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Breast Metastases of Rectal Cancer: A Case Report and Review of the Literature

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Abstract

Breast metastasis from gastrointestinal cancers is uncommon, accounting for 0.5% to 2% of breast cancer cases. The clinical and radiological manifestations may resemble those of primary breast cancer, making accurate diagnosis challenging. Here, we present the case of a 26-year-old female with breast metastasis from rectal cancer. This report describes the patient's clinical presentation, diagnostic workup, and management, as well as a review of current literature. The aim of this case report is to highlight a rare clinical presentation, raise awareness of uncommon metastatic sites of rectal cancer, and emphasize the importance of distinguishing between primary and metastatic breast cancer to guide appropriate treatment. Key findings include the rapid progression of the disease, the challenges in management, and the poor prognosis associated with such metastases.

Keywords

Rectal Cancer, Breast Metastasis, Immunohistochemistry, Colorectal Cancer, Metastatic Disease

1. Introduction

Mammary metastases from digestive cancers are rare and exceptionally reported in the literature. They account for about 2% of breast cancers. Mammary metastases can be confused with a primary cancer and lead to inappropriate and mutilating treatment. The clinical and radiological signs of mammary metastases are not specific. Given the differences in management and prognosis, it is crucial to distinguish between primary and metastatic breast cancer. Metastatic disease spreading from the rectum to uncommon sites, such as the breast, is associated with a significantly poor prognosis. This case report highlights the diagnostic and

therapeutic challenges in managing such rare metastases and underscores the importance of considering metastatic disease in patients with a history of rectal cancer who present with new breast masses.

2. Case Presentation

2.1. Patient

26-year-old female with no significant comorbidities.

2.2. History of Current Illness

The patient initially presented with anal pain, mild rectal bleeding, and episodes of constipation lasting four months. She consulted a gastroenterologist, who performed a colonoscopy and biopsy, revealing a rectal tumor. She was subsequently referred to the University Hospital for further evaluation and management.

2.3. Initial Physical Examination

-General Examination: WHO performance status 0; conjunctiva normally colored.

-Abdominal Examination: Soft abdomen, normal breathing, no signs of tumor syndrome (e.g., no hepatomegaly or splenomegaly).

-Anal Margin Examination: No fissures or fistulas.

-Digital Rectal Examination: Presence of an exophytic process 5 cm from the anal margin; good sphincter tone.

-Lymph Nodes: No palpable inguinal or supraclavicular lymphadenopathy.

2.4. Laboratory Tests

-Liver function tests and complete blood count were within normal limits.

-Serology for hepatitis B, hepatitis C, and human immunodeficiency virus were negative.

-Serum carcinoembryonic antigen (CEA) levels were mildly elevated.

2.5. Colonoscopy Findings

An ulcerative, exophytic lesion located 8 cm from the anal margin on the left lateral wall of the rectum, extending over 5 cm. The mucosa beyond this point appeared macroscopically normal.

Conclusion: Ulcerative-exophytic rectal lesion.

2.6. Histopathological Analysis

Rectal biopsy revealed a poorly differentiated and infiltrating Lieberkühnian adenocarcinoma.

2.7. Imaging Studies

Thoraco-abdominal-pelvic CT Scan:

-Tumor involving all three segments of the rectum with extramural extension > 5 mm and a circumferential resection margin (CRM) < 1 mm.

-Mesorectal and left internal iliac lymphadenopathy.

-No distant metastases.

-Classification: T3 N2 M0.

2.8. Treatment

-The patient underwent ovarian transposition before starting radiotherapy.

-Initial treatment included concurrent radiochemotherapy using the Cap50 protocol (The Cap50 protocol, consisting of capecitabine-based chemoradiotherapy, was chosen due to the locally advanced stage of the tumor (T3N2), aiming for tumor downstaging and potential organ preservation), followed by two cycles of Folfox (organ preservation protocol), then the patient was lost to follow-up for two months due to personal reasons.

2.9. Evolution

Upon returning, the patient reported the appearance of bilateral breast nodules shortly after completing the two cycles of Folfox.

