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THE OPTIMAL TREATMENT OF INVASIVE DUCTAL AND LOBULAR CARCINOMA OCCURRING AT THE SAME TIME NEEDS TO BE ESTABLISHED

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ABSTRACT

Bilateral breast cancer with distinct histological subtypes poses a significant clinical challenge, requiring an individualised approach to management. This case discusses a 61-year-old postmenopausal woman with concurrent invasive ductal carcinoma (IDC) in the right breast and invasive lobular carcinoma (ILC) in the left breast. IDC, the most common breast cancer subtype, is known for its aggressive behaviour, nodal involvement and metastatic potential, while ILC, representing a smaller percentage of breast cancers, often exhibits an indolent course with diffuse growth patterns. Both tumours in this patient were hormone receptor-positive (ER/PR-positive) and HER2-negative, warranting targeted endocrine therapies. The complexity of this case was further heightened by a significant family history of breast and colon cancers, and comorbid conditions including borderline diabetes, hypertension and coronary artery disease (CAD), which required careful therapeutic consideration to balance efficacy and tolerability.

Pathological evaluation confirmed stage II, grade 2 IDC in the right breast with one positive sentinel lymph node and stage I, grade 1 ILC in the left breast with no nodal involvement. Given her extensive family history, the patient opted for bilateral mastectomy with sentinel lymph node biopsy. Multidisciplinary tumour board discussions emphasised the integration of genetic testing, including BRCA1/2 evaluation, and Oncotype DX genomic profiling to assess recurrence risk and guide adjuvant chemotherapy decisions. Recommendations included adjuvant radiation therapy for the right breast, endocrine therapy for both tumours and the incorporation of CDK 4/6 inhibitors based on recent evidence from the NATALEE trial, which demonstrated improved outcomes in high-risk, hormone receptor-positive, HER2-negative breast cancers.

The case highlights the need for further research into the optimal treatment strategies for synchronous breast cancers, a potential knowledge gap in current oncology practice. A literature review revealed limited reports addressing similar cases, underscoring the lack of consensus guidelines. Our approach integrates the best available evidence with multidisciplinary expertise to inform a personalised treatment plan. The learning points emphasise the need for establishing evidence-based strategies for managing synchronous bilateral breast cancers.

KEYWORDS

IDC, ILC, ER/PR positive, HER2-negative

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LEARNING POINTS

- The optimal treatment of synchronous bilateral breast cancers with differing histological subtypes remains uncertain.
- This case illustrates the importance of leveraging existing evidence, multidisciplinary collaboration and patient-centred decision-making when addressing knowledge gaps.
- There is a call for further research to establish guidelines for managing simultaneous, histologically distinct breast cancers.

INTRODUCTION

Bilateral breast cancer with distinct histological subtypes represents a complex clinical scenario that requires a highly individualised approach to management. This case involves a 61-year-old postmenopausal woman with invasive ductal carcinoma (IDC) in the right breast and invasive lobular carcinoma (ILC) in the left breast. IDC is the most common subtype of breast cancer, accounting for approximately 70–80% of cases, and is characterised by its aggressive behaviour and higher likelihood of nodal involvement and distant metastasis[1,2]. In contrast, ILC accounts for 10–15% of breast cancer cases and is typically associated with an indolent clinical course, high hormone receptor positivity and HER2-negative status, often leading to better long-term outcomes[3]. These distinct biological and clinical profiles necessitate tailored therapeutic strategies to address the unique features and risks associated with each tumour.

The complexity of this case is further compounded by the patient's significant family history of breast cancer in her paternal grandmother and aunt, and colon cancer in her father. A family history of breast cancer increases the risk of developing the disease by two to three times, particularly when first-degree relatives are affected[4]. This underscores the need for comprehensive genetic testing to assess for hereditary cancer syndromes, such as BRCA1/2 mutations, which may influence treatment decisions and risk management for the patient and her family members[5]. The presence of comorbid conditions, including borderline diabetes, hypertension and coronary artery disease (CAD), adds another layer of complexity, as these conditions can limit the therapeutic options available and increase the risk of treatment-related complications[6,7].

Molecular profiling and genetic testing are integral to the development of a personalised treatment plan. Tools such as Oncotype DX testing provide valuable insights into recurrence risk and the potential benefit of adjuvant chemotherapy, particularly for hormone receptor-positive, HER2-negative breast cancers such as those seen in this patient[8]. Additionally, the high oestrogen receptor and progesterone receptor positivity in both tumours highlight the central role of endocrine therapy in reducing recurrence risk. Advances in precision medicine, such as the incorporation of CDK 4/6 inhibitors for high-risk hormone receptor-positive breast cancers, provide further opportunities to enhance treatment efficacy[9].

