

## Hoof beats could mean zebras: A rare late metastasis of breast carcinoma in the rectum

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### ABSTRACT

Breast cancer metastasis is most commonly observed in bone, lung, liver, and brain and is rarely observed in the gastrointestinal tract (GI). In rarer cases, GI metastasis reaches the rectum and generally presents as late metastasis. The type of breast cancer usually associated with GI metastasis is invasive lobular carcinoma; however, few case reports also show their association with invasive ductal carcinoma (IDC). Here, we report a case that unfortunately is a coalescence of all these atypical events, with metastatic rectal linitis plastica (RLP) of the breast, 15 years after the treatment of the primary tumor, originating from IDC. This is the first case report from India, reporting the late metastatic presentation of breast cancer as RLP. The report emphasizes the need to correlate persistent GI symptoms to breast cancer history; however, late the presentation may be.

**Key words:** Breast cancer, Invasive ductal carcinoma, Late metastasis, Linitis plastica, Rectal metastasis


Metastatic disease though an important contributor to cancer-associated mortality still remains elusive. In the case of breast cancer, metastasis may manifest itself within months of completion of treatment or in rare cases, may also relapse after decades [1]. The most common sites of metastasis of breast cancer are the bone, lung, liver, and brain while gastrointestinal (GI) metastasis is rare. Of these GI metastasis cases, only about 4% metastasize to the rectum. Most GI metastasis from the breast is from a lobular primary [2]. There have been only a handful of case reports of ductal carcinoma metastasizing to the rectum and very few of these present features of linitis Plastica [3,4]. In most reported cases, Linitis is of lobular origin but in this case, the ductal carcinoma recurs as linitis plastica of the rectum. This is the first case report from India, reporting the late metastatic presentation of breast cancer as Rectal Linitis Plastica (RLP). The aim to present this case report is to highlight that the diagnosis of current unrelated symptoms still needs to be correlated with breast cancer case history even though it might be archived.

### CASE REPORT

A 57-year-old patient presented with recurrent GI symptoms and sudden extensive weight loss. Since September 2015, she had

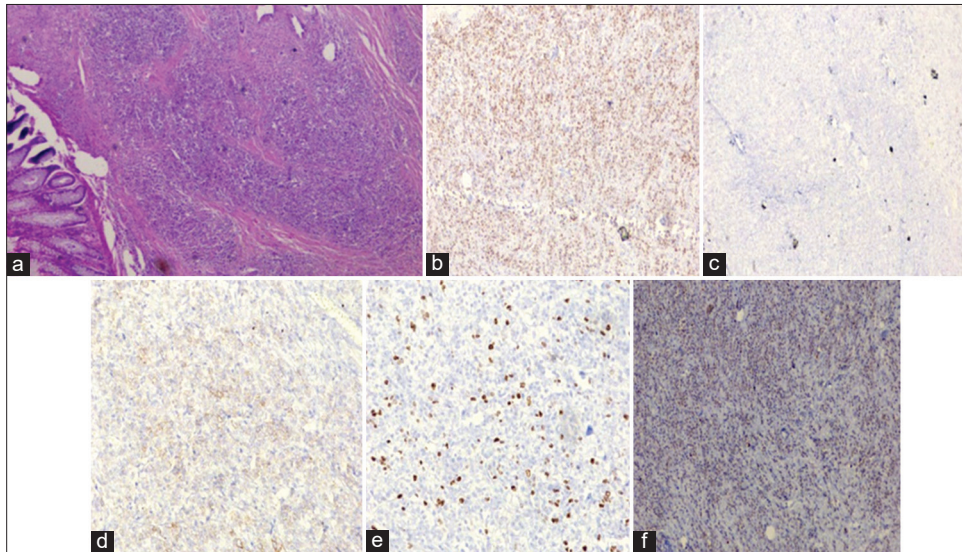
been suffering from abdominal pain, cramps, and rectal tenesmus. For almost a year, she was treated with symptomatic medications comprising of Cifran, Protobid, Vibact, Normaxin, Darolac IBS, SOS Imodium along with diet restriction of triggers (milk, wheat, and fruit juices). Rectal endoscopies were done twice in this period with mucosal biopsies which turned out to be normal. In June 2016, magnetic resonance imaging of the pelvis revealed double-layered symmetrical circumferential wall thickening, preserved mucosa, involving rectal and anal canal with mesorectal fat stranding suggestive of the diffuse infiltrating lesion and mixed plastic and lytic bone lesions likely representative of metastatic spread. A trucut deep biopsy was then performed of the rectal wall which finally revealed metastatic rectal adenocarcinoma consistent with the following immunohistochemical profile: Estrogen Receptor (ER), Progesterone Receptor (PR), Ki 67, and GATA Binding Protein (GATA3) positive, and CK7, CDX-2, and human epidermal growth factor receptor 2 (ERBB2/Her2) negative (Fig. 1).

