CASE REPORT

CONTRASTING OUTCOMES IN BILATERAL HORMONE POSITIVE BREAST CANCER: COMPLETE PRIMARY TUMOUR REGRESSION WITH PERSISTENT NODAL METASTASIS

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ABSTRACT

Introduction: Bilateral breast carcinoma (BBC) is an uncommon but clinically significant condition, with an incidence ranging from 1.4% to 12%. It can present synchronously or metachronously and poses diagnostic and therapeutic challenges due to its rarity and heterogeneous biological behavior. Complete primary tumor regression refers to the complete disappearance of the primary tumor at the site of origin in response to treatment with no detectable cancer cells remaining either clinically, radiologically or pathologically.

Case Presentation: We present the case of a 56-year-old postmenopausal woman who presented with complaint of right breast lump and bilateral axillary lymphadenopathy which was incidentally detected during routine screening. Initial biopsy confirmed hormone receptor positive and Human Epidermal Growth Factor Receptor-2 (HER-2) negative status. Imaging revealed Breast Imaging Reporting and Data System (BIRADS)-6 in both breasts, yet a pre-treatment biopsy of the left breast was not performed due to the absence of a palpable mass. The patient received neoadjuvant chemotherapy and thereafter bilateral modified radical mastectomy. Postoperative histopathology showed no residual tumor in either breast but revealed metastatic disease in 2 of 5 sampled lymph nodes from the left axilla, which were also hormone receptor positive and HER2-negative. These findings raised two possible diagnoses: (1) synchronous bilateral hormone receptor positive breast cancer with complete primary tumor regression and residual nodal disease or (2) right-sided primary with contralateral axillary metastasis (CAM).

Conclusion: The case illustrates a rare scenario of complete bilateral primary tumor regression with persistent nodal metastasis, highlighting the unpredictable nature of hormone receptor-positive breast cancers. It emphasizes the need for meticulous assessment of both breasts and lymphatic regions, especially in patients with bilateral lymphadenopathy, to ensure accurate diagnosis and optimal therapeutic planning. It also contributes to the limited literature on such complex presentations from Sub-Saharan Africa.

Keywords: Bilateral breast carcinoma, synchronous breast cancer, complete tumour regression, contralateral axillary metastasis.

INTRODUCTION

Bilateral breast carcinoma (BBC) is a relatively uncommon clinical scenario, though not extremely rare, with incidence of 1.4-12%.[1] Due to its low frequency, standardized guidelines for diagnosis and management remain unclear. Invasive lobular carcinoma in the initial breast, a family history of breast cancer, younger age at the time of first diagnosis, and the presence of BRCA gene mutations are all recognized as significant risk factors that increase the likelihood of developing bilateral breast cancer.[2]

Bilateral breast cancers can be classified according to the time of their presentation as synchronous (within 6 months of primary breast cancer) or metachronous (after 6 months of primary breast cancer).[3] Patients with metachronous bilateral breast cancer tend to have a worse disease-free survival compared to those with synchronous bilateral or unilateral breast cancer. However, overall survival rates remain similar across these groups.[4]

Metastasis is the multiple process by which an original primary tumor develops into a distal secondary tumor. The typical metastatic spread of breast carcinoma involves regional lymph nodes, particularly the ipsilateral axillary nodes, and distant organs such as bones, lungs, liver, and brain.[5] Contralateral axillary lymphadenopathy (CAM), where cancer cells spread to the axillary lymph nodes opposite the primary tumour, is an uncommon clinical presentation, with reported incidences ranging from 1.9% to 6%.[6] CAM can manifest either synchronously, at the time of initial breast cancer diagnosis, or metachronously, as a recurrence following prior treatment.[7]

We present a case of bilateral hormone positive breast cancer with complete regression of the primary tumour and persistence of nodal metastasis, one of the few case reports on this from Sub-Saharan Africa.

CASE REPORT

A 56-years-old postmenopausal woman presented to our facility in early January 2024 with complaints of a right breast lump and bilateral axilla lymphadenopathy which were incidentally detected during a breast cancer awareness screening program. There was no pain in either breast or axillae. The breast lump was not associated with nipple retraction or abnormal discharge. There was no cough, chest pain or respiratory distress. Furthermore, she had no of history bone pain, abdominal swelling or symptoms suggestive of intraabdominal metastases. There were no neurological symptoms. However, she had a history of bilateral benign breast lumps 10 years ago, which were excised. On clinical examination of the right breast, a single firm, mobile, and irregularly shaped mass was palpated in the upper outer quadrant; it was non-tender and not fixed to the overlying skin or underlying structures. No palpable mass was detected in the left breast. There were multiple bilateral lymph nodes which were mobile, firm, non-tender located at level I and II.

