing to the rectum is a rare event, physicians should be aware of this differential diagnosis, even in patients with a remote history of breast cancer.

## 1. Introduction

Breast cancer is the most common cancer in women. Breast cancer often metastasizes to the lymph nodes, bones, brain, liver, and lungs. Metastasis to the gastrointestinal tract (GI tract) is rare, accounting for only 0.7% [1]. Of which the stomach and small intestine are more commonly involved compared to colorectum [2]. Distinguishing this condition from primary colorectal cancer is crucial since the treatment and prognosis are completely different. Here we report a case of rectal metastatic from breast cancer after eleven years of initial diagnosis and briefly review the literature. This work has been reported in line with the SCARE 2020 criteria [3].

## 2. Case presentation

A 49-year-old female patient came to our hospital with complaints of hematochezia and dull abdominal pain that manifested for about two weeks. She has no symptoms of cough, no shortness of breath, or chest pain. She also reported a history of stage II right-sided breast cancer that was treated with mastectomy, adjuvant chemotherapy, and radiotherapy eleven years ago. The pathology finding at that time was invasive ductal carcinoma, a triple-negative subtype with three out of fourteen positive axillary lymph nodes. The patient had no other comorbidities, no history of smoking, drug or alcohol use. The patient was discharged from the hospital and continued to be examined annually. However, in the last two years, due to the covid pandemic, the patient did not go to the hospital for medical examination. On clinical examination, she showed no signs of mild anemia and no abnormal abdominal mass. No lesions were detected on the right chest wall and left breast as well. Digital rectal examination revealed an ulcerated-like rectal lesion located 4 cm from the anal verge. Colonoscopy was then performed, which revealed an infiltrating rectal lesion occupying half of the rectal circumference. (Fig. 1). Abdominal-pelvic computerized tomography (CT) showed mild thickening of the rectal wall and no suspected abnormal regional lymph nodes. (Fig. 2). The chest computed tomography scan showed multiple opacities, regular margins, and scattered two lung fields, which were indicative of lung metastases. Bone scan did not detect bone metastases. A core biopsy of the rectal lesion was performed, and histopathological findings indicated a carcinoma, which raised the initial diagnosis of primary rectal carcinoma metastasis to the lung. However, given her medical history of breast cancer, immunohistochemistry (IHC) staining was performed, which

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https://doi.org/10.1016/j.amsu.2022.103841
Received 21 April 2022; Received in revised form 17 May 2022; Accepted 17 May 2022
Available online 20 May 2022

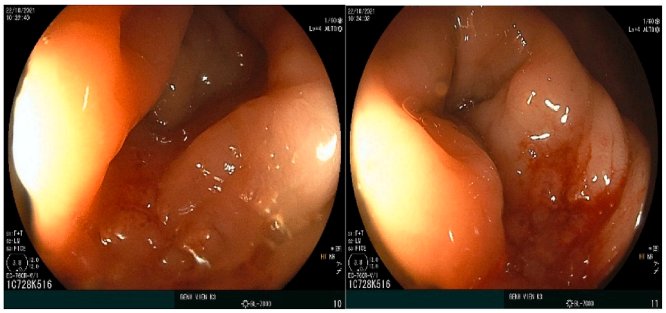

**Fig. 1.** The endoscopic image of the rectum shows 4cm from the anal margin; there is a complex infiltrating ulcerative lesion occupying half of the circumference.

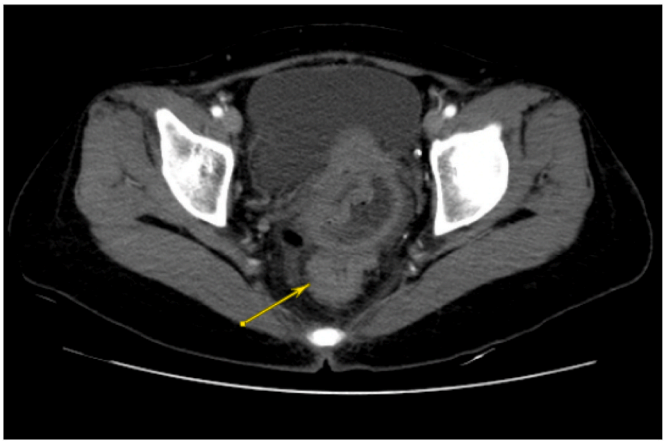

**Fig. 2.** On the computed tomography image shows slight thickening of the rectal wall.

was confirmed as original from breast cancer (positive staining for GCDFP-15, Mamaglobin, GATA3, E-cadherin, CK7, ER (+) 5%, PR (++) 3%, and negative staining for CK20, CDX2, Her2/neu). (Figs. 3 and 4). No other sites of recurrence were detected elsewhere. Thus, she was diagnosed with recurrent breast cancer metastasizing to the rectum and the lung. BRCA germline mutation testing was performed and showed a negative result. Our tumor board had decided to treat the patient with gemcitabine-carboplatin regimen and stopped hematochezia after two cycle. However, after six cycles of chemotherapy, the disease progressed to bone metastases, so we decided to switch to a 3-week cycle of paclitaxel. It has now been six months since the diagnosis of relapse; she just completed the second cycle well tolerated without any complication. We intend to continue the 3-week paclitaxel chemotherapy regimen until disease progression or when the patient cannot tolerate it.

