Occurrence of contralateral breast cancer in a \textit{BRCA}-positive breast cancer patient who underwent free TRAM flap reconstruction: a case report

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This report presents a case of contralateral breast cancer in a \textit{BRCA} mutation-positive patient who had previously undergone delayed free transverse rectus abdominis myocutaneous flap reconstruction for unilateral breast cancer. Having used up the available abdominal autologous tissue in the first reconstruction, a direct-to-implant procedure was employed for the reconstruction of the second, contralateral breast. Therefore, one breast was reconstructed using autologous tissue from the abdomen, while the other was asymmetrically reconstructed with an implant. If the risk of contralateral breast cancer had been anticipated initially, we might have opted for implant-based reconstruction from the start to facilitate a more symmetrical outcome in the event of subsequent contralateral reconstruction. This case underscores the importance of reviewing the risk of contralateral breast cancer in patients with unilateral breast cancer who also carry mutations in \textit{BRCA} and other breast cancer susceptibility genes. Furthermore, it encourages consideration of how mutations in breast cancer susceptibility genes, including \textit{BRCA}, influence the choice of plastic surgery reconstruction techniques. The findings from genetic testing for breast cancer susceptibility are now crucial to achieving aesthetic completeness in breast reconstruction.

\textbf{Keywords} Breast / Genes / Mutation / Case reports

INTRODUCTION

Rates of post-mastectomy breast reconstruction have increased over the past several years [1,2]. Patients referred to the department of plastic and reconstructive surgery for breast reconstruction include those diagnosed with breast cancer, as well as those who have not been diagnosed but meet the criteria for prophylactic mastectomy following genetic testing for breast cancer-associated genes 1 and 2 (\textit{BRCA1} and \textit{BRCA2}). \textit{BRCA1} and \textit{BRCA2}, which are types of breast cancer susceptibility genes—similar to tumor suppressor genes (\textit{TP53} and \textit{PTEN})—are recognized as the most common causes of hereditary breast cancer [3,4].

In South Korea, the rates of \textit{BRCA1} and \textit{BRCA2} genetic testing, along with prophylactic mastectomy, have seen a rapid increase. Jung et al. [5] reported a nearly 10-fold rise in \textit{BRCA1/2} genetic testing, from 578 cases in 2010 to 5,880 cases in 2017. Additionally, the incidence of contralateral risk-reducing mastectomy among affected carriers has increased approximately 5.8-fold, from five cases in 2013 to 29 cases in 2017. \textit{BRCA1} or \textit{BRCA2} mutations significantly increase the lifetime risk of developing breast cancer by age 70, with rates reaching 46\%–87\% for \textit{BRCA1} and 26\%–84\% for \textit{BRCA2} [6-9]. In contrast, the lifetime risk for the general population is approximately 10\% [10]. For \textit{BRCA} carriers, the risk of developing contralateral breast cancer is notably high at 53\%, compared to just 2\% in the general population. 

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population [11]. Furthermore, following a diagnosis of unilateral breast cancer, the risk of developing contralateral breast cancer increases by 0.4% annually over a period of 25 years [12]. The case presented herein indicates that even when unilateral breast cancer reconstruction is requested by BRCA carriers, it is crucial to consider a bilateral reconstruction plan due to the high risk of contralateral breast cancer.

CASE REPORT

A 49-year-old woman with a history of modified radical mastectomy and axillary lymph node dissection, followed by delayed free transverse rectus abdominis myocutaneous (TRAM) flap reconstruction for left-sided breast cancer, presented at the hospital with a palpable 1.5 cm mass in her right breast. Ultrasound examination revealed an irregular, indistinct hypoechoic mass measuring 1.3 × 1.3 × 1.0 cm in the lower outer quadrant at the 7 o'clock position. An ultrasound-guided core needle biopsy was performed (Fig. 1).

The biopsy confirmed invasive ductal carcinoma, prompting bilateral chest contrast magnetic resonance imaging for preoperative evaluation of the mass (Fig. 2). The patient had no family history of breast or ovarian cancer. However, she was diagnosed with left breast cancer at age 33 and subsequently developed primary breast cancer in the right breast at age 49, classifying her as a bilateral breast cancer patient. Genetic testing was conducted to assess for mutations linked to breast cancer susceptibility, using next-generation sequencing to examine a total of 29 genes, including BRCA1, BRCA2, CHEK2, and PALB2, among others. A pathogenic variant in the BRCA2 gene was identified. Further imaging with contrast-enhanced chest computed tomography (CT), abdominal and pelvic CT, and a bone scan showed no signs of local or distant metastasis. A nipple-sparing mastectomy with sentinel lymph node biopsy was planned for the newly diagnosed contralateral breast cancer, with immediate reconstruction referred to the plastic surgery department.

