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CASE REPORT

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Poorly differentiated rectal cancer with breast metastases; A case report

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ABSTRACT

Objective: Rectal cancer can rarely metastasize to the breast. It is an indicator of widespread stage and poor prognosis. We aim to present a rectum cancer patient who developed breast metastasis.

Case: A 48-year-old female patient, underwent an abdominoperineal resection operation due to obstruction. She has been diagnosed with Stage-IIIC poorly differentiated rectal adenocarcinoma. Multiple metastases were detected in the 4 month of adjuvant therapy. The patient was diagnosed with rectal cancer that had metastasized to the breast and soft tissue. FOLFIRI-Aflibercept treatment was started for microsatellite stabile-stable, KRAS mutant, and BRAF wild, metastatic rectal carcinoma. Progression was detected after three cycles of treatment. The patient died 9 months after diagnosis.

Conclusion: The breast is an unexpected site of metastasis for non-mammary solid tumors. Taking a biopsy from every metastatic lesion and a detailed evaluation are important.

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Breast metastases; prognosis; rectum cancer; soft tissue metastasis

Introduction

Colorectal cancers (CRCs) are the third most common cancer type in the world [1]. It can spread to lymph nodes, the liver, lungs, bone, and pelvic organs [2]. The breast is an organ where extramammary metastases are rare. Tumors that metastasize to the breast are rapidly growing tumors with a very poor prognosis [3]. We aim to present a case of poorly differentiated rectal adenocarcinoma with breast and subcutaneous metastases.

Material and Methods

The data of case who was treated between November 2020 and July 2021 were evaluated retrospectively.

A written informed consent form was obtained from the patient and the study was carried out in accordance with the Declaration of Helsinki.

Case Presentation

A 48-year-old female patient presented with pain, obstruction, and rectal bleeding. A colonoscopy revealed a bleeding ulcerovegetant malign lesion that allowed a passage starting from 1 cm at the anal canal entrance. In preoperative abdominal imaging, irregular wall thickening in the anorectal region, multiple lymph nodes in the perirectal fat planes, and bilateral internal iliac chain were observed.

An abdominoperineal resection operation was performed. In pathology, 5.5 cm poorly differentiated rectal adenocarcinoma perforated the intestinal wall, tumor invaded the serosa, lymphovascular invasion, perineural invasion, and moderate necrosis was found. The tumor was detected in 11 of 15 lymph nodes and surgical margins were clean. No distant metastasis was detected in the staging images. The patient was diagnosed with pT4aN2bM0 (Stage-IIIC) rectal adenocarcinoma. The tumor markers were found to be cancer antigene (CA)125: 45.1 (high), CA15.3: 44.8 (high), carcinoembryonic antigen (CEA):3.2, and CA19.9 normal. Because she was a young woman and had high CA125 and CA 15.3 levels, a gynecological examination and breast imaging were planned to rule out synchronous tumors. Breast Imaging-Reporting and Data System-2 changes were detected in the

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mammography of the patient whose gynecological examination was normal.

In the adjuvant treatment, due to perforation and extensive lymph node involvement, it was planned to start systemic treatment first, followed by chemoradiotherapy. During the fourth month of adjuvant Folfox-6 chemotherapy, the patient developed severe rectal pain. 18F-flourodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) was performed due to new symptoms developing in the patient. Locoregional recurrence and breast and subcutaneous fat tissue metastases were detected in the rectum and pelvic region (Fig. 1). CA15.3 and CA125 elevations continued but, CEA and Ca19.9 increase was not observed.

A biopsy was taken from the lesion in the breast, lumbar region, and rectum. The biopsy result was ''undifferentiated carcinoma with mesenchymal/spindle cell component, dedifferentiated from poorly differentiated adenocarcinoma.'' In the immunohistochemical (IHC) examination, CK7(+), CK20(+), CDX2(−), EMA(+), Vimentin(+), GCDFP-15(−), and GATA-3(−) were detected (Fig. 2). It was observed that the tumor in the breast, lumbar region, and rectum reflects the same tumor and it has undifferentiated carcinoma in most areas and glandular component in focal areas.

The patient was diagnosed with poorly differentiated rectal adenocarcinoma with spindle cell components. No malignancy was detected in the gynecological examination performed again on the patient. Microsatellite instability (MSI), KRAS, NRAS and BRAF mutation tests were done. MSI-stable, BRAF wild but, KRAS exon-2 codon-12 (Gly12Ala) mutation detected. Folfiri-Aflibercept chemotherapy was planned for the patient who developed diffuse metastasis under adjuvant oxaliplatin-based chemotherapy. However, since the patient presented with severe pain in the rectal region, the first 30 Gy radiotherapy was administered palliatively. After three cycles of chemotherapy, progression was detected (Fig. 1). The Eastern Cooperative Oncology Group (ECOG) performance status dropped to three and she was taken to the palliative care unit. The patient died nine months after diagnosis.

