OXFORD

Oxford Medical Case Reports, 2022, **9**, 303–305
https://doi.org/10.1093/omcr/omac095
Case Report

Management of Crohn's disease relapse during neoadjuvant chemotherapy for bilateral breast cancer: a case report

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Abstract

Diagnosis of breast cancer in a patient with Crohn's disease (CD) is uncommon. However, cytotoxic chemotherapy might help control CD during the treatment period. Here, we report a case of CD relapse during treatment with neoadjuvant chemotherapy (NAC) for bilateral breast cancer. A 39-year-old woman with CD controlled by infliximab and mesalazine was diagnosed with bilateral breast cancer. Infliximab treatment was discontinued temporarily so that the patient could receive NAC. However, her CD symptoms intensified during chemotherapy, and after her symptoms improved after a one-time administration of infliximab, the remainder of NAC was completed with a corticosteroid. Bilateral breast conservation surgery was performed. Histopathological examination revealed partial response of the left breast cancer and no residual cancer in the right breast. Breast irradiation and hormone therapy were added and no signs of recurrence have been observed for 5 years. CD has been well controlled with adalimumab and mesalazine.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer in women worldwide [1]. Crohn's disease (CD) is a chronic inflammatory condition of the gastrointestinal tract. When a patient with CD is diagnosed with breast cancer, the management of both CD and breast cancer can be challenging. Generally, anti-tumor necrosis factor (TNF) agents (infliximab, adalimumab) for CD should be stopped during chemotherapy [2], because the use of anti-TNF agents, especially during treatment with cytotoxic chemotherapy, may cause severe immunosuppression. Previous reports suggested that cytotoxic chemotherapy for cancer may induce or maintain CD remission during cancer therapy [3]. We report a case of CD relapse during treatment with neoadjuvant chemotherapy (NAC) for bilateral breast cancer after interruption of infliximab.

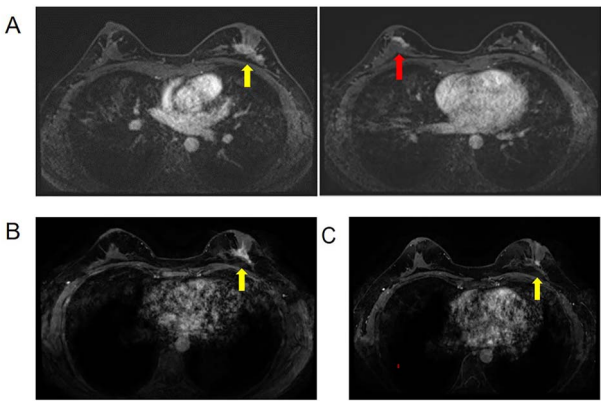

Figure 1. MRI findings; (A) initial breast MRI of the bilateral breast tumor; (B) tumor in the left breast after 4 cycles of taxane; (C) tumor in the left breast after the completion of NAC.

CASE REPORT

A 39-year-old pre-menopausal woman had CD, which has been well controlled by 5-mg/kg intravenous infliximab every 8 weeks and 2000 mg per day oral mesalazine for the last 7 years. She was referred to our hospital due to complaints of a palpable mass in the left breast. She had no family history.

Breast examination revealed a 3.5-cm lump in the left breast without swollen axillary lymph nodes. Dynamic contrast-enhanced magnetic resonance imaging (MRI) showed a 50-mm mass in the left breast and an 18-mm lesion in the right breast (Fig. 1A). Core needle biopsy (CNB) of the left breast tumor revealed invasive ductal carcinoma (IDC) that was estrogen receptor (ER)-positive, progesterone receptor (PgR)-positive and human epidermal growth factor receptor-2 (HER2)-negative with a Ki-67 proliferation index of 5%. CNB of the right breast tumor revealed ductal carcinoma in situ that was ER-positive, PgR-positive and HER2-negative with a Ki-67 proliferation index of 7%. Computed tomography (CT) and bone scintigraphy showed no findings of distant metastasis. She was diagnosed with bilateral breast cancer. BRCA genetic test was not performed because she had no family history of breast or ovarian cancer. PI3K test and NGS were not performed because these were not covered by national health insurance in Japan.

Received: May 24, 2022. **Revised:** July 17, 2022. **Accepted:** August 1, 2022

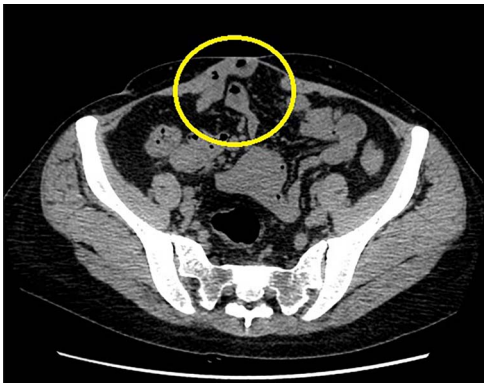

Figure 2. CT findings; abdominal CT showed mild ileus.

