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CASE REPORT

Bilateral Primary Breast Cancer: A Case of Synchronous Diagnosis and Management of Ductal Carcinoma *In Situ* and Invasive Ductal Carcinoma

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Abstract

Aims/Background Bilateral breast cancer (BBC) is an uncommon subtype of breast cancer which occurs either synchronously or metachronously. Synchronous BBC with distinct histological types in the left and right breasts is particularly rare.

Case Presentation This report presents a case of a 57-year-old female patient diagnosed with bilateral primary breast cancer, characterized by ductal carcinoma *in situ* (DCIS) in one breast and invasive ductal carcinoma (IDC) in the other. The patient initially sought medical attention due to a palpable mass and pain in her left breast, leading to a diagnosis confirmed through imaging studies and biopsy. The patient was treated with three cycles of neoadjuvant therapy, followed by a modified radical mastectomy on the left breast and a lumpectomy on the right breast. Postoperatively, the patient received endocrine therapy and radiotherapy, with no evidence of recurrence observed to date.

Conclusion Further research and clinical advancements are necessary to optimize treatment and care strategies for patients with bilateral breast cancer, ensuring that their unique therapeutic needs are effectively addressed.

Key words: case report; breast neoplasms; ductal carcinoma *in situ*; invasive ductal carcinoma; neoadjuvant therapy

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Introduction

Breast cancer ranks among the most prevalent malignancies affecting women globally (Niang et al, 2022). Bilateral breast cancer (BBC) is a rare subtype characterized by the occurrence of independent tumor lesions in the bilateral mammary glands. The reported incidence of BBC ranges from 1.4% to 11.8% (Kheirelseid et al, 2011). BBC is stratified into synchronous (occurring within 6 months of the primary breast cancer) or metachronous (occurring more than 6 months after the primary breast cancer) based on the timing of its presentation (Kuo et al, 2009). Moreover, synchronous BBC with distinct histological subtypes in the left and right breasts is particularly rare, especially when one breast is affected by ductal carcinoma *in situ* (DCIS) and the other by invasive ductal carcinoma (IDC) (Bai et al, 2022). The complexity of diagnosing and treating this condition necessitates a thorough evaluation of the patient's clinical presentation, tumor pathology, and therapeutic responses. This case report, prepared in accordance with the CARE

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framework (**Supplementary Material**), explores the diagnostic and therapeutic approaches employed in this rare case and highlights the challenges of effectively balancing the treatment approaches for both DCIS and IDC.

Case Report

A 57-year-old female patient discovered a lump in her left breast two years ago during a routine check-up. The lump was accompanied by left nipple retraction and significant localized pain but was not associated with nipple discharge. The patient had an unremarkable medical history, had undergone menopause at the age of 50, and had three children (two sons and one daughter). She reported no family history of hereditary tumors.

Upon admission, a physical examination revealed asymmetry between the breasts, with the left nipple retracted and a palpable lump measuring 3.0 cm × 3.5 cm behind the left nipple. The lump had a hard texture, unclear borders, a rough surface, and poor mobility, and it caused significant pain upon palpation. Notably, the skin above the mass was ulcerated, though no adhesion to the underlying chest muscle was observed. The right breast appeared normal, with no palpable lumps, and no significantly enlarged lymph nodes were detected in either axilla.

Following admission, relevant examinations were conducted. Laboratory tests revealed no significant abnormalities in (cancer antigen 125) CA125 and CA153 levels. Ultrasound imaging identified a 5 mm × 6 mm hypoechoic area located 23 mm from the nipple at the 8–9 o'clock position of the right breast, characterized by an irregular shape, unclear borders, and multiple punctate echogenic foci. Additionally, a 15 mm × 20 mm hypoechoic lesion was observed in the glandular tissue beneath the left nipple, characterized by an irregular shape, indistinct borders, and posterior echo attenuation. A linear arterial blood flow signal was detected, with an arterial resistance index of 0.7. No significantly enlarged lymph nodes were identified in the right axilla. However, several lymph nodes measuring less than 5 mm × 7 mm were palpable in the left axilla. These lymph nodes exhibited a regular shape, distinct borders, no significant cortical-medullary differentiation, and a longitudinal-to-transverse ratio of less than 2. Ultrasound diagnosis suggested hypoechoic nodules with calcifications at the 8–9 o'clock position of the right breast (Breast Imaging Reporting and Data System (BI-RADS) IVb–IVc) and hypoechoic nodules in the left breast areola region (BI-RADS IVc), along with abnormal enlargement of lymph nodes in the left axilla (Fig. 1A–C).