## 3. Discussion

The gastrointestinal tract (GI tract) is not commonly involved in breast cancer, which accounts for only less than 1% of all breast carcinoma cases [1]. Of which the stomach and small intestine are more commonly involved compared to colorectum. In a large review, of 206 patients with GI tract metastases originating from breast cancer, only 7% had metastases to the rectum [2]. Notably, despite being accounted for only less than 15% of all histologic breast cancer subtypes, invasive lobular carcinoma (ILC) is much more frequently encountered in metastasizing to the GI tract, rather than the more common invasive ductal carcinoma (IDC) [2]. In a study of 96 breast cancer patients with GI metastases, there were 56 patients who had lobular carcinoma, while only 17 patients had ductal carcinoma [4]. Another study conducted by McLemore et al. also revealed that ILC contributed to 64% of all GI metastases [5]. The concrete mechanism for this phenomenon is still unclear, though this could be attributed to the different methods of invasion in ILC with loss of E-cadherin and the distinct shape of lobular cells that favoring trapped in the GI tract [6]. Thus, our patient with an IDC subtype metastasizing to the rectum is rarely encountered and reported.

As breast cancer patients live longer, the rate of recurrence and metastasis gradually increases over time. Rectal metastases from breast cancer may present as late as many years after treatment, even when the patient is diagnosed at an early stage. Notably, GI metastases could occur after a long-term latency of up to 30 years [7]. The median time to metastasis was 6 years (0.25–12.5 years), as was 11 years in our case [8]. Thus, oncologists and gastroenterologists should be aware of the relatively high prevalence of late disease metastasis in breast cancer patients even with an unusual site like the rectum.

Clinical symptoms of breast cancer metastasized to the rectum include abdominal pain, bloody stools, constipation, or bowel obstruction, so it can be easily confused with inflammatory bowel disease or primary rectal cancer. Imaging findings could help to differentiate between these diagnoses. On colorectal endoscopy, rectal metastasis lesions usually present with diffuse infiltrate pattern, as shown in our case, different with mass-like lesions protruding into the lumen in most primary rectal cancers [8]. This characteristic could be clarified on magnetic resonance imaging, which showed diffuse concentric rectal wall thickening relating to submucosa and musclaris propria involvement with sparing of the mucosa and hypointensity on T2-weighted imaging. In contrast, primary rectal cancer lesions tend to have more eccentric wall thickening with mucosal disruption and intermediate to hyperintense on T2-weighted imaging [8]. In our case, an abdominopelvic CT scan was performed, instead of a pelvic MRI at the discretion of her physician. In fact, her diagnosis CT scan, as shown above, brought little information of the rectal lesion. Therefore, cases with endoscopic appearance unfavoring primary rectal lesions like our case should be undergone pelvic MRI and be carefully diagnosed before treatment.

Immunohistochemistry staining is the most important result needed to identify the origin of rectal lesions. Our patient had positive staining for CK7(+), and negative for CK20(−), suggesting that metastases may be of breast, ovarian, lung, endometrial, or thyroid origin [9]. This is an important finding since only 2% of primary rectal cancers have CK7 (+)/CK20 (−) [10]. CDX2 is a homeobox gene that encodes a transcription protein factor critical for the development of intestinal epithelium. CDX2 is expressed in 97% of rectal tumors [11]. Our patient had CDX2 (−), CK20(−), CK7(+), so primary rectal cancer could be safely excluded. GCDFP-15 is a glycoprotein originally isolated in human breast gross cystic fluid, and a marker of apocrine differentiation, including apocrine carcinoma of the breast. Thus, it is a diagnostic marker for mammary differentiation in histopathology. Mammaglobin is also a marker for breast tumors, and it is positive in about 84% of metastatic breast cancers [12]. Mammaglobin is more sensitive but not as specific as GCDFP-15 for diagnosis [13]. Therefore, our patient with positive staining for Mammaglobin and GCDFP-15 could be diagnosed as breast cancer metastasizing to the rectum.

