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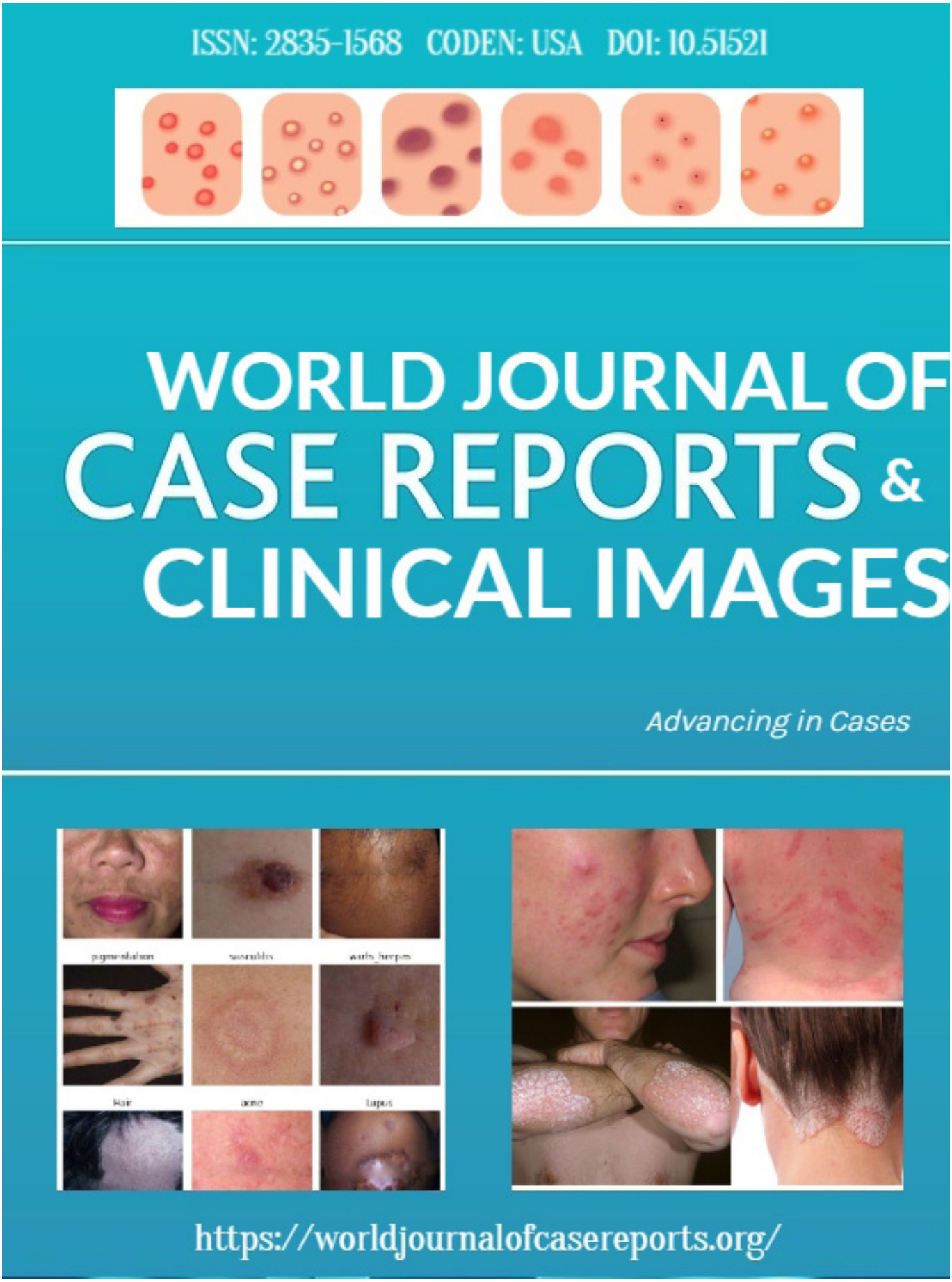

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CASE REPORT

Synchronous Bilateral Breast Carcinoma Treated with Breast Conserving Surgery. Presentation of Two Cases and Literature Review

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Abstract

Synchronous bilateral breast carcinoma (sBBC) is an uncommon entity, with great challenges, as far as optimal surgical treatment concerned. Two women, with synchronous bilateral breast cancers were referred to the Breast Department of our hospital. According to the multidisciplinary team decision, both of them were treated with breast conserving surgery. At present, both of them are free of disease. So far, there are no clear guidelines about sBBC, and the treatment is scheduled according to the more advanced tumor. Advancements in radiotherapy and oncoplastic techniques have made breast conserving surgery (BCS) both feasible and safe. Treatment of such cases demand a careful preoperative planning and therefore treatment should be individualized by a multidisciplinary team (MDT).

Keywords: Breast Conserving Surgery, Case Report, Multidisciplinary Team, Radiotherapy, Synchronous Bilateral Breast Cancer.