A breast magnetic resonance imaging (MRI) was performed without contrast, followed by contrast enhancement, and several significant findings were revealed. The left breast exhibited irregular skin, nipple retraction, and a mass-like lesion characterized by protracted T1 and T2 abnormal signals posterior to the left breast. This lesion displayed rough edges with multiple spiculations, measuring approximately 30 mm × 14 mm. The diffusion-weighted imaging (DWI) demonstrated a high signal, while the apparent diffusion coefficient (ADC) exhibited a slightly lower signal, with an average ADC value ranging from 0.852 to 0.976 × 10^{-3} mm^2/s. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) re-

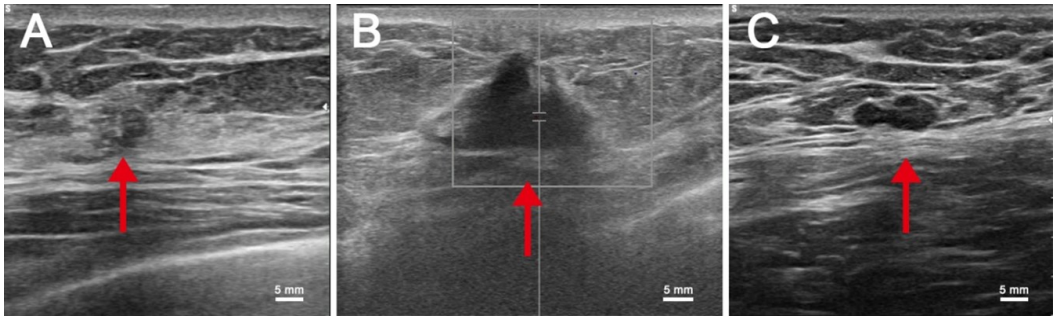

Fig. 1. Ultrasound images of breast cancer and left axillary lymph nodes at initial diagnosis. (A) Ultrasound image of the right breast showing a hypoechoic, nodule-like lesion at the 8–9 o'clock position, 23 mm away from the nipple (the red arrow). (B) Ultrasound image of the left breast showing a hypoechoic mass-like lesion beneath the nipple (the red arrow). (C) Ultrasound image of the left axilla showing enlarged lymph nodes (the red arrow).

vealed substantial heterogeneous enhancement, with the time-intensity curve (TIC) suggesting an outflow pattern. Maximum intensity projection (MIP) imaging revealed thickened and dilated vascular shadows surrounding the lesion. Additionally, a small nodular lesion with a long T2 signal was noted in the right breast, characterized by indistinct borders, high DWI signal, and contrast enhancement. Multiple small lymph nodes were observed within the left axilla. MRI diagnostic interpretation indicated an irregular mass-like abnormality posterior to the left breast, classified as BI-RADS IVc, along with a small nodular abnormality in the right breast designated as BI-RADS IVa (Fig. 2A,B). No significant metastatic lesions were detected in the brain, thoracic cavity, liver, bilateral supraclavicular regions, or skeletal structures.

Subsequently, a bilateral breast mass core needle biopsy was performed, revealing pathological findings of high-grade ductal carcinoma *in situ* in the right breast (Fig. 3A) and invasive ductal carcinoma, no special type (grade 2) in the left breast and left axilla (Fig. 3B).