Discussion

CRC is the third most common malignancy seen in both men and women [1]. Because of clinicopathological and genetic features, the frequency of CRC increases in young people. The rectum is an organ without serosa. Therefore, locoregional and distant metastases are common. Rarely, skin and breast metastases have been reported [3,4].

The breast is not a region where solid tumors metastasize frequently, its incidence is around 3%

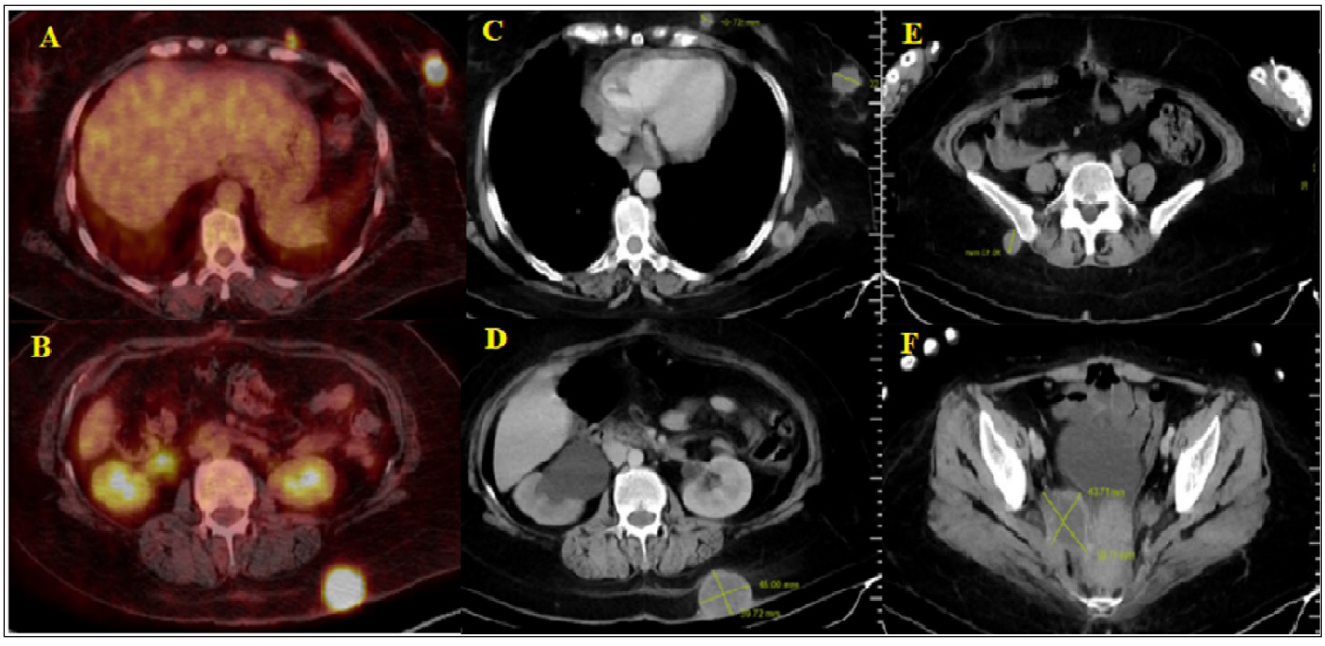


Figure 1. (A) Left breast metastases in FDG-PET/CT images; (B) subcutaneous fat tissue metastases in FDG-PET/CT images; (C) left breast metastases after folfiri aflibercept treatment in thorax computer tomography images; (D) subcutaneous metastases after folfiri aflibercept treatment in abdomen computer tomography images; and (E,F) an abscess in the left perineal radiotherapy area findings observed in abdomen computer tomography images.