Consequently, Tru-Cut biopsy of the right breast lump was done which revealed Invasive Ductal Carcinoma (IDC) Non-Special Type (NST); Scarff-Bloom-Richardson (SBR) Grade 5/9. Immunohistochemistry (IHC) was positive for Estrogen Receptor (ER), focal positivity for Progesterone Receptor (PR), and negative for Human Epidermal Growth Factor Receptor (Her-2). An Excisional biopsy was later done which further confirmed the diagnosis. During follow up, mammography was done which showed scattered fibroglandular density (ACR-Type-B) on both

breasts. Multiple spiculated lesions were also seen in all quadrants of the right breast, while only fewer similar lesions were seen in the left breast. There was also distortion of the parenchyma with few macrocalcifications in both breasts. Furthermore, an oval shaped well circumscribed opacity was seen in the retromammary spaces around the upper quadrants of the left breast. Additionally, bilateral lymph nodes were noted in both axillae with pop-corn calcifications. A conclusion of Breast Imaging Reporting and Data System (BIRADS) score of 6 on both breasts with bilateral axilla lymphadenopathies was made.

MANAGEMENT AND OUTCOME

Following institutional guidelines, the patient was commenced on neoadjuvant chemotherapy (NACT) with the AC regimen i.e. cyclophosphamide 600mg/m^2 and doxorubicin 60mg/m^2 every 3 weeks for six cycles. She completed NACT and was evaluated. There was clinical resolution of the right breast lump and axillary mass. Chest X-ray and abdominopelvic ultrasound scan showed no evidence of distant metastasis. She was referred to the General Surgeons for modified radical mastectomy of the right breast. However, based on the result of previous bilateral mammography which showed suspicious mass in the left breast, patient voluntarily opted for bilateral modified radical mastectomy. She had a double mastectomy after which she was started on letrozole 2.5mg daily. The post mastectomy pathology report showed that there was no detectable tumor in both mastectomy specimen, there was extensive fibrosis seen in both breasts with negative resection margins. Out of 5 lymph nodes sampled from the left axilla, 2 showed tumor involvement; IHC revealed that the tumor was ER-negative, PR-patchy positive, and Her-2 negative. This result necessitated a revision of her diagnosis in retrospect from right hormone positive breast cancer to bilateral hormone positive breast cancer with primary tumour regression and persistent nodal metastasis. However, a differential diagnosis of right hormone positive breast cancer with CAM was made because the left breast was not biopsied prior to NACT and there could be possibility of a benign lesion. The treatment plan was reviewed. The patient was subsequently referred for external beam radiotherapy to the chest wall and regional nodal irradiation. As at the last visit, the patient was stable and did not have any symptoms of residual disease, recurrence, or distant metastasis.

DISCUSSION

BBC is a rare clinical condition, most often occurring metachronously, while the synchronous form comprising about 0.2% to 3% of newly diagnosed breast cancer cases.[3] Synchronous BBC often involves slower growing, less aggressive tumors and occurs in older patients, making simultaneous detection more likely due to subclinical presentation.[8]

Current evidence suggests that primary synchronous BBC represent independent primary tumors rather than metastatic dissemination from a unilateral lesion.[3]

In most patients with BBC, the second tumour is identified at an early stage than index tumours supporting the importance of contralateral breast cancer screening at the time of primary diagnosis and during follow-up. BBC occurs more frequently in old age group and majority of these tumours are estrogen dependent.[10] There is strong pathological similarity between the index tumour and the contralateral breast cancer.[9]

Indicators that the tumors are separate primary cancers include the presence of an intraductal component, differences in histological types, or varying degrees of differentiation between the tumors.[3]

In cases of BBC, distinguishing between metastatic spread from one breast to the other and the presence of an independent primary tumor in the contralateral breast is essential for informing optimal treatment strategies and accurately evaluating the patient's prognosis.[10] Histological features suggesting a second primary tumor rather than an intra-breast metastasis include differences in tumor types, variations in the degree of differentiation, and the presence of an in-situ component.[11]

However, in the case of our patient although the histology report of the right breast lump biopsy done before NACT showed Hormone positive and Her2 negative, no biopsy was done on the left breast because there was no palpable lump observed. Additionally, the histology report of the resected breast tissues following double mastectomy revealed no evidence of malignancy, although 2 out of the 5 left axillary lymph node biopsy confirmed tumour involvement with also hormone positive and Her2 negative.

Bilateral axillary lymphadenopathy in primary breast cancer may result from an undetected primary tumor in the opposite breast, CAM, or a non-mammary tumor. This case underscores the importance of thorough testing and detailed evaluation when a patient presents with unilateral breast cancer with bilateral lymphadenopathy. Such an approach is essential to identify or rule out BBC and CAM, which may exhibit features distinct from those of the initial tumor. We present this case to provide initial evidence of the rare occurrence of contrasting outcomes in complete bilateral primary tumour regression with persistent nodal metastasis.

CONCLUSION

This case underscores the complex and sometimes paradoxical behaviour of bilateral hormone receptor-positive breast cancer, where complete regression of the primary tumours can occur alongside persistent nodal metastasis. Such contrasting outcomes demonstrates the heterogeneity of tumour biology, even within the same molecular subtype. Furthermore, the persistence of nodal metastasis despite complete tumor regression emphasizes the need for tailored treatment planning and vigilant follow-up. It also emphasizes the need for thorough pre-treatment evaluation, including biopsy of the contralateral breast when imaging indicates malignancy, even if there are no clinical symptoms and signs. This is with a view to ensuring prompt and effective diagnosis management of bilateral breast cancer.

DECLARATIONS

Ethical Considerations

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal

Competing Interests

The authors declare that they have no competing interests

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