Highlights:

- To emphasize that synchronous bilateral breast carcinoma (sBBC) poses great therapeutic challenges
- To highlight the critical role of multidisciplinary team involvement in managing sBBC
- To stress the fact that the more advanced breast tumor guides treatment in sBBC
- To demonstrate Breast conserving surgery (BCS) for sBBC is both feasible and safe

Introduction:

Bilateral breast cancer (BBC) is a relatively uncommon, challenging entity. So far there is lack of consensus in terms of definitions, staging and treatment [Mishra et al. 2023]. It may present as synchronous bilateral breast cancer (sBBC) or metachronous bilateral breast cancer (mBBC). The incidence is variable and represents 2.9-3.9% of all breast cancers [Tada 2025]. Advances in breast imaging techniques have resulted in an increase in the incidence of sBBC [Mishra et al. 2023, Naik et al. 2023]. Herein, we present two cases of sBBC, both treated with breast conserving surgery followed by radiotherapy.

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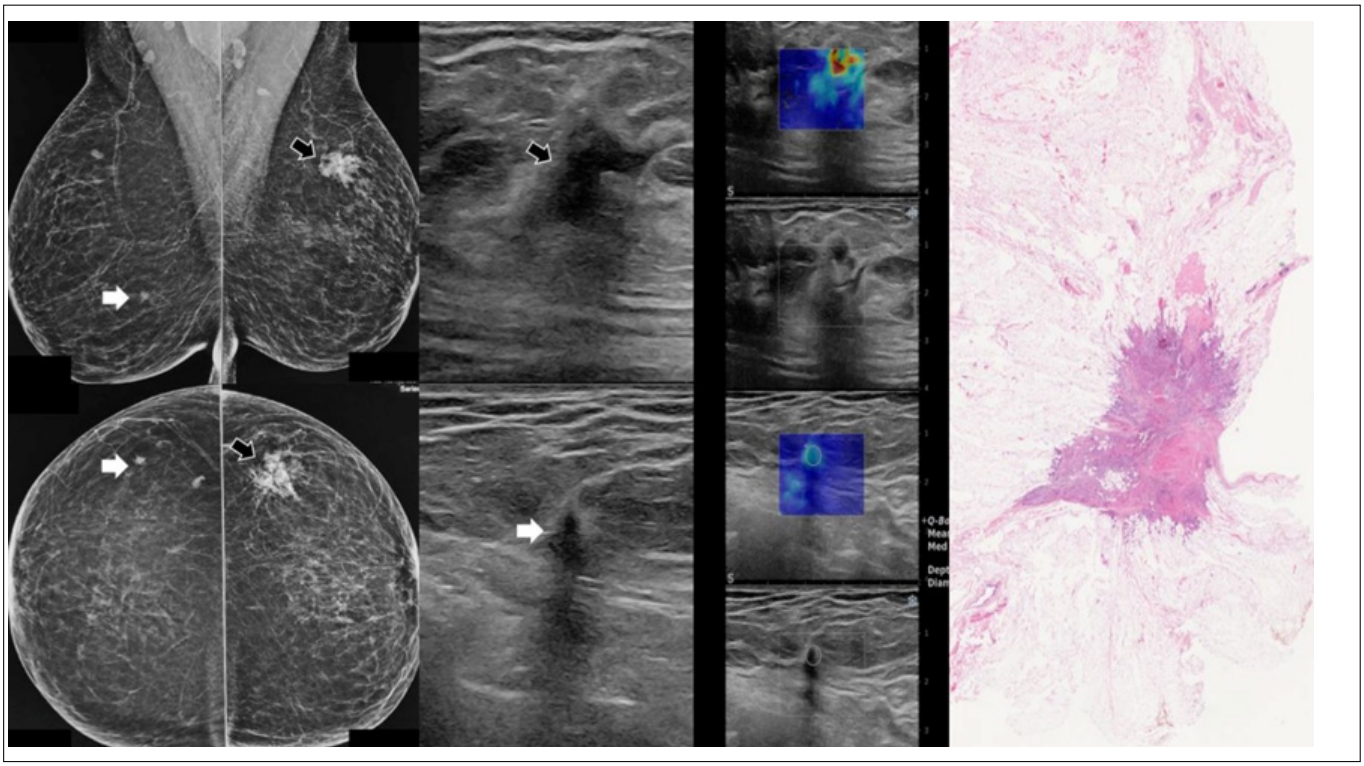

Graphical Abstract

Case Presentation:

Case 1:

A 66-year-old post-menopausal female was referred to the Breast Department of our hospital with a palpable mass in the upper outer quadrant of the left breast. She had a clear past medical history and did not receive any drugs. She reported no family history of breast or ovarian cancer. Clinical examination of the contralateral breast and both axillae was normal.