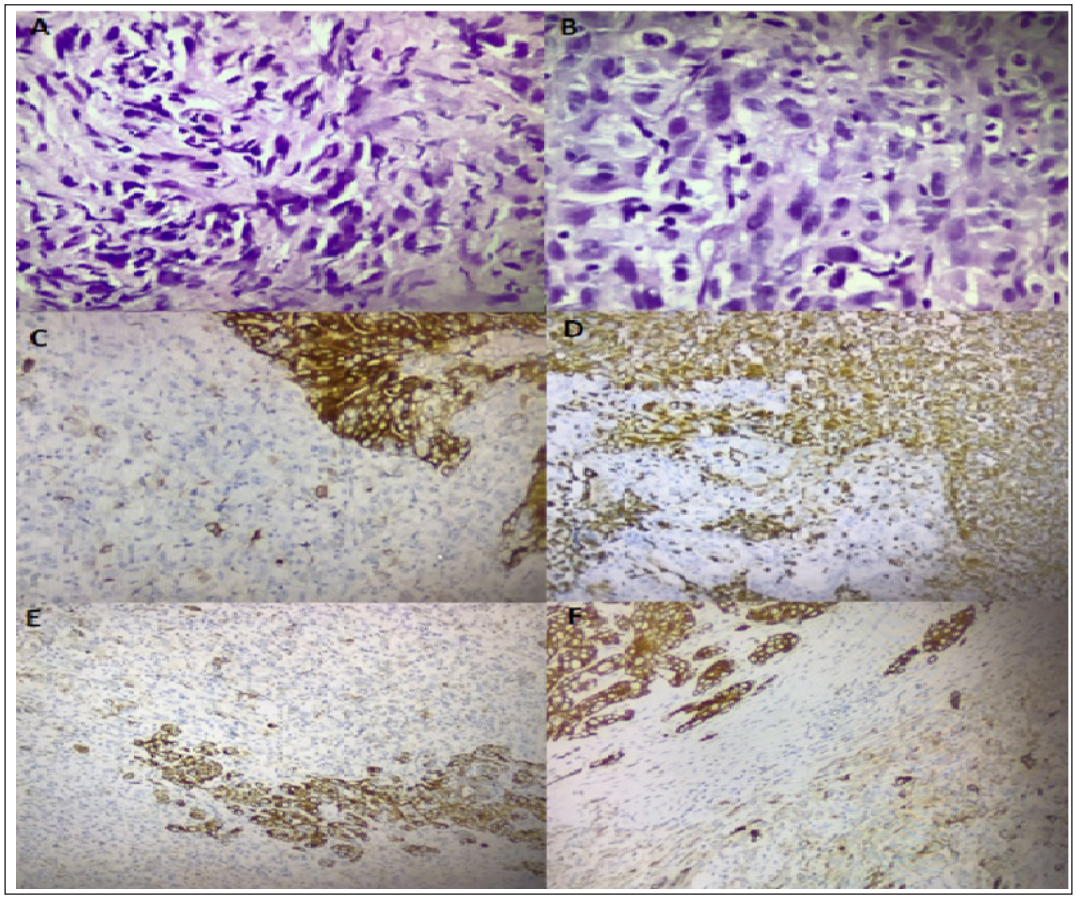


Figure 2. Breast and lumbar region biopsy pathology samples, poorly differentiated adenocarcinoma with carcinoma and sarcoma components. (A) hematoxylin and eosin × 20; (B) hematoxylin and eosin magnification × 40; (C) EMA magnification × 10; (D) vimentin magnification × 10 (mesenchymal/spindle cell component was stained); (E) CK7 magnification × 10; and (F) PanCK magnification × 10.

[5]. The majority of the cases are women, with a median age of 50 years, with tumors with a large metastasis diameter, usually localized in the upper outer quadrant of the left breast [6]. The seed soil hypothesis is being considered to explain breast metastasis of rectal cancer, but it remains unclear why breast metastasis of rectal cancer, is more common in women than men. It is thought that the effect of estrogen on breast angiogenesis may trigger this condition [3].

It is important to differentiate metastases of the breast from primary breast tumors. History, clinical and radiological features, evaluation of tumor morphology, and differential diagnosis with IHC are required. Rectal cancer is CK7(−) CEA(+) CK20(+) CDX-2(+), SATB-2(+) ER(−) PR(−) HER-2(−) and GCDFP-15(−) with IHC, however, primary tumors of the breast are stained with CK7(+) CK20(−) GATA-3(+) ER(−/+) PR(−/+) HER-2(−/+). Rectal cancer breast metastasis usually presents with in situ component deficiency, lymphovascular invasion prevalence, and ER(−) PR(−) HER-2(−) status [3]. This is also supported in our case.

Patients with rectal cancer and breast or skin metastases have a poor response to therapy, and have a poor prognosis with rapid progression. The main treatment is systemic and supportive treatment [4,6].

Breast metastasis of rectal cancer is a very rare, aggressive, and specific condition. Differential diagnoses should be made correctly. Synchronous and metachronous tumors should be excluded.

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