Case Report

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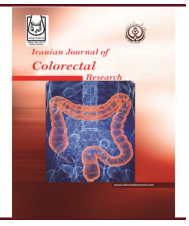

Incidentally Diagnosed Breast Cancer in a Patient with Rectal Cancer: A Case Report

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Abstract

The development of screening and therapeutic approaches has improved the prognosis of colorectal cancer (CRC) patients, leading to an expected increase in the incidence of second primary cancers (SPCs). CRC has been correlated with several extracolonic SPCs, including malignancies of the small intestine, stomach, breast, and ovary. We report a case of a 50-year-old woman with a history of rectal bleeding who was diagnosed with rectal adenocarcinoma. She underwent total neoadjuvant therapy followed by abdominoperineal resection in the colorectal surgery ward at Ghaem Hospital, Mashhad, Iran, in December 2023. Five months after surgery, a soft tissue mass (10*13 mm) in her left breast was incidentally detected on a chest computed tomography scan. Suspecting breast cancer, she underwent mammography and a core needle biopsy, which confirmed the diagnosis. She subsequently underwent a left partial mastectomy, and pathological evaluation revealed invasive ductal carcinoma. This case highlights the importance of considering SPCs in CRC survivors. Regular follow-up is recommended for these patients to detect early signs of recurrence, progression, or the presence of SPCs, enabling prompt and appropriate treatment.

Keywords: Breast neoplasms; Case reports; Colorectal neoplasms; Second primary neoplasms

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Introduction

Colorectal cancer (CRC) ranks as the third most prevalent cancer and the second leading cause of cancer-related death worldwide, with an estimated 1.9 million new cases, representing 10% of all new cancer diagnoses, and 935,000 related deaths (1). Recent advances in CRC screening, early diagnosis, and treatment have improved patient prognosis; however, CRC remains a major global health concern. Long-term health issues, such as an increased risk of second primary cancers (SPCs),

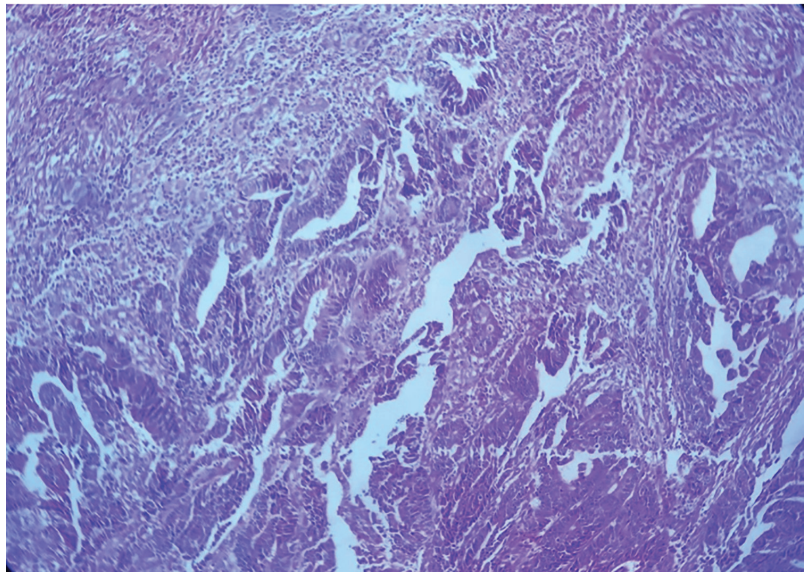

Figure 1: Histopathological findings of the resected rectal specimen showing well-differentiated adenocarcinoma consisting of atypical cells in a desmoplastic stroma, with invasion to the submucosa (treatment effect: partial response) (stain, hematoxylin and eosin; magnification: x100).

affect the growing population of CRC survivors (2). SPCs are defined as subsequent, distinct types of cancer that develop in cancer survivors, excluding any recurrences, extensions, or metastases of the identified index malignancy (3). CRC patients have a higher risk of developing SPCs compared to the general population. Recognizing the clinical characteristics of SPCs in these patients is crucial for early diagnosis and curative treatment (4). Several population-based studies have focused on second primary malignancies occurring after CRC, revealing a significantly elevated risk of developing second malignancies in the gastrointestinal tract, including the colorectum, as well as lung, bronchus, and gynecologic cancers (5-7). In this study, the authors describe a 50-year-old female with rectal cancer who was incidentally was diagnosed with breast cancer.