Mammography and ultrasound of both breasts was performed with the following findings. The findings were reported according to the Breast Imaging Reporting and Data System (BI-RADS). Left breast: BI-RADS 4C lesion, at two o'clock, 7 cm from the nipple. The dimensions were 20 x 17 mm. Right breast: BI-RADS 4C lesion, max diameter 7 mm, 10 cm from the nipple at eight o'clock. (Figure 1) Core needle biopsy (CNB) of both lesions was performed. Both breast lesions were ductal carcinomas of No Special Type (NST). Left breast lesion was Estrogen receptor (ER) positive, Progesterone Receptor (PR) negative and Human Epidermal Growth Factor Her2-low (score 1+). Right breast lesion was ER positive, PR positive and Her2 negative. The staging was completed with thoracic and abdominal computed tomography (CT) and bone scan, that were negative for metastases.

The case was discussed in the MDT meeting. Bilateral breast conserving surgery (BCS) with bilateral sentinel lymph node biopsy (SLNB), using the blue dye technique was performed. Two sentinel lymph nodes from the left axilla and one sentinel lymph node from the right axilla were negative both in the frozen section and the final histopathologic exam. No drains were placed. She was discharged on postoperative day 1. The postoperative course was uneventful.

The findings of the postoperative histologic examination were as following: Left breast: Ductal carcinoma NST grade 2, d=2.5 cm. Immunohistochemistry: ER positive (Allred score 8), Progesterone Receptor (PR) negative (Allred score 0), Her2 low (1+), Ki 67=18%. Negative margins achieved. Lymph invasion present, no vascular invasion. Stage T2N0. Right breast: Ductal carcinoma NST grade 2, d=0.6 cm, ER positive (Allred score 8), PR positive (Allred score 4), Her2 negative (0), Ki 67=12%. Negative margins achieved. No lymphovascular invasion. Stage T1bN0 (Figures 2 & 3).

The oncotype recurrence score was 18, so the patient received no chemotherapy. She received bilateral radiotherapy and she continues hormonal therapy (letrozole 2.5 mg) for 5 years according to the guidelines. She is followed up six months postoperatively. Clinical examination revealed no recurrence. She has neither lymphedema, nor upper arm paresthesia.

Case 2:

A 53-year-old postmenopausal female was referred to the Breast Department of our hospital with a palpable mass in the upper outer quadrant of the right breast. She had a clear past medical history and did not receive any drugs. She reported no family history of breast or ovarian cancer. Clinical examination of the contralateral breast and both axillae was normal.

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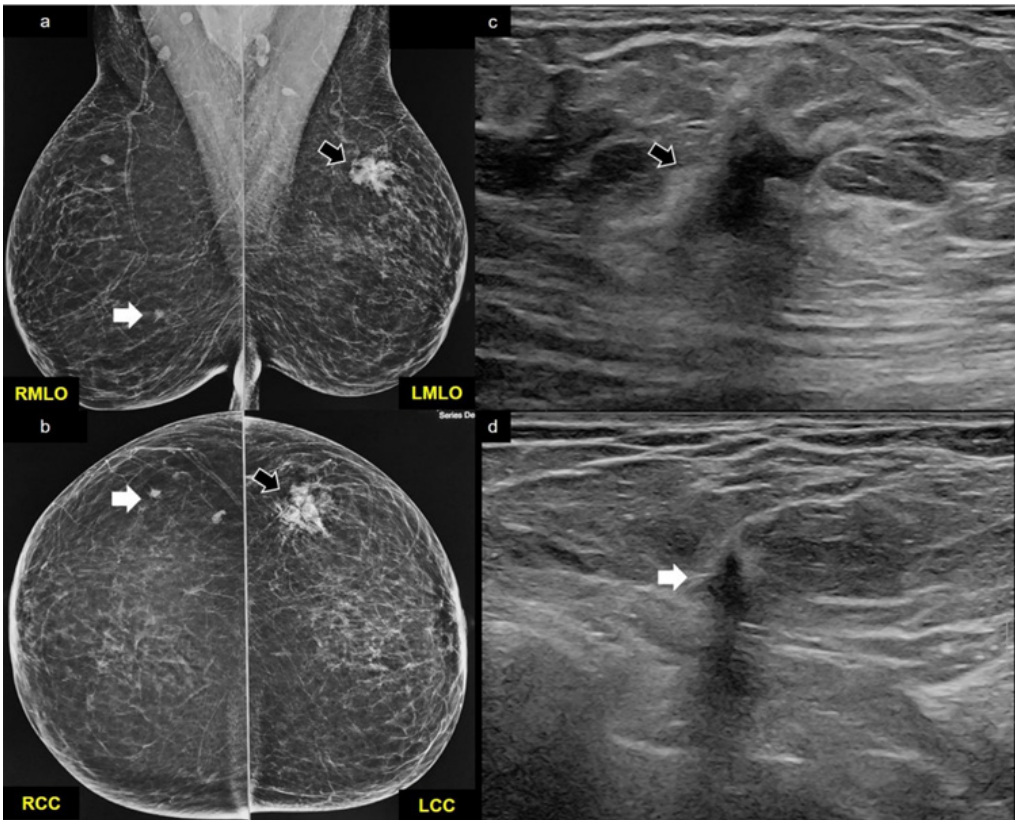

Figure 1: Radiologic examinations: The lateral oblique (a) and the craniocaudal (b) mammographic images demonstrate breast tumors both on the right breast (white arrows) and on the left breast (black arrows). The findings were verified with ultrasound examination (c-d: black arrow shows tumor on the left and white arrow tumor on the right breast).