Fifteen years ago, at age 37 years, she had been diagnosed with invasive ductal carcinoma (IDC) of the breast. At that time, she underwent a modified radical mastectomy and was staged as T1N0M0 with the following immunohistochemical profile: ER and PR positive. She was subsequently treated with Tamoxifen (10 mg) for five years. She also had a familial history of cancer

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**Figure 1: Immunohistochemical analysis of rectosigmoid colectomy (a) H&E Staining (b) ER Positive (c) PR Negative (d) HER2 Negative e. Ki67 (30%) f. p53 (50%)**

with her mother being diagnosed with breast carcinoma at age 67 years with metastases to bones and lungs. The patient was started on Injection Denosumab + Anastrozole + CCM. A colonoscopy in September 2016 demonstrated clinical disease regression. Whole body positron emission tomography-computed tomography (PET-CT) done in Feb 2017 showed stable disease. In July 2017, a follow-up PET-CT showed disease progression in the form of an increase in the size and extent of circumferential wall thickening involving the rectum and anal canal as compared to the previous PET scan. As such, it was decided to excise the tumor and in August 2017, the patient underwent robotic abdominoperineal resection. She was put on hormonal therapy (Exemestane and Inj Exgeva).

In Nov 2017, she developed posterior vaginal wall metastatic nodules. PET-CT done in Dec 2017 showed some increase in F-fluorodeoxyglucose uptake in L2 vertebral lesion. She then underwent palliative radiation of 30 Gy in Dec 2017. In March 2018, she developed new metastatic deposits in the right lower abdominal skin, possibly at the scar site. She was started on Fulvestrant, Exgeva, and Palbociclib. She developed post-treatment complications and was hospitalized for symptom management but unfortunately, the patient passed away in 2018.

## DISCUSSION

RLP represents 0.1% of rectal cancers and most of them are from metastatic deposits. Rectal involvement in the form of linitis plastica has always been in the form of anecdotal case reports. Diagnosis is often delayed as GI symptoms are often non-specific such as rectal pain, tenesmus, changed bowel habit, etc. Endoscopy can miss these cancers due to the lack of mucosal involvement [5] and hence, a deeper biopsy involving submucosa and muscularis propria is needed to diagnose these tumors. Differentiating a metastasis from a primary colonic tumor is difficult and can be done by noting normal colonic epithelium surrounding the tumor deposit without dysplasia or atypia.

Our patient too had these features wherein diagnosis of Linitis was delayed by a year while endoscopic findings seemed benign. She suffered a lot for a year from 2015 to 2016. She had severe loose motions sometimes also causing incontinence and making her confined to her home. Twice she underwent colonoscopy and superficial mucosal biopsies which were obviously unable to pick up a deeper problem. Due to this delay, she already had significant rectal and lymph node involvement with skeletal metastasis by the time she was finally diagnosed and despite excision and chemotherapy, she succumbed to the disease.

The GI tract is an unusual site for metastatic breast cancer. The colon and rectum are even rarer as sites of metastasis [1]. GI involvement has also been seen more frequently with lobular breast cancer [6]; however, in this case, the primary was an IDC. The preponderance of lobular carcinoma showing GI metastasis is attributed to the tropism of lobular cells, their preponderance of being Her2 negative, and the lack of cohesion of cells due to E-cadherin inactivation [7].

ER-positive tumors do have a tendency to delay recurrences, at the rate of about 2% per annum for at least 15 years, even after 5 years of tamoxifen therapy [8]. Metastases have been reported from 6 to 12 years after primary cancer by Schwarz *et al.* [9] It has been suggested that certain estrogen-positive tumors, about 20%, which have a high Ki 67 index upward of 10%, even 2–4 weeks after starting therapy may be endocrine resistant and might respond better to other systemic therapy [10]. Our patient had a Ki 67 of about 8–10%.

The NSABP B-33 had to stop the accrual of patients and offer all of them additional 5 years of Exemestane after 5 years of Tamoxifen due to significant benefits with regards to DFS and RFS [11]. Similar results were shown in the ATLAS trial where women with hormone receptor-positive early-stage breast cancer were randomized to 5 versus 10 years of Tamoxifen which showed further reduction in recurrence and mortality, particularly after 10 years [12].

As this patient's germline testing did not reveal any disease-causing mutation or novel variant that was considered deleterious, her disease might have been sporadic and not due to an inherited germline mutation. Somatic mutational analysis of the tumor identified a mutation in the Helical Domain (exon 9) of PIK3CA (c.1633G>A p.E545K). Although a few PI3K inhibitors have been developed and are in varying stages of clinical testing, the patient declined to enroll in any clinical trial. RLP resembles the rare primary colon adenocarcinoma, signet ring cell carcinoma. Although PIK3CA mutational burden is reported to be low in primary signet ring cell carcinomas, PIK3CA mutations are associated with recurrence in colon cancers [13,14]. Interestingly, while the report suggests an association of germline PIK3CA mutations with recurrence in breast cancer cases, data on mutational profiles specific to RLP recurrence are lacking [15].

## CONCLUSION

GI metastasis from primary breast cancer is known to occur many years after the primary has been treated. Clinicians and oncologists need to keep in mind this when dealing with persistent, new-onset GI symptoms of such patients. A high index of suspicion is necessary for these to be diagnosed and treated early. Furthermore, hormonal therapy should be extended for 10 years in hormone receptor-positive patients to reduce the risk of distant recurrence and metastasis.

## ETHICS STATEMENT

Written informed consent was obtained from the patient's guardian for performing and publishing this study.

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