In our case, our patient had an ER (+) 5%, a PR (++) 3%, even though the histopathological result of the primary tumor was triple negative. In many studies, the change in the endocrine profile of primary and metastatic tumors ranged from 10.3% to 14.2% [14,15]. Although, this change is usually from positive to negative HR. However, the opposite change was still reported. Subgroup analysis in the study by Thomas et al. showed that in triple-negative breast cancer, 18% of patients had phenotypic change compared with the primary tumor, with most HR gain (79%) [15]. Survival was reported to be worse for positive to negative endocrine change but not different for negative to positive change [15]. Therefore, we should re-biopsy metastatic tumors in breast cancer to assess ER, PR, and HER2 status. The mechanisms responsible for changes in biomarker expression between primary and recurrent

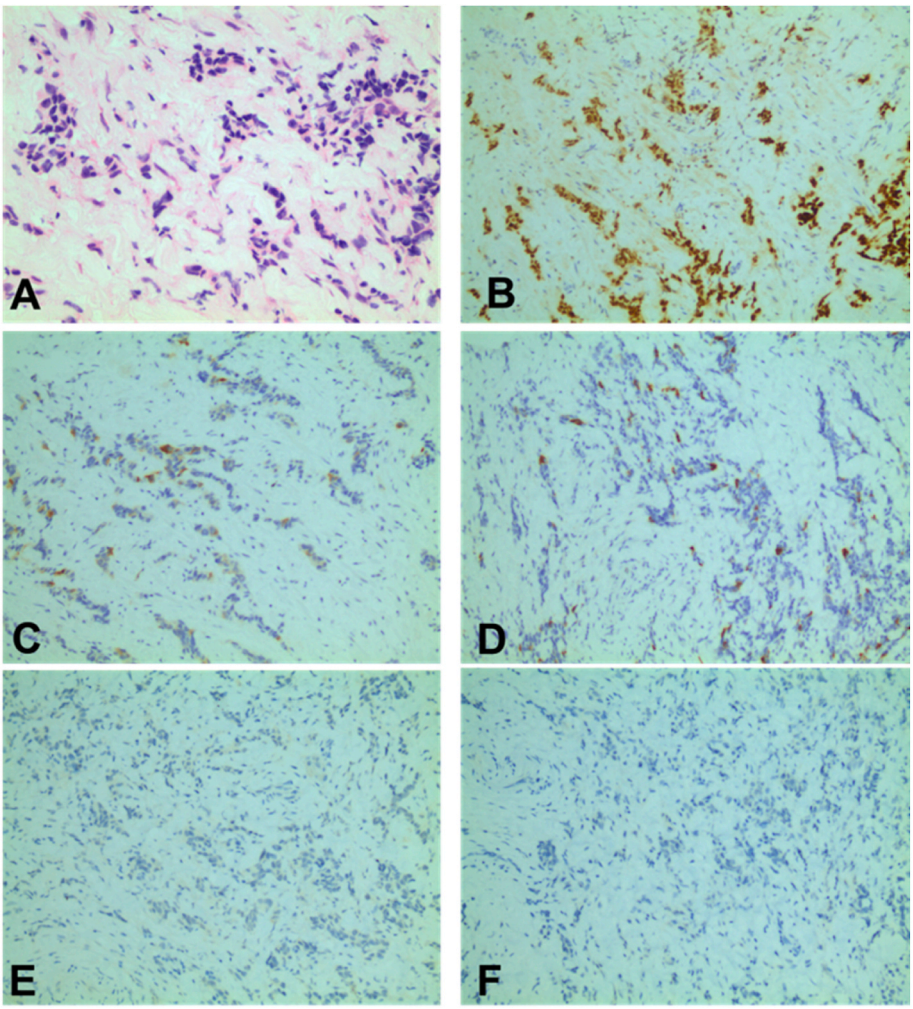


**Fig. 3.** Histopathology and immunohistochemical stain. Invasive carcinoma with nests and cords of tumor cells that have mild pleomorphic nuclei and a high nuclear-cytoplasmic ratio (A). Tumor cells positive for GATA3 (B), GCDFP-15 (C), Mammaglolin (D), and negative for CK20 (E), CDX-2 (F) (A-Hematoxylin and eosin, x400; B, C, D, E F- Immunohistochemical stain, x200).

breast cancer are not clearly understood; however several hypotheses have been put forward. One is methodological and technical errors; the other is intra-tumor and inter-tumor heterogeneity, the ability of tumors to generate tumor clones and clones with different molecular properties, and biological changes in tumor tissue after treatment [15]. Therefore, we should re-biopsy metastatic tumors in breast cancer to assess ER, PR, and HER2 status. In terms of treatment in low-estrogen positive (positive in 1%–10% of nuclei staining) and Her-2/neu negative breast cancer, the available options include PARP inhibitors, endocrine therapy, and conventional chemotherapy. However, it has been well documented that low-estrogen positive breast cancer patients had no significant difference in terms of recurrence-free survival, disease-free survival, and overall survival, compared to ER-negative ones, even if treated with endocrine therapy [16,17].Besides, our patient had a negative result for germline BRCA testing that ruled out the PARP inhibitors option. Thus, we decided to give her chemotherapy with gemcitabine and carboplatin doublet regimen.