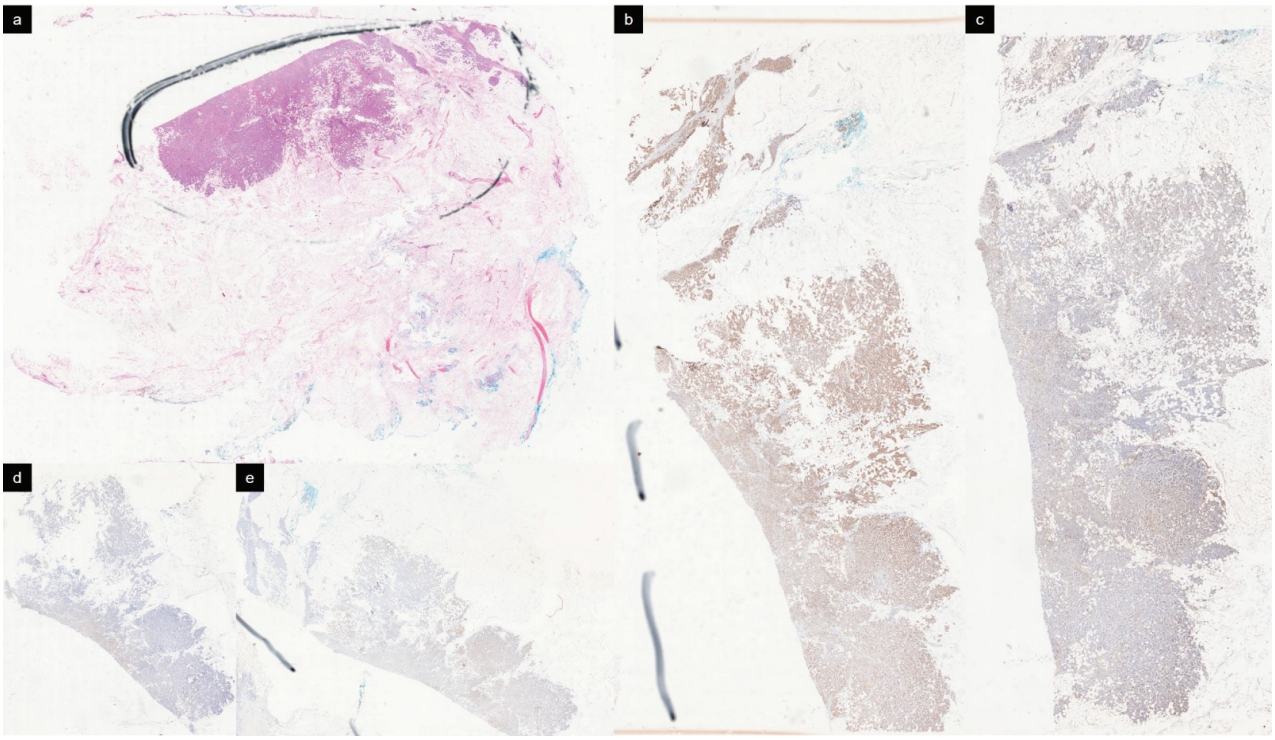

Figure 2: Histopathologic images of the right breast tumor: (a) hematoxylin-eosin stain shows neoplastic cells magnification view x20, (b) ER positive immunohistochemistry stain (Allred score 8), magnification view x20, (c) ki67 immunohistochemistry stain, magnification view x20, (d) PR positive immunohistochemistry stain (Allred score 4), magnification view x20 (e) HER2 negative immunohistochemistry stain, magnification view x20.