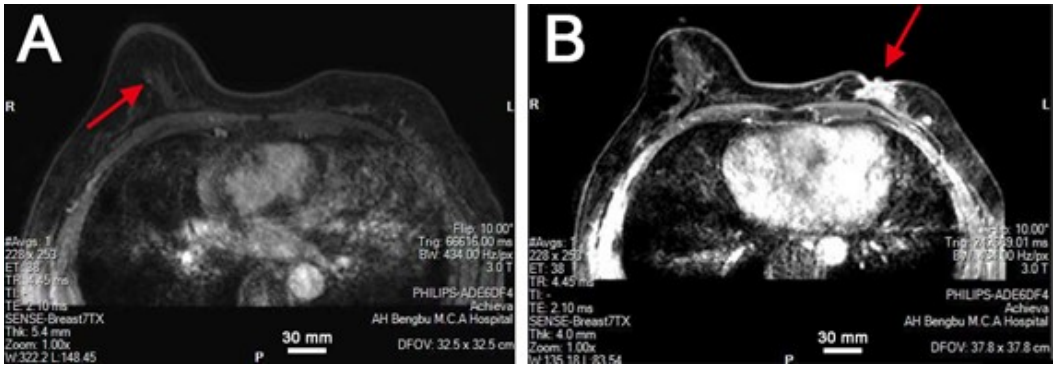

Fig. 2. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) of bilateral breast cancer at initial diagnosis. (A) DCE-MRI image of the right breast cancer lesion (the red arrow). (B) DCE-MRI image of the left breast lesion (the red arrow).

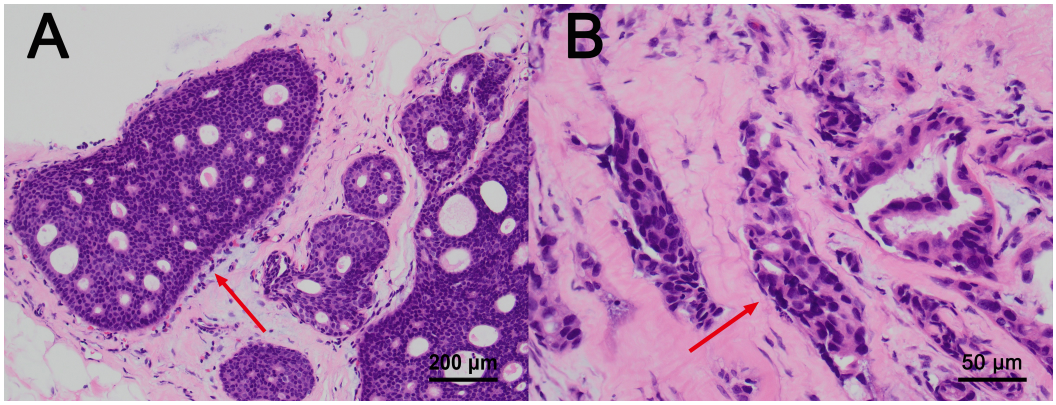

Fig. 3. Pathological images of core needle biopsy specimens from bilateral breast lesions at initial diagnosis. (A) Pathological image of the right breast lesion demonstrating high-grade ductal carcinoma *in situ* (the red arrow). (B) Pathological image of the left breast lesion showing invasive ductal carcinoma (the red arrow).

Immunohistochemical analysis of the right breast mass revealed strong estrogen receptor (ER) and progesterone receptor (PR) positivity, both at 3+ with 90% expression. Human epidermal growth factor receptor 2 (HER2) expression was equivocal at 2+, but fluorescence *in situ* hybridization (FISH) testing was negative, and the Ki-67 antigen (Ki-67) proliferation index was positively low at 5%. In the left breast tumor, ER was strongly positive at 3+ with approximately 90% expression, while PR was 3+ with 70% expression. HER2 expression ranged between 1+ and 2+, with FISH confirming a negative result, and Ki-67 positivity was higher at 30%. Similarly, the left axillary lymph nodes showed strong ER and PR positivity at 3+, with expression levels of 90% and 80%, respectively. HER2 expression was 2+, but FISH testing was negative, and Ki-67 positivity remained at 30%.

Following a multidisciplinary team (MDT) discussion, it was determined that the patient would initially receive neoadjuvant therapy with (docetaxel, doxorubicin, and cyclophosphamide) TAC. After three cycles of treatment, tumor lesions were reassessed using MRI and ultrasound. However, the response was classified as stable disease (SD) according to the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria, suggesting poor efficacy of neoadjuvant therapy. Consequently, on 12 September 2024, the patient underwent right breast-conserving surgery with right axillary sentinel lymph node biopsy, followed by a left breast modified radical mastectomy.