Although there have been many advances in diagnosing and treating breast cancer, patient survival times have improved. However, the prognosis of the gastrointestinal metastatic breast cancer group is still poor. The average survival time from detecting gastrointestinal metastases is 1 years [4]. As in our case, the patient presented with rectal and lung metastases simultaneously; although bleeding and difficult defecation were partially improved, the patient also progressed rapidly after six cycles of chemotherapy gemcitabine - carboplatin Due to limited data, surgery such as low anterior resection and abdominoperineal resection has not been shown to improve survival in this situation. However, physicians should closely monitor patients, and consider the role of surgery in cases of life-threatening conditions like massive bleeding, obstruction, and perforation.

## 4. Conclusion

Though breast cancer metastasizing to the rectum is a rare event, physicians should be aware of this differential diagnosis, even in patients with a remote history of breast cancer. Treatment guidelines for this condition are unavailable due to the scattering data. At this time, first-line systemic therapy is widely used, but the role of local therapy in rectal lesions still needs further validation.

## Sources of funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Ethical approval

The manuscript approved by ethical committee of Viet Nam National cancer hospital.

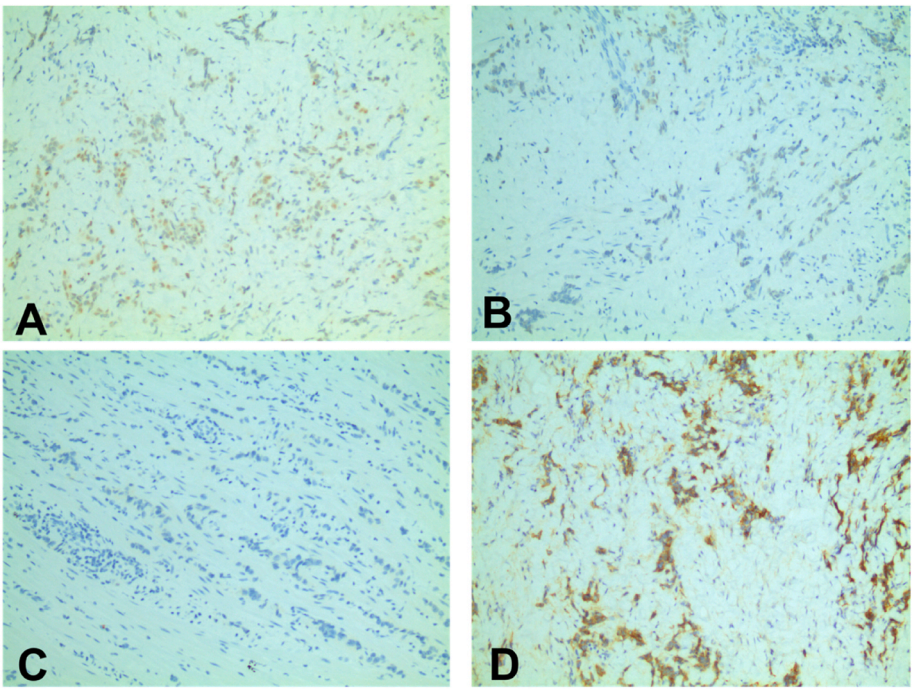


**Fig. 4.** Hormonal receptors immunohistochemistry. (A) Estrogen receptor (ER +, 5%), (B) Progesterone receptor (PR ++, 3%), (C) Human epidermal receptor protein-2 (HER-2) negative and (D) E-cadherin positive (A, B, C, D, x200).

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. The manuscript is carefully reviewed to avoid patient identification details and/or figures.

## Author contributions

Dung Anh Hoang: primary doctor who treated the patient, revised manuscript.

Anh Quang Nguyen: doctor who treated the patient, wrote manuscript.

Manh Duy Pham: doctor who treated the patient, revised manuscript.

Khuyen Thi Nguyen: Follow up the patient, revised manuscript.

## Registration of research studies

This is not an original research project involving human participants in an intervantional or observational study but a case report. This registration is was not required.

## Guarantor

Anh Quang Nguyen is guarantor of this submission.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

There is no conflict to be declared.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103841.

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