Mammography and Ultrasound:

- Nodules in the upper-inner quadrant of the right breast and the upper-inner quadrant of the left breast.
- Heterogeneous hypoechoic tissue structure, classified as ACR 4 (BI-RADS classification).

Immunohistochemical Analysis:

- GATA3: Negative.
- CDX2: Intense and diffuse expression (indicative of gastrointestinal origin).
- RO: Positive.
- RP: Positive.
- HER2: Score 0.
- KI67 Index: 70%.

Physical Examination:

- **Right Breast:** 7 cm nodule in the upper-inner quadrant (UIQ), mobile, no skin changes or nipple discharge.
- **Left Breast:** 9 cm nodule in the upper-inner quadrant (UIQ), mobile, no skin changes or nipple discharge.
- **Lymph Nodes:** Free.
- **Gynecological Examination:** Hard cervix with involvement of the cul-de-sac.

Further Investigations:

- Elevated CA19.9 levels.
- **Thoraco-Abdominal-Pelvic CT Scan:**
  - Slight regression of rectal tumor thickening.
  - Appearance of bilateral breast masses invading the pectoral major muscle.
  - Appearance of hepatic metastasis in segment IV.

Multidisciplinary Consultation Meeting (RCP):

- Decision to initiate Folfox with biotherapy based on RAS status.

Emergency Surgery and outcome:

- The patient presented with signs of acute colonic obstruction, including abdominal distension, vomiting, and absence of bowel movements.
- **CT Scan Findings:**
  - Rapid disease progression with pneumomediastinum, increased breast masses, pulmonary metastasis, and peritoneal carcinomatosis.
  - Intravaginal air-filled formation (no clear fistula).
- Emergency laparotomy revealed an obstructive tumor in the descending colon. A loop colostomy was performed for decompression. Post-operative recovery was initially uneventful; however, the patient declined further systemic treatment, citing treatment fatigue and psychosocial distress. Palliative care discussions were held, and psychological support was offered.

3. Discussion

The majority of breast metastases originate from the contralateral breast [1]. Metastases to the breast from extra-mammary cancers are rare, occurring in only 0.43% of cases. Common extra-mammary primary malignancies that metastasize to the breast include lymphoma, melanoma, sarcoma, lung carcinoma, and ovarian tumors. The first reported case of breast metastasis from colon cancer was by McIntosh, and from rectal cancer by Lal in 1999 [2]. A few cases of colorectal cancer (CRC) metastasizing to the breast have been reported, with the two largest studies presenting two new cases each [3]. It is essential to distinguish these metastatic lesions from primary breast tumors based on patient history, clinical and radiological features, tumor morphology, and immunohistochemistry [4].

The mechanisms underlying the rare phenomenon of breast metastases from colorectal cancer remain unclear. Possible explanations include hematogenous spread via the systemic circulation or retrograde lymphatic dissemination. Circulating tumor cells (CTCs) that survive in the bloodstream and adapt to the breast microenvironment may play a role. The breast's rich vascularization, hormonal milieu, and immune microenvironment may occasionally favor the seeding and growth of colorectal tumor cells. Further research on tumor cell plasticity and metastatic niche biology is warranted.

3.1. Clinical and Radiological Features

Most metastases appear as palpable breast masses, sometimes adhering to the skin, with a slight predominance on the left side, typically located in the upper outer quadrant. Multiple or bilateral lesions are rarely observed [3]. Schakelford *et al.* reported that 55% of breast metastases occurred on the left, 30% on the right, and only 3% involved bilateral breast metastasis. Toombs and Kalisher noted that pain, tenderness, or discharge are rarely observed, and nipple retraction has not been reported, although adherence to the skin has been reported in 25%. Axillary node involvement was frequently encountered. Rumana, Rakesh Kumar, Ruiz, *et*

al. [5] [6] reported cases of bilateral breast metastasis in young patients exist. Suganthi Krishnamurthy documented the youngest patient, a 23-year-old, with rectal cancer metastasizing to the breast. Hisham *et al.* [1] described an unusual case of rectal carcinoma metastasizing to the breast, accompanied by ocular involvement. Mihai *et al.* reported a 53-year-old woman who developed breast metastasis followed by cutaneous metastasis after chemotherapy, exhibiting a disease progression [7].