This patient underwent nipple-areolar complex reconstruction

![Fig. 1. Ultrasonography of the patient’s right breast, showing a 1.3 × 1.3 × 1.0 cm irregular, indistinct, hypoechoic mass.](image1)

![Fig. 2. Magnetic resonance imaging of the right breast, showing a 1.6 × 1.4 × 1.1 cm irregular, heterogeneous, fast-washout mass.](image2)

![Fig. 3. Photograph of the patient before mastectomy of the right breast.](image3)
Fig. 4. Photograph of the patient 13 months after mastectomy of the right breast. Implant reconstruction on the right, autologous tissue reconstruction on the left.

using a modified C-V flap following free TRAM flap surgery on the left breast, and a vertical mastopexy with a superior pedicle on the right breast to align with the left (Fig. 3). Despite multiple operations aimed at achieving bilateral symmetry after the delayed free TRAM flap reconstruction, the diagnosis of contralateral breast cancer significantly burdened the patient both emotionally and physically. This situation also presented a challenge for the plastic surgeon, as the option to use autologous abdominal tissue for reconstruction was no longer available. Due to the patient’s significant fatigue from previous surgeries, she opted for a reconstruction method that would allow for a shorter surgical time, reduced hospital stay, and a quicker return to daily activities. Given the absence of a plan for radiation therapy and the upcoming nipple-sparing mastectomy, it was decided to proceed with direct-to-implant reconstruction after consulting with the patient. The chosen implant, a Mentor MemoryGel Smooth Round Moderate Classic Profile 130 cc, was wrapped in an 18 × 18 cm acellular dermal matrix (Bellacell) and placed in the prepectoral layer. The patient was discharged without complications following the right breast surgery and was seen in an outpatient clinic 13 months later (Fig. 4). She is currently content with her condition, experiencing no discomfort. No further operations are planned, and she continues to be monitored in an outpatient setting.

DISCUSSION

Pathogenic variants in BRCA1 and BRCA2 are the most common cause of hereditary breast and ovarian cancer, observed in 2% to 10% of all breast cancers [13]. Although mutations in breast cancer susceptibility genes, including BRCA, are well known to increase the risk of breast cancer, it is less commonly known that they also raise the risk of contralateral breast cancer in patients previously diagnosed with the disease. Recent studies have begun to analyze the risk of contralateral breast cancer associated with mutations in other genes such as CHEK2 and PALB2, in addition to BRCA. In premenopausal women, the 10-year cumulative incidence of contralateral breast cancer was observed to be 33% for BRCA1, 27% for BRCA2, 13% for CHEK2, and 35% for PALB2 in cases of estrogen receptor-negative breast cancer. In postmenopausal women, these rates were measured at 12% for BRCA1, 9% for BRCA2, and 4% for CHEK2 [14]. If the risk of contralateral breast cancer is sufficiently high, this consideration can influence the decision to preserve abdominal autologous tissue during initial reconstructive surgery. Therefore, the presence of BRCA mutations should be a key consideration in planning reconstructive surgery.

If genetic testing had been conducted at the time of the initial breast cancer diagnosis and had confirmed a positive BRCA2 result, the patient and surgeon could have considered the significant 16.9% risk of developing contralateral breast cancer associated with BRCA2 positivity. This information might have led to the consideration of alternative reconstruction methods [14]. Consequently, the chosen approach could have resulted in higher aesthetic completeness, including improved shape, symmetry, and texture of both breasts, ultimately enhancing patient satisfaction. This scenario indicates that the treatment plan might have been modified based on the information shared with the patient. Although no established guidelines currently exist for patients classified as having a high probability of developing contralateral breast cancer, it appears beneficial to initially use implants for reconstruction and then monitor the patient for a sufficient period. If contralateral breast cancer does not develop after this observation period, the implants could be removed, and a delayed free TRAM flap reconstruction could be considered. Conversely, if contralateral breast cancer develops during the follow-up, both implants could be removed, and bilateral free TRAM flap reconstruction could be undertaken [15]. Furthermore, for patients with unilateral breast cancer who are at high risk of developing contralateral breast cancer, it may be necessary to discuss whether mastopexy of the contralateral breast should be postponed for a certain period following unilateral breast reconstruction.

The question of risk percentage that qualifies as sufficiently high certainly remains open for debate. It is also unclear at what level of risk it becomes more beneficial to preserve abdominal autologous tissue and opt for reconstruction using implants. Moreover, the advantages of choosing autologous tissue flap options are significant and should not be overlooked based solely on the potential risk of developing contralateral breast cancer, which has not yet occurred. In the long term, autologous reconstruction offers several benefits,
including freedom from complications such as infection, implant rupture, capsular contracture, and rippling. This approach is particularly beneficial for patients with ample abdominal fat, an irradiated chest, or thin and tight skin around the mastectomy scar. Additionally, some patients may prefer autologous reconstruction over implants due to the numerous advantages provided by living tissue.

Currently, we inform patients about their genetic mutation status and the associated risk percentage for contralateral breast cancer prior to surgery. We utilize this information to collaboratively decide on reconstructive surgical methods with the patients. At our institution, for patients with mutations in **BRCA1**, **BRCA2**, **CHEK2**, or **PALB2** who undergo free TRAM flap surgery for unilateral breast cancer, we are actively monitoring the development of contralateral breast cancer. Research into breast cancer susceptibility genes is ongoing, and further data collection is necessary. It may be too early to establish specific guidelines for plastic surgery reconstruction based on the results of genetic testing. Nevertheless, it is crucial for surgeons to consider this information when planning reconstructive surgery.

**NOTES**

Conflict of interest
No potential conflict of interest relevant to this article was reported.

Ethical approval
The study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB No. B-2312-870-701).

Patient consent
The patient provided written informed consent for the publication and use of her images.

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