Case Presentation

A 50-year-old Iranian woman was referred to the colorectal surgery ward at Ghaem Hospital, Mashhad, Iran, in December 2023 with a 10-month history of rectal bleeding. The patient had no significant past medical history and no history of smoking, tobacco use, or alcohol consumption. She reported a family history of breast cancer in a second-degree relative (her cousin). Colonoscopy revealed an infiltrative ulcerative lesion in the distal rectum, along with a polypoid lesion protruding through the anal canal. Biopsy confirmed adenocarcinoma of the distal rectum. Staging computed tomography (CT) scans of the thorax, abdomen, and pelvic indicated a T4bN1bM0 tumor. The patient underwent total neoadjuvant therapy followed by abdominoperineal resection. Pathologic evaluation of the resected tumor showed well-differentiated adenocarcinoma of the rectum without lymphovascular or perineural invasion. The pathological stage was ypT_1N_0 (Figure 1). Five months after surgery, a soft tissue mass in her left breast was incidentally detected on a chest CT scan (Figure 2). Suspecting breast cancer, she underwent mammography (Figure 3), and a core needle biopsy revealed low-grade invasive ductal carcinoma. Immunohistochemistry demonstrated

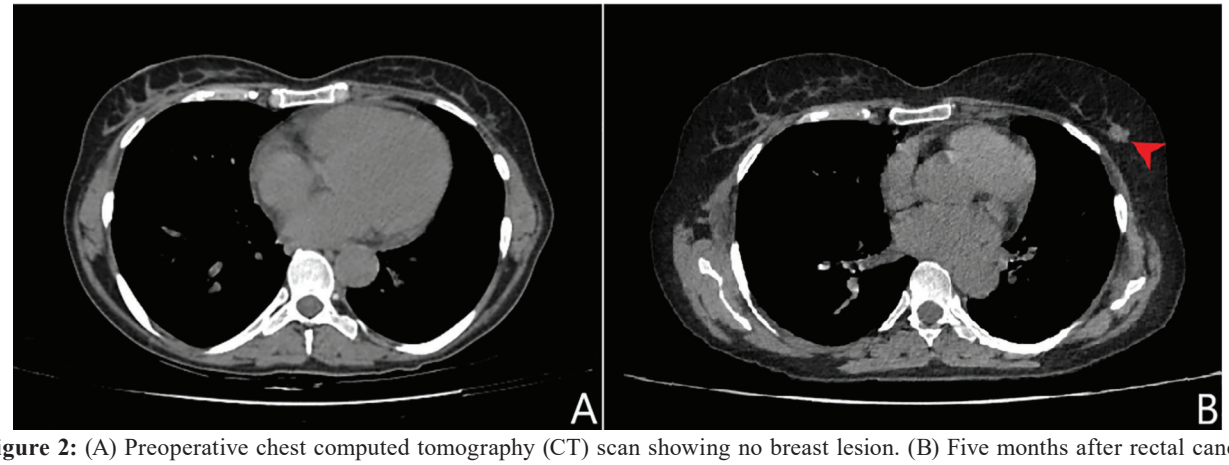

Figure 2: (A) Preoperative chest computed tomography (CT) scan showing no breast lesion. (B) Five months after rectal cancer surgery, chest CT scan showed a soft tissue density mass (10*13 mm) in the left breast (red arrow).