The management of this patient required multidisciplinary collaboration, with input from oncology, surgery, genetics and cardiology specialists. Given the node-positive IDC in the right breast, adjuvant radiation therapy was recommended to minimise locoregional recurrence risk. Furthermore, the findings from the NATALEE trial supported the inclusion of CDK 4/6 inhibitor therapy in combination with endocrine therapy, which offers significant recurrence risk reduction in high-risk hormone receptor-positive, HER2-negative breast cancer[10]. The patient's decision to undergo bilateral mastectomy rather than breast-conserving surgery reflects her preference for a definitive approach, influenced by her extensive family history.

CASE DESCRIPTION

The patient is a 61-year-old postmenopausal woman with a complex medical history that includes borderline diabetes, hypertension and CAD. She also has a remote history of smoking and alcohol use, both of which ceased years prior to presentation. Her family history is significant for breast cancer in her paternal grandmother and aunt, and colon cancer in her father. Given this familial predisposition, she underwent routine screening mammography, which identified a 1.5 cm mass in the right breast and a 0.5 cm mass in the left breast.

An ultrasound evaluation of both axillae showed no evidence of lymphadenopathy. Subsequent ultrasound-guided core needle biopsies of both breast masses were performed; pathological evaluation confirmed IDC in the right breast and ILC in the left breast. Considering her extensive family history and personal preference for a more definitive approach, the patient opted for a bilateral mastectomy with sentinel lymph node biopsy, rather than breast-conserving surgery.

Post-surgical pathological examination revealed stage II, grade 2 IDC in the right breast, with one sentinel lymph node-positive for metastatic carcinoma. This tumour demonstrated oestrogen receptor positivity (80%) and progesterone receptor positivity (80%). The left breast showed stage I, grade 1 ILC, with no nodal involvement and high hormone receptor positivity (ER 95%, PR 85%). Both tumours were HER2-negative, and there was no evidence of lymphovascular invasion. Surgical margins were negative for residual disease, confirming complete resection.

To further evaluate the patient's cancer risk and guide adjuvant therapy decisions, genetic testing and Oncotype DX genomic testing were initiated. Genetic testing aimed to assess the presence of hereditary cancer syndromes, such as BRCA1/2 mutations, which could influence both her

treatment plan and her family's cancer risk management strategies. Oncotype DX testing was performed to quantify the likelihood of recurrence and evaluate the potential benefit of adjuvant chemotherapy for her hormone receptor-positive, HER2-negative tumours.

The patient's case was reviewed by a multidisciplinary tumour board, which considered her dual diagnosis of IDC and ILC, tumour pathology and molecular profile. Based on the node-positive status of the right breast IDC, adjuvant radiation therapy was recommended for the chest wall and regional nodes to reduce the risk of locoregional recurrence. Additionally, given the high-risk features of her IDC and findings from the NATALEE trial, the tumour board deemed her eligible for adjuvant endocrine therapy in combination with a CDK 4/6 inhibitor, such as abemaciclib. This recommendation was made to address the increased risk of recurrence associated with her node-positive, hormone receptor-positive breast cancer, despite the absence of HER2 amplification. The treatment plan for this patient emphasises a personalised and evidence-based approach, integrating multiple modalities:

- *Adjuvant radiation therapy:* targeting the right breast and axillary region due to node-positive disease.
- *Endocrine therapy:* initiating aromatase inhibitor therapy as part of standard treatment for postmenopausal women with hormone receptor-positive tumours.
- *CDK 4/6 inhibitor therapy:* adding a targeted agent to enhance the efficacy of endocrine therapy and mitigate recurrence risk, supported by the NATALEE trial findings.
- *Monitoring and follow-up:* regular imaging and clinical evaluations to assess response to therapy and to detect any recurrence.

This case highlights the complexity of managing bilateral breast cancer with distinct histological subtypes, requiring a multidisciplinary and tailored approach to optimise outcomes. The integration of molecular diagnostics, advanced therapeutic strategies and close monitoring ensures a comprehensive care plan tailored to the patient's unique clinical scenario.

DISCUSSION

This case underscores the contrasting biological behaviours of IDC and ILC, necessitating tailored management strategies. IDC, the most common subtype of breast cancer, is associated with aggressive behaviour, frequent nodal metastases and a higher risk of recurrence[1]. Conversely, ILC typically follows a more indolent course, characterised by hormone receptor positivity and HER2 negativity, leading to a generally favourable prognosis[2].