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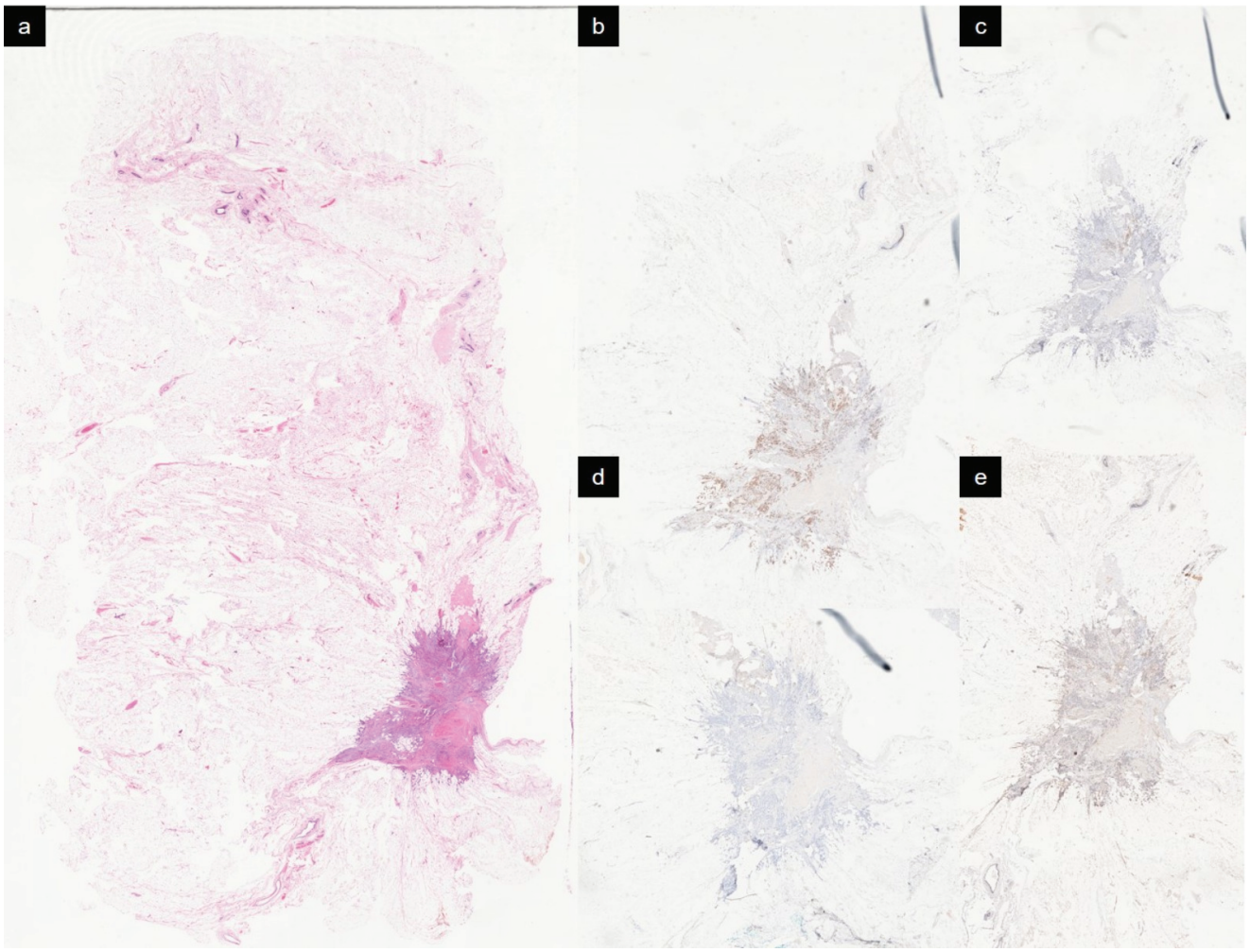

Figure 3: Histopathologic images of the left breast tumor: (a) hematoxylin-eosin stain shows neoplastic cells magnification view x20, (b) ER positive immunohistochemistry stain (Allred score 8), magnification view x20, (c) PR negative immunohistochemistry stain (Allred score 0), magnification view x20 (d) HER2 low immunohistochemistry stain 1+, magnification view x20 (e) ki67 immunohistochemistry stain, magnification view x20.

Mammography had abnormal findings. The ultrasound revealed abnormal findings in both breasts. Right breast: hypoechoic and vascularized lesion with lobulated margins and vertical axis at nine o' clock. The distance from the nipple was 8-10 cm. The dimensions were 26 x 23 x17 mm. Left breast: hypoechoic lesion with vertical axis and architectural distortion at twelve o'clock, 5 cm from the nipple. The dimensions were 11 x 8 x 7 mm (Figure 4).

Core needle biopsy (CNB) of both lesions was performed. Left breast: invasive carcinoma NST. Right breast: invasive papillary carcinoma. Both cancers were ER positive, PR positive and Her2 low (1+). The staging was completed with a thoracic and abdominal CT scan and a bone scan, that were negative for metastases.

The case was discussed in the MDT meeting. Bilateral breast conserving surgery (BCS) was performed with bilateral sentinel lymph node biopsy, using blue dye technique. Four sentinel lymph nodes from the left axilla were negative in the frozen section. In the right axilla, two sentinel lymph nodes were positive in the frozen section and therefore, an axillary lymph node dissection (ALND) was performed. The postoperative course was uneventful. She was discharged on postoperative day 1, with a drain, which was removed 12 days later.