The time from the initial diagnosis to the development of breast metastasis ranges from 1 month to 15 years, with an average of 1 to 5 years. Hasukic *et al.* [8] reported a 69-year-old patient who developed breast metastasis 30 months after undergoing an abdominoperineal resection. Ting Wang *et al.* reported a 38-year-old male who, after undergoing an anterior resection,developed breast metastasis 7 years later. Differentiating between primary and metastatic breast neoplasms can be challenging. Mammograms are useful in resolving uncertainties. The typical mammographic finding is a rounded, well-circumscribed mass without speculation, microcalcifications,or skin thickening [3].

The typical ultrasound (US) features of hematogenous metastases include single or multiple well-defined, round to oval-shaped, hypoechoic masses without spiculations, calcifications, or architectural distortion. These masses are typically located superficially in the subcutaneous tissue or directly adjacent to the breast parenchyma.

3.2. Histopathological and Immunohistochemical Findings

Histologically, metastatic tumors display the same morphological characteristics as the primary tumors. Excisional or incisional biopsy is the most frequently employed procedure for differential diagnosis [9]. There is a growing preference for needle core biopsy over fine needle aspiration cytology. In his study, Silverman reported 2529 FNA breast biopsies, of which 666 were malignant, with only 18 originating from extra-mammary malignancies. In a series of 10,650 breast biopsies from the Mexican population, Alvarado *et al.* reported 24 cases of extra-mammary malignancies. In most cases, immunohistochemistry is useful for making an accurate diagnosis. Testing for the expression of CK7 and CK20 is particularly helpful. The majority of primary breast cancers are CK7-positive and CK20-negative, whereas colorectal carcinomas are typically CK7-negative and CK20-positive. Mucinous differentiation in colorectal cancer is linked to a poor prognosis. In this case, the intense CDX2 expression confirmed the gastrointestinal origin of the breast nodules.

3.3. Prognosis and Management

Most patients with secondary breast cancer succumb to the aggressive progression of the disease within a year of the primary tumor diagnosis. Surgical treatment is typically palliative, with mastectomy playing a limited role. Systemic chemotherapy is essential for these patients, and while metastasectomy combined with effective chemotherapy can extend survival, its primary role remains palliative [3].

Treatment options for patients with metastatic colorectal cancer (mCRC) have evolved significantly with the advent of anti-epidermal growth factor receptor (EGFR) therapies that target the EGFR signaling pathway. KRAS genotyping is essential before starting anti-EGFR monoclonal antibody therapy in mCRC patients, as KRAS mutations are a strong and reliable negative predictive factor for the effectiveness of anti-EGFR monoclonal antibody treatments.

3.4. Comparative Analysis

This case is consistent with previous reports of rapid disease progression and poor outcomes in young patients with breast metastases from rectal cancer. The patient's refusal of further treatment highlights the psychosocial challenges in managing advanced cancer.

Table 1. Literature review of case reports.

References	Age	Sex	Primary cancer	Metastasis	Location of breast metastasis	Radiology	Histology	Management	OPD
Lal and Joffe [2]	69	F	Rectal cancer T3N2R0 Mo	Breast, liver, lung, brain, skin	Left upper outer quadrant	CT TAP, FNA, wide local excision, elevated CEA, CA19.9	Moderately differentiated mucin secreting adenocarcinoma breast histology moderately differentiated adenocarcinoma, ER negative	Radical anterior resectional wide local excision Poor response to chemotherapy	RIP 4/12 after breast diagnosis
Sanchez *et al.*	36	F	Rectal cancer	Breast metastasis	Left outer upper quadrant 6 cm in size				
Hisham *et al.* [1]	32	F	Rectal cancer	10 months after APR, breast, spine, left eye, orbit	Left breast metastasis	Colonoscopy, CT abdomen pelvis Lumbosacral xray, MRI brain	Poorly differentiated mucinous adenocarcinoma of the rectum, Breast Bx similar	APR and total mesorectal excision, excision of posterior vaginal wall, cuff of the tissue in the lateral pelvic wall	RIP 2/12
Mihai *et al.* [7]	53	F	Rectal cancer	Lung, breast metastasis, skin metastasis	Breast lump	Ultrasound, mammogram, FNA, core biopsies, local excision		Chemotherapy, local excision, Post op chemotherapy	RIP
Wakeham *et al.* [3]	43	F	Rectal Cancer	Bilateral breast	Breast lump 2 × 2.2 cm^2		Dukes C rectal		
Li *et al.* [4]	51	F	Perforated rectal cancer	Breast, lung, soft tissue	3 cm mass in the right upper quadrant	CT abdomen pelvis, Mammogram, US breast, axilla	Invasive poorly differentiated adenocarcinoma rectal carcinoma T4N0M0, Core Bx breast and axilla triple negative similar to rectal histology	Laparotomy colostomy, preop radiochemotherapy	RIP 12 months