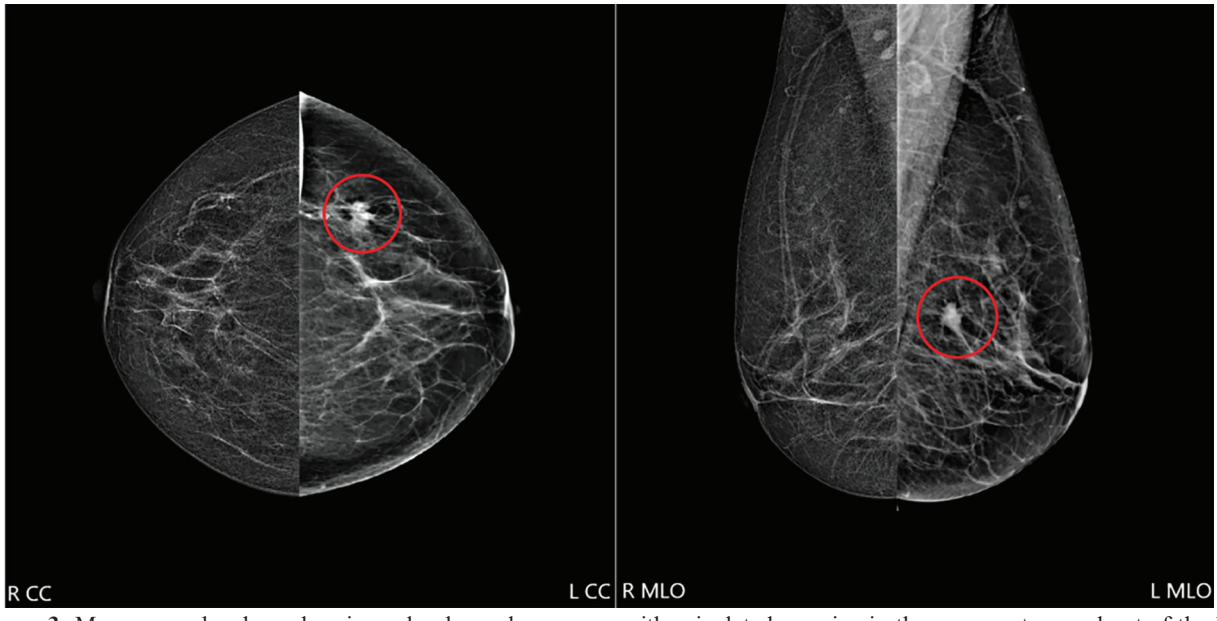

Figure 3: Mammography showed an irregular, hyperdense mass with spiculated margins in the upper outer quadrant of the left breast (BIRADS=5) (red circle).

estrogen and progesterone receptor: positive, HER2/neu: 1+/negative, and Ki-67: positive in 27% of tumor cells. A left partial mastectomy was performed, and pathological analysis confirmed invasive ductal carcinoma (modified Bloom–Richardson: grade 1) without skin and lymphovascular invasion (Figure 4). Unfortunately, genetic testing was not performed for further evaluation. The patient has been followed up since discharge and is currently receiving postoperative adjuvant therapy. This patient's information was obtained from the colorectal cancer registry (NO#4001728) at Mashhad University of Medical Sciences, Mashhad, Iran.

Discussion

Advances in early diagnosis, supportive care, and multimodal therapeutic strategies have significantly improved the survival rates of CRC patients in recent decades (8). However, a major concern regarding the long-term survival of CRC patients is their increased risk of developing SPCs. The overall survival of these patients is influenced by both the nature of the initial CRC and the subsequent SPCs. In cases of advanced-stage CRC with residual cancer post-surgery or mutations that are unresponsive to targeted therapies, the prognosis tends to be poor, and the impact of SPCs on survival is not evident. In contrast, if the CRC is in its early stages and follows curative surgery, the survival of these patients is likely to be affected by the SPCs, which have high morbidity and mortality rates, such as melanoma and thoracic malignancies (2).