The findings of the postoperative histologic examination were as following: Left breast: Invasive carcinoma, tubular and NST grade 1, d=1.5 cm. Immunohistochemistry: ER positive (Allred score 8), PR positive (Allred score 8), Her2 low (1+), Ki 67=4%. Four axillary lymph nodes removed without infiltration. Stage T1c, N0, M0. Right breast: Invasive carcinoma NST, solid and papillary type grade 1, d=2.6 cm. Immunohistochemistry: ER positive (Allred score 8), PR positive (Allred score 6), Her2 equivocal (2+), Ki 67=9%. Fluorescence in Situ Hybridization (FISH) test was performed and the neoplasm was Her2 negative. Nine out of sixteen nodes were infiltrated. Stage T2N2a (Figures 5 & 6).

The patient was referred to the MDT for further treatment. She received chemotherapy, 4 cycles epirubicin-cyclophosphamide and 4 cycles docetaxel, followed by whole

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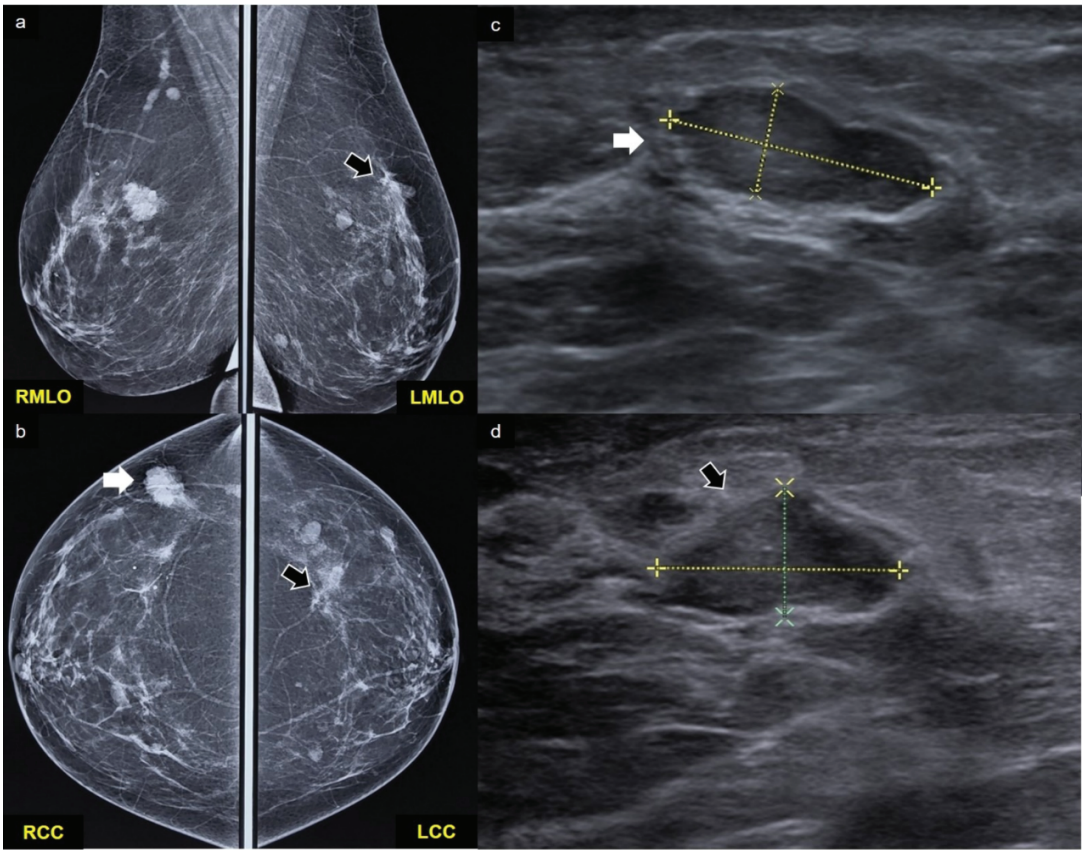

Figure 4: Radiologic examinations: The lateral oblique (a) and the craniocaudal (b) mammographic images demonstrate breast tumors both on the right breast (white arrows) and on the left breast (black arrows). The findings were verified with ultrasound examination (c-d: black arrow shows tumor on the left and white arrow tumor on the right breast).