Postoperative pathological examination of the right breast revealed high-grade ductal carcinoma *in situ* with no definitive evidence of infiltration (Fig. 4A). The right axillary sentinel lymph node biopsy yielded negative results (0/11), although one lymph node exhibited focal necrosis consistent with granulomatous inflammation. All surgical margins (upper, lower, inner, outer, and base) were confirmed to be negative. The left breast specimen from the modified radical mastectomy contained a solitary lesion located at the nipple, classified as invasive breast cancer of no special type, grade 2. This lesion was associated with local necrosis of tumor cells, displaying atypical nuclear changes and fibrotic tumor stroma with lymphocytic infiltration, alongside a negative skin base margin. According to the

Miller-Payne grading system, the primary breast lesion was graded as 3. Additionally, left axillary lymph node dissection revealed metastases in 2 out of 25 lymph nodes (Fig. 4B).

Following the surgical intervention, the patient underwent endocrine therapy with letrozole and received 25 sessions of radiotherapy. No evidence of recurrence has been observed to date.

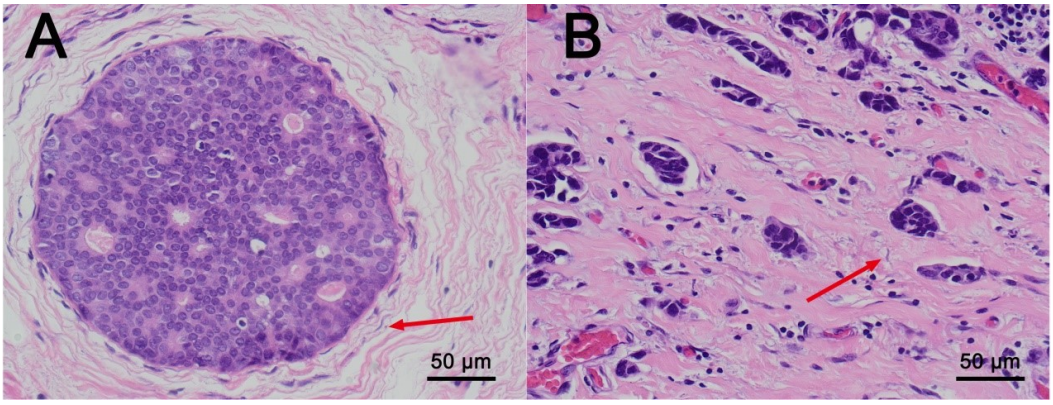

Fig. 4. Postoperative pathological images of bilateral breast lesions. (A) Pathological image of the right breast showing high-grade ductal carcinoma *in situ* (the red arrow). (B) Pathological image of the left breast lesions revealing invasive carcinoma with localized tumor cell necrosis, atypical nuclear changes, and Miller-Payne grade 3 (MP3) classification (the red arrow).

Discussion

Bilateral breast cancer is a rare clinical presentation, and recommended treatment guidelines remain unclear. In this study, we present a case of synchronous BBC, characterized by IDC in one breast and DCIS in the contralateral breast. This case highlights the complexity of BBC and underscores the importance of a comprehensive approach when making treatment decisions.

The clinical characteristics of tumors on both sides are vital factors influencing treatment selection. DCIS is often considered a direct precursor to IDC, with approximately 25–60% of untreated cases progressing to IDC within 9–24 years (Wang et al, 2024). However, the natural history and definite etiology of these two diseases differ significantly. IDC is an invasive malignancy with a higher risk of distant metastasis, necessitating more aggressive treatment to improve survival outcomes. In contrast, DCIS is a non-invasive lesion with a high overall survival rate and normal life expectancy after appropriate treatment (Wang et al, 2024). In cases of bilateral breast cancer, treatment decisions are typically guided by the tumor with the worst prognosis (Kuo et al, 2009), often leading to the selection of more aggressive treatment interventions, such as bilateral mastectomy (Schulze et al, 2024).