The development of SPCs may be influenced by

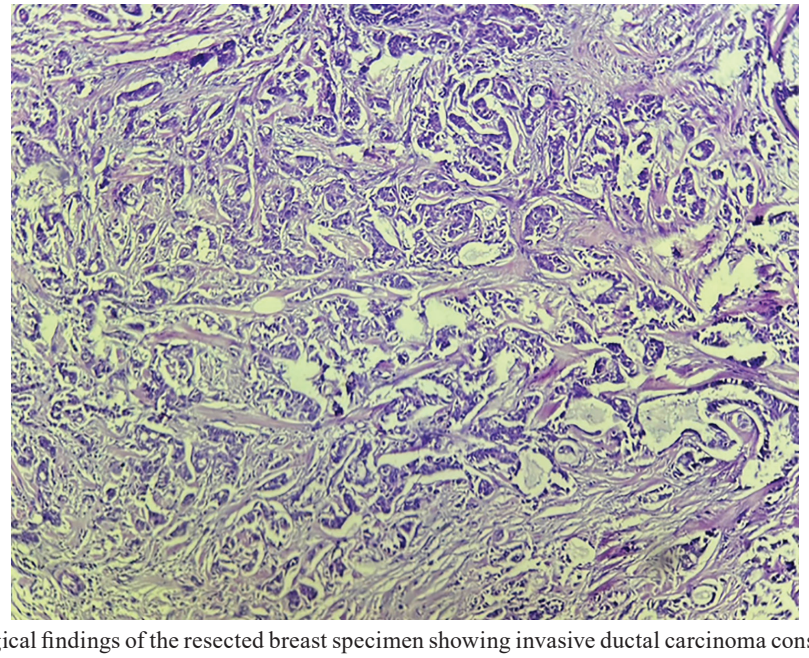

Figure 4: Histopathological findings of the resected breast specimen showing invasive ductal carcinoma consisting of nests and ducts lined by atypical cells exhibiting moderate pleomorphism in a desmoplastic stromal (stain, hematoxylin and eosin; magnification: x100).

various factors, including genetic predispositions, hormonal effects, molecular phenotypes, environmental exposures or shared lifestyles, therapeutic strategies for the primary cancer, or a combination of them (9, 10). Age is a significant risk factor contributing to the development of SPCs in CRC survivors. In a study conducted by Shin et al. (10), CRC patients under 55 years of age exhibited a higher risk of breast and gynecological malignancies compared to those over 55 years (hazard ratio, 3.51 vs. 2.59). Since younger individuals generally have a lower frequency of comorbidities, the estimated risk for SPCs in these patients may be attributed to genetic susceptibility (11). However, some studies have reported that elderly patients have a higher risk than younger individuals (12, 13). Dasgupta et al. (9) demonstrated that the risk of female breast cancer in CRC patients increased with longer follow-up, in contrast to the risk of other SPCs, which was generally higher shortly after the initial CRC diagnosis. The differing patterns of second primary breast cancer risk may be explained by its relatively long preclinical duration and the cumulative effects of hormonal exposures and other factors.

Patients with different index CRC subsites exhibit a high risk of SPCs in specific sites. Previous right-sided colon cancer has been linked to increased risks of cancers in the stomach, small intestine, pancreas, breast, thyroid, renal pelvis, and ureter, and there was a correlation between left-sided colon cancer and secondary CRC. Additionally, rectal cancer is a risk factor for developing lung, urinary bladder, and vaginal cancers (14). Treatment modalities also influence the development of subsequent malignancies. surgical intervention for CRC has been identified as an independent risk factor for increased risk of SPCs, even with the exclusion of multiple primary CRCs (9). In the study by Chen et al. (4), surgery was associated with an elevated risk of second primary breast cancer in female patients with CRC. Although the underlying mechanism remains unclear, evidence-based guidelines suggest heightened medical surveillance following CRC surgery may enhance the detection of SPCs. Moreover, radiation therapy and chemotherapy are correlated with subsequent malignancies due to their long-term effects (5, 15). Genetic predisposition to treatment agents is also believed to be associated with developing subsequent malignancies. Due to genetic variations, such as polymorphisms affecting drug metabolism (e.g. glutathione transferase), may increase individual sensitivity to these treatments, thereby elevating the risk of SPCs (10).