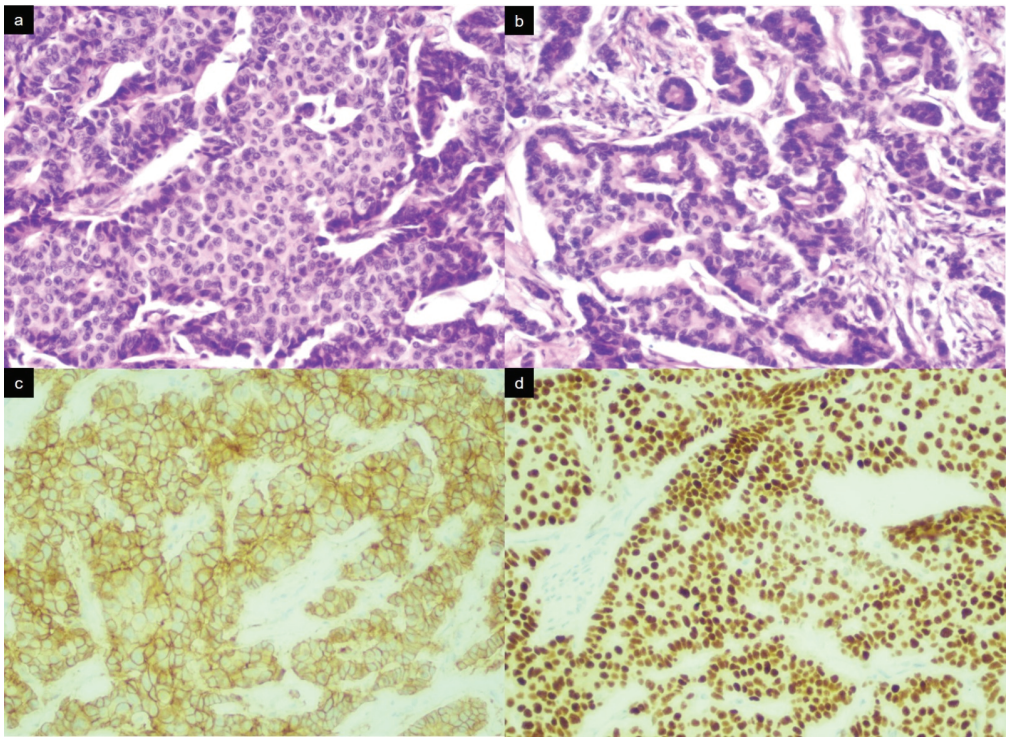

Figure 5: Histopathologic images of the right breast tumor: (a-b) hematoxylin-eosin stain, show solid trabecular and cribriform patterns of neoplastic cells, magnification view x20. (c) ER strong and intermediate positive immunohistochemistry stain, magnification view x20. (d) HER2 equivocal immunohistochemistry stain 2+, magnification view x20.

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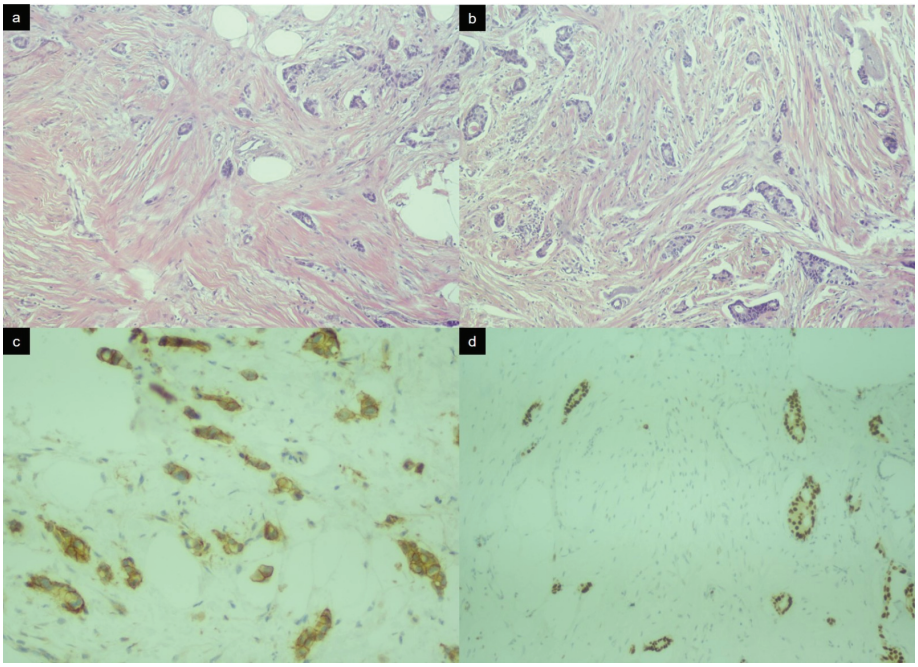

Figure 6: Histopathologic images of the left breast tumor: (a-b) hematoxylin-eosin stain, shows tubular pattern of the neoplastic cells, magnification view x10. (c) ER strong positive immunohistochemistry stain, magnification view x10. (d) HER2 low immunohistochemistry stain 1+, magnification view x20.

breast radiotherapy (WBRT) in both breasts and hormone therapy (exemestane 25mg daily).