Continued

Rumana Makhdomi [5]	28	F	Rectal cancer 4 cm away from anal verge	Bilateral breast metastasis	Largest 3×2 cm^2 and smallest 2×1 cm^2	Sigmoidoscopy, colonoscopy, contrast enhanced computed tomography, mammography, FNAC	Mucus secreting adenocarcinoma with signet-ring differentiation, metastatic mucinous adenocarcinoma of the breast, ER/PR negative	Anteroperineal resection, adjuvant chemotherapy	OPD follow up
Singh *et al.* [9]	42	F	Rectal cancerT4 N1M0	Right Breast lump	Outer upper quadrant 5×4 cm	Mammogram, FNAC, pleural fluid cytology, core needle biopsy, CEA mildly elevated	Mucin secreting adenocarcinoma with signet ring cell Signet cell carcinoma CK20 positive, CK7, ER/PR negative	Anterior resection, chemoradiation, chemothreapy	RIP 2/12 after breast metastasis
Hasukic *et al.* [8]	63	F	Rectal cancer T3N1M0	Right breast mass 3×2 cm	Right upper outer quadrant	Mammography, Ultrasound	Rectal adenocarcinoma T3N1M0, breast biopsy, Adenocarcinoma ER/PR neg	APR, Adjuvant chemoradiotherapy, open excisional breast biopsy	RIP post 4/12 breast pathology
Ruiz *et al.* [6]	36	F	Rectal cancer	Bilateral breast left axilla right groin	Bilateral breast	CT abdomen pelvis, Mammogram Ultrasound	Poorly differentiated rectal carcinoma with signet ring cellT3N1M0	APR with hysterectomy, adjuvant radiochemotherapy exploratory laparotomy, incisional bx of both breast, chemotherapy nine cycles	RIP 6 /12 after breast mets diagnosis
Ting Wang *et al.* [10]	38	M	Rectal cancer	Right mammary mass 7 years after surgery				Anterior resection, core needle bx, neoadjuvant chemotherapy, modified radical mastectomy	
Suganthi Krishnamurthy *et al.* [11]	23	F	Rectal cancer	Breast/ axillary metastasis two 1/2 months later	Right upper outer quadrant	Colonoscopy, CT TAP, FNAC, Core Bx	Poorly differentiated adenocarcinoma with signet cell	Emergency laparotomy, loop colostomy, palliative chemotherapy	

Among the 13 cases summarized in Table 1, the majority occurred in women aged 23 to 69, with a tendency toward unilateral presentation, particularly in the upper outer quadrant. The most frequently used diagnostic tools included ultrasound, CT, and core needle biopsy. Immunohistochemistry was consistently useful in confirming gastrointestinal origin through CDX2 positivity and absence of GATA3. Treatment strategies varied, but outcomes were generally poor, with a survival time post-breast metastasis ranging from 2 to 12 months [10].

4. Conclusion

This case underscores the importance of considering breast metastases in patients with a history of rectal cancer, despite its rarity. A new breast mass in such patients should be evaluated with a high index of suspicion for metastatic disease. Accurate diagnosis, aided by immunohistochemistry and imaging, is essential to guide appropriate management. Future research should focus on understanding the molecular mechanisms underlying such rare metastases and developing targeted therapies to improve outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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