In the present case, the patient underwent breast-conserving surgery on the DCIS-affected side and a modified radical mastectomy on the IDC-affected side to prolong survival and improve life quality. This decision was based on a compre-

hensive evaluation of tumor characteristics and the patient's preferences. The IDC lesion was larger and had metastasized to the axillary lymph nodes, both indicating poor prognosis (Sinha and Gill, 2019). Consequently, a more aggressive surgical approach, including mastectomy combined with axillary lymph node dissection, was selected to reduce the risk of recurrence. On the contralateral side, the DCIS lesion was small and considered low-risk. Therefore, a less invasive surgical approach, such as breast-conserving surgery or lumpectomy, was chosen to minimize surgical complications and improve patient's quality of life. A recent study also showed that the difference in disease-free survival between patients treated with bilateral lumpectomy and those undergoing bilateral mastectomy is not statistically significant; furthermore, breast-conserving surgery does not compromise survival outcomes (Schulze et al, 2024).

Postoperative adjuvant therapy should be considered based on pathological findings (Deniffel et al, 2023). In cases of IDC, treatment may require a combination of adjuvant treatments, including chemotherapy, radiotherapy, endocrine therapy, and HER2-targeted therapy, depending on individual risk profiles (Luo et al, 2023). Conversely, for DCIS, additional adjuvant therapy is recommended only when the excision margins of lesions are positive or other high-risk factors are present (Co and Kwong, 2018). In the present case, the patient underwent neoadjuvant therapy before surgery. However, the efficacy was unsatisfactory. The poor effectiveness may be attributed to several factors, including the tumors' pathological characteristics, heterogeneity, and the patients' inherent resistance to chemotherapeutic agents (Foutadakis et al, 2024). Recent studies have indicated that the HER2-low expression subgroup of breast cancer (HER2 1+ or HER2 2+) exhibits a lower pathological complete response (pCR) rate compared to the HER2-null (no staining) subgroup after neoadjuvant therapy (Guan et al, 2024; Zhang et al, 2024). The low HER2 expression observed in this case may partially explain the suboptimal response to neoadjuvant therapy.

Additionally, a multidisciplinary team (MDT) collaboration in oncology has emerged as an essential approach for managing complex cases (Mangada et al, 2023). Collaboration with different multidisciplinary professionals enhances the comprehensiveness of the treatment and ensures that patients receive personalized care and support tailored to their unique needs.

Our study has several limitations. First, due to the lack of gene expression profiling and immune status assessment for the patient, we were unable to conduct a more in-depth analysis of the treatment efficacy. Additionally, as the patient's postoperative chemoradiotherapy was completed recently, long-term follow-up data are not yet available. Future studies should address these limitations by incorporating comprehensive molecular and immunological analyses, as well as providing extended follow-up data to better assess the long-term effectiveness of treatment options.

Conclusion

This case report presents a clinical example of the diagnosis and management of synchronous bilateral breast cancer, highlighting the critical role of multidisciplinary teamwork in managing complex breast cancer cases. An in-depth analysis of this case illustrates the significance of individualized treatment strategies and precision medicine in breast cancer management. Future research and clinical practice should focus on optimizing treatment and care for these patients to ensure that their unique needs are addressed effectively.

Learning Points

- Tailor treatment strategies based on tumor characteristics and patient-specific conditions.
- Optimize treatment planning through the integration of expertise from multiple medical disciplines.
- Continuously assess the efficacy of neoadjuvant therapy and adjust treatment approaches when necessary.

Availability of Data and Materials

The datasets used or analyzed in the current study are available from the corresponding author upon reasonable request.

Author Contributions

YW was primarily responsible for the conception and design of the study, the acquisition of data, and drafting the initial manuscript. YC and BZ contributed to the acquisition and analysis of data. XL contributed to the conception and design of the study, provided guidance and supervision throughout the research process. All authors contributed to revising the manuscript critically for important intellectual content. All authors gave final approval of the version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of Bengbu Medical University (approval number: 2024. No. 207). Written informed consent was obtained from the patient for the publication of this case report.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.1013.

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