During the three-year follow-up, the patient did not have any recurrence of the disease. Follow-up included clinical examination every six months, annual mammography and breast ultrasound and symptom-directed imaging. She has neither lymphedema, nor upper arm paresthesia. She continues hormone therapy (exemestane 25mg daily) for five years according to guidelines.

Discussion:

BBCs may present as synchronous bilateral breast cancer (sBBC) or metachronous bilateral breast cancer (mBBC), according to the time interval between the diagnosis of bilateral primary breast tumors. So far, different time intervals have been used to discriminate these two entities, varying from one month to 12 months. The most common time interval used in large retrospective studies, is six months [Jiang et al. 2021]. In both our cases the diagnosis of synchronous bilateral cancers is clear, since both cancers were diagnosed and treated simultaneously.

So far there is a lack of consensus over the optimal management of BBC. It has been suggested that choice of surgical treatment in BBC should be similar to that of unilateral cancers [O'Brien et al. 2015]. Multiple factors affect the management of BBC and such cases should be discussed in MDT meetings. According to some studies, tumor size and disease stage seem to have a significant difference between both breasts [Jiang et al. 2021]. In the case of sBBC, the treatment is scheduled according to the side with the more advanced stage [Mishra et al. 2023]. Consequently, if a breast conserving surgery is technically feasible in the side with the more advanced stage, then breast preservation is feasible bilaterally. In both presented cases the decision of bilateral breast preservation was taken according to the breast with the more advanced stage. Moreover, in both cases, tumors were located in the outer quadrants of both breasts and therefore symmetry was feasible with common oncoplastic techniques with an acceptable cosmetic result.

In some studies, bilateral mastectomy seems to be preferred [O'Brien et al. 2015; Jiang et al. 2021; Mishra et al. 2023], although second tumors are diagnosed at an earlier stage. However, the factors that define the final surgical decision making, including the patient preference [O'Brien et al. 2015] and the stress related to diagnosis of two cancers are not yet fully identified [Padmanabhan et al. 2015]. Breast conservation therapy in sBBC is feasible but demands a careful planning of postoperative radiotherapy, because of the overlapping of radiation fields in the medial aspects of both breasts. Nowadays, this is minimized by CT simulation and newer radiation techniques, such as three dimensional (3D) conformal radiotherapy, intensity modulated radiotherapy (IMRT), and volumetric modulated arc therapy (VMAT) [Mishra et al. 2022]. As far as unilateral breast cancer concerned, randomized controlled trials and a recent meta-analysis have showed that breast conserving surgery combined with RT offers a survival benefit compared to mastectomy [Rajan et al. 2024]. However, more studies are needed to verify if breast conserving surgery combined with RT offers a survival benefit in case of bilateral cancers.

According to the literature, BBC are more commonly invasive

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ductal carcinomas, hormone receptor positive, Her2 negative [Mishra et al. 2022]. The histopathologic type, the grade and the ER, PR, Her 2 status of sBBC is more usually concordant in both breasts [Jiang et al. 2021, Mishra et al. 2022]. As far as ER and PR positivity concerned, there are no statistically significant differences, according to most studies [Jiang et al. 2021]. According to Baretta et al, bilateral ER positive cancers seem to have better prognosis than those with different ER status, while ER negative seem to have the worst prognosis [Baretta et al. 2015]. Therefore, both ER positivity and concordance seem to affect prognosis. In our first patient both cancers were NST. In general, there was concordance regarding ER and Her2 status but discordance in PR status. In our second patient there were differences in histology and specifically the right breast cancer was NST, solid and papillary type and the left breast cancer was tubular type and NST. As far as immunohistochemistry concerned, there was concordance regarding ER, PR and Her2 status.

From the genomic point of view, there is no association of BBC with strong genetic mutations. Only 5% of BBC carry BRCA1 or BRCA2 mutations [Carmichael et al. 2002]. Several genetic studies have showed that BBC are genomically independent and are not clonally related. However, in the case of sBBC, the extrinsic factors related to the host (i.e. sex, age and BMI), the environment (i.e. tobacco, alcohol) and the immune microenvironment are the same. This probably explains the similar genetic portraits of sBBC, but there is no evidence of a common genetic alteration. Therefore, sBBC seem to be two different and independent diseases that might develop incidentally at the same time [Hamy et al. 2023].

Conclusion:

Synchronous bilateral breast cancer is a relatively uncommon entity. They seem to be independent tumors, but the histopathologic and immunohistochemistry profiles are more usually concordant.

So far there are no clear recommendations about the optimal treatment, that seems to be defined according to the more advanced tumor. Breast conserving surgery is feasible with acceptable cosmetic results. Consequently, such cases should be discussed in the multidisciplinary team, including breast surgeon, oncologist, radiation oncologist, radiologist, pathologist and plastic surgeon, in order to provide the best treatment option and a maximum survival benefit for patients.

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Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

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Conflicts of Interest: The authors declare no conflict of interest.

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