Several previous studies have reported an increased risk of breast cancer following CRC (4, 16). Additionally, patients with breast cancer exhibit a higher risk of developing CRC (17, 18). According to Yang et al. (5), breast cancer was the most prevalent SPC (22.2%) in female patients, and ranked fourth (9.33%) among all CRC survivors. Chang et al. (7) found that female patients with CRC had a 39% higher incidence of the four types of gynecological cancers (breast, ovary, cervix, and endometrium) compared to women without CRC (2.99 vs. 2.14 per 1000 person-years). Breast cancer was the most common SPC, with a hazard ratio (HR) of 1.24. In another study analyzing 56,682 patients with CRC, the overall risk of gynecological malignancies was significantly higher in CRC patients (HR: 2.91) than in non-CRC controls. CRC was associated with a subsequent breast cancer risk with an HR of 1.85. This study also demonstrated that CRC patients with dyslipidemia had a greater risk of developing breast cancer compared to individuals without dyslipidemia (10). In a meta-analysis by Robertson et al. (2), which included 7,716,750 cases from 13 retrospective studies, CRC survivors had a significantly higher overall risk of extracolonic SPCs than the general population. However, this study did not find a significant difference in the risk of second primary breast cancer.

A large retrospective study conducted by Fisher et al. (19) investigated the mortality rates among patients with synchronous or metachronous CRC and breast cancer. They found that the five-year cumulative risk of death in women diagnosed with both CRC and breast cancer is three times higher for CRC than for breast cancer. This finding holds true regardless of which cancer was diagnosed second. Furthermore, CRC-specific mortality increased over time, while mortality from breast cancer decreased. Another study by Tantiphlachiva et al. (20) compared survival differences between individuals with single CRC or breast cancer and those with both cancers. The five-year survival rates were 63.2% for the single cancer group and 74.6% for the double cancer group. The single cancer group with CRC had a significantly shorter survival time than the double cancer group in which CRC was diagnosed first. Survival did not seem to be affected by the development of a second primary breast cancer following CRC. However, the mean survival time did not differ significantly between the single cancer group with breast cancer and the double cancer group in which breast cancer was diagnosed first. Future studies evaluating the risk of SPCs in patients with CRC are necessary, as establishing effective surveillance and management strategies is crucial to reducing the burden of SPCs in this growing patient population.

Conclusion

In conclusion, advances in the diagnosis and management of CRC have led to an increase in the number of patients with SPC following index CRC diagnosis. Therefore, it is crucial to understand the clinical characteristics of individuals with multiple primary malignancies, and more attention should be given to the occurrence of SPCs during the follow-up care of CRC survivors.

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None.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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Availability of Data and Materials

The data supporting the findings of this study are available upon reasonable request from the corresponding author.

Ethical Approval

Written informed consent was obtained from the patients for participation in this study. According to the guidelines of the Ethics Committee of our university, single case reports do not require separate ethical approval, as they do not contain identifying information and do not involve experimental treatment.

Authors' Contribution

M.R.: Writing_original draft, Writing_review, and editing; A.A.: Conceptualization, Supervision; F.S.: Project administration, Resources; E.Z.: Resources; A.H.J.: Resources; M.A.O.: Resources; A.J.N.: Resources, Supervision; M.A.: Conceptualization, Resources, Supervision. All authors read and approved the final manuscript.

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