NAC consisting of taxane and anthracycline was scheduled to enable breast-conservation surgery, after temporary discontinuation of infliximab. She received NAC with 4 cycles of nanoparticle albumin-bound paclitaxel (260 mg/m^2) every 2 weeks and was treated with mesalazine for CD. The left breast tumor decreased to 30 mm (Fig. 1B). However, at that time, she complained of slight-to-moderate abdominal distension and diarrhea 4–5 times per day and severe fatigue for 1 week. There were no other symptoms including fever or weight loss. Abdominal CT revealed mild ileus caused by small intestine stenosis (Fig. 2), and her C-reactive protein level was 0.17 mg/dl, while her baseline was 0.01 mg/dl. The CD activity index was moderately active, which indicates exacerbated CD. NAC was temporarily interrupted, and 250-mg infliximab was administered once. CD remission was induced in 1 week. Eight weeks later, NAC consisting of 4 cycles of epirubicin (90 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks was resumed with 40-mg predonine for CD. After the completion of NAC, the left breast tumor decreased to 8 mm (Fig. 1C). The patient underwent bilateral partial mastectomy and left sentinel lymph node biopsy followed by axillary lymph node dissection. Histopathological examination of surgical specimens showed a 40-mm IDC in the left breast and no residual cancer in the right breast.

After surgery, she received adjuvant radiation therapy to both breasts and has remained on tamoxifen and leuprorelin. She has survived without any signs of breast cancer recurrence for 5 years. Her CD has also been well controlled by adalimumab and mesalazine.

DISCUSSION

This is a case report of CD relapse during NAC for breast cancer after interruption of infliximab. A breast cancer diagnosis in a patient with CD increases the difficulty in managing the treatment of both CD and breast cancer. The European Crohn's and Colitis Organization guideline suggested that anti-TNF agents should be stopped during chemotherapy because of their ability to aggravate the bone marrow suppression induced by cytotoxic chemotherapy [2]. Previous studies reported that the risk of CD relapse after anti-TNF agent withdrawal ranged from 30 to 40% at 1 year [4] and that patients in long-standing stable remission probably had a lower risk of relapse after anti-TNF cessation [5]. Axelrad *et al.* [3] reported that cytotoxic chemotherapy for cancer may induce or maintain CD remission by causing cell death or preventing cell division in rapidly dividing cells such as T lymphocytes and malignant cells. Koc *et al.* [6] also reported that of 41 patients, none showed exacerbation of inflammatory bowel disease during chemotherapy. We chose NAC because chemotherapy is recommended over endocrine therapy for premenopausal women with hormone receptor-positive disease who warrant neoadjuvant therapy by clinical evidence and guideline. We discontinued infliximab because this patient had maintained a long-term remission of CD and because the cytotoxic chemotherapy for breast cancer could also effectively control CD through its immunosuppressant effect. However, CD symptoms intensified after discontinuation of infliximab even though the patient was receiving cytotoxic chemotherapy. We supposed that infliximab was very effective in controlling CD in this patient. Although we should have ruled out the presence of other disease including cytomegalovirus and *Clostridium difficile* infections, re-administration of infliximab was effective because these symptoms were due to CD relapse. Fecal calprotectin test was not performed because it was not covered by national health insurance in Japan. In cases where CD symptoms flare during chemotherapy, it is not clear whether corticosteroids or anti-TNF should be given [7]. Although CD symptoms remitted after one-time administration of infliximab, a corticosteroid was used during continuation of NAC because combination of chemotherapy and infliximab might cause severe immunosuppression. Interleukin inhibitors were not approved for CD in Japan and might also cause severe immunosuppression in combination with chemotherapy.

This case report highlights the important suggestion that CD may relapse after interruption of infliximab treatment even during treatment with NAC for breast cancer. It is necessary to assess the appropriate management of breast cancer in patients with CD, as well as CD in patients with breast cancer.

ACKNOWLEDGEMENTS

We thank Ms Akiko Yuzuriha for her excellent technical assistance.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

FUNDING

No funding was received for this report.

ETHICAL APPROVAL

Not applicable.

CONSENT

Informed consent for the publication of the case details was obtained from the patient.

GUARANTOR

H.J. is the guarantor of this report.

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