In this patient, the IDC presented as stage II, grade 2, with one positive sentinel lymph node, indicating a significant risk of recurrence and necessitating additional therapeutic interventions. Meanwhile, the stage I, grade 1 ILC tumour, with no nodal involvement, suggested a more favourable prognosis. Both tumours' hormone receptor positivity highlighted the pivotal role of endocrine therapy in the treatment plan, reflecting standard evidence-based practices[6].

The patient's substantial family history of breast and colon cancers elevated her risk of hereditary cancer syndromes. Studies show that having a first-degree relative with breast cancer increases risk by two to three times, particularly when multiple relatives are affected[3]. Genetic testing, including evaluation for BRCA1/2 mutations, is crucial in such cases. The identification of a hereditary predisposition would not only guide treatment decisions but also inform risk reduction strategies for the patient's family[4]. Moreover, this testing provides insights into potential therapeutic targets, such as poly-ADP ribose polymerase inhibitors, in cases involving BRCA mutations.

Managing a case of synchronous bilateral breast cancers requires a multidisciplinary approach. The tumour board considered critical factors such as tumour grade, receptor status, nodal involvement and the patient's cardiovascular comorbidities to devise an optimised treatment plan.

The inclusion of Oncotype DX testing provided prognostic insights into the recurrence risk and informed decisions regarding adjuvant chemotherapy. However, the patient's cardiovascular comorbidities necessitated a careful evaluation of chemotherapeutic agents, as agents such as anthracyclines and taxanes carry cardiotoxic risks[5].

Adjuvant therapy strategies are:

- *Endocrine therapy:* Given the high oestrogen receptor and progesterone receptor positivity in both tumours, aromatase inhibitors were recommended as the cornerstone of adjuvant treatment. Aromatase inhibitors are particularly effective in reducing recurrence risk in postmenopausal women with hormone receptor-positive breast cancers[6].
- *CDK 4/6 inhibitors:* The NATALEE trial demonstrated the efficacy of CDK 4/6 inhibitors, such as abemaciclib, in reducing recurrence risk in high-risk, hormone receptor-positive, HER2-negative breast cancers. The patient's node-positive IDC qualified her for this therapy, adding a layer of protection against recurrence[7].
- *Radiation therapy:* Adjuvant radiation therapy targeting the right breast and axillary region was recommended to address the node-positive disease. This aligns with standard guidelines for reducing local recurrence in such cases[2].

The patient's comorbid conditions, including CAD, underscore the importance of supportive care during treatment. Strategies to mitigate endocrine therapy-related side effects, such as osteoporosis and cardiovascular risks, are particularly relevant for postmenopausal women. Collaboration with cardiology was essential to optimise the patient's cardiovascular health throughout her treatment[8]. Additionally, lifestyle modifications, including a healthy diet and regular physical activity, should be encouraged to reduce overall cancer risk and improve long-term outcomes.

A significant knowledge gap exists regarding the optimal treatment of synchronous bilateral breast cancers with

distinct histological subtypes. While individual tumour characteristics often guide management, their concurrent occurrence presents unique challenges. Balancing the aggressive management required for IDC with the generally favourable prognosis of ILC requires careful consideration.

A review of the literature revealed limited case reports addressing similar scenarios, many of which pre-date advancements in molecular profiling and modern therapeutic approaches. This highlights the need for further research to establish evidence-based guidelines for managing synchronous malignancies. By comparing our management approach to historical cases, this report aims to contribute to the growing discourse on this topic.

CONCLUSION

This case underscores the challenges of managing synchronous bilateral breast cancers with distinct subtypes, highlighting the importance of a personalised, evidence-based approach. The integration of genetic testing, molecular profiling and innovative therapies, such as CDK 4/6 inhibitors, demonstrates how individualised care can address the unique complexities of such cases. The limited guidance in current literature emphasises a significant knowledge gap, underscoring the need for further research to develop consensus guidelines. This case contributes to the discourse by showcasing the role of multidisciplinary collaboration and precision medicine in improving patient outcomes and informing future oncology practice. Upon conducting an extensive review of the available literature, we found no previously documented cases of IDC and ILC occurring concomitantly. Consequently, the management of our case was meticulously guided by a multidisciplinary tumour board's consensus discussion, ensuring a collaborative and comprehensive approach, and was aligned with the most current National Comprehensive Cancer Network guidelines.

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