Gender-affirming surgery requires a multidisciplinary clinical approach. Some transfeminine patients may undergo a complex and highly individualized transition process. Medical transition can include feminizing hormone therapy like conjugated estrogens and antiandrogens. However, prolonged estrogen hormone exposure and genetic mutations are known risk factors for breast cancer. There have only been 21 reports of breast cancer in transgender female patients since 1968. It remains unclear whether the use of feminizing hormone therapy augments this risk in transgender women in the setting of genetic predisposition.

There is a lack of literature addressing the approach to breast cancer treatment and reconstruction in transgender women. We aim to contribute our findings to the small data set by presenting the second ever reported case of BRCA2-associated invasive ductal carcinoma in a transgender woman. We then discuss the shared decision-making process that led to bilateral nipple-sparing mastectomy (NSM) and prosthetic implantation. Finally, we explore the challenges associated with reconstructing a transfeminine chest.

CASE REPORT

Full informed consent for participation and photography was obtained from the patient. A 70-year-old transgender woman of Ashkenazi Jewish descent began taking 1.8 mg estradiol and 50 mg spironolactone daily in 2018 as part of her gender-affirmation transition. Baseline mammography done 1 year after beginning hormone therapy was normal. Six months later, she developed prominent asymmetry in the right breast (Fig. 1). Repeat mammography revealed a 1.8 cm lobulated spiculated mass in the right retroareolar region and no axillary adenopathy. Pathology showed estrogen and progesterone receptor positive (ER/PR+), human epidermal growth factor receptor 2 negative (HER2-) invasive ductal carcinoma.

Estrogen and spironolactone were discontinued. Orchiectomy was recommended to decrease peripheral testosterone conversion to estrogen. However, the patient declined orchiectomy because she did not wish to undergo any genital operations before vaginoplasty. She was agreeable to neoadjuvant endocrine therapy with tamoxifen. Following 3 months of therapy, the patient underwent bilateral NSM with ipsilateral sentinel lymph node biopsy and immediate subpectoral tissue expander and acellular dermal matrix placement.

Surgical pathology revealed a 1.8 cm high grade invasive ductal carcinoma with less than 1 mm nipple margin and lymphovascular invasion. One sentinel node was positive with 1 mm nodal deposit. In the setting of her pathologic findings, adjuvant chemotherapy and radiation were recommended.

Genetic evaluation revealed both sets of grandparents were of Eastern European Ashkenazi Jewish descent. Family history was notable for both lung and breast cancer. The patient met National Comprehensive Cancer Network

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criteria for genetic testing. She was found to have a heterozygous BRCA2 gene mutation (c.6070C>T; p. Gln2024).

**DISCUSSION**

Diagnosis of breast cancer in transgender women requires a high index of suspicion. Twenty-one cases1,3–17 of nonimplant associated breast cancer (age: 30–74 years) have been reported worldwide since 1968 (Table 1). Among the 21 cases, duration of hormone replacement therapy ranged from 2 to 30 years. We present the second ever reported case of BRCA2-associated breast cancer in a transgender woman. We explore the shared decision-making process that informed our reconstruction plan and discuss challenges we faced when attempting to create an aesthetic outcome.

Upon discussion with our multidisciplinary team, our patient elected to undergo bilateral nipple sparing mastectomies with immediate tissue expander placement. Traditional guidelines for NSM include tumor-to-nipple distance (TND) greater than 2 cm, no breast skin involvement and negative retroareolar resection margins at the time of mastectomy.18 However, a recent study by Wu et al showed no significant difference in 5-year cumulative local, nipple areolar complex, regional or distal recurrence rates between patients with a TND greater than 2 cm versus patients with a TND of 1 cm or less.19 Similar studies have shown no significant differences in disease free-survival rates between TND of 2 cm or less and TND greater than 2 cm cohorts.20,21 Our patient was involved in an evidence-based discussion about the risks and benefits of bilateral NSM with immediate breast reconstruction before her surgery. She expressed her goals of care with careful consideration of her gender-affirmation process. However, once her surgical pathology resulted and BRCA2 mutation was revealed, we revisited conversations about the need for adjuvant chemotherapy, radiation, and potential removal of the nipple areolar complex given her unique increased risk of recurrence.

During our patient’s reconstruction, we encountered challenges unique to transgender women. Transfeminine chests are generally broader due to wider sternums and greater pectoralis major muscle bulk than cisfeminine chests.22 Creating a reconstructed breast with upper pole fullness and “cleavage” was more difficult in our patient given her anatomy. However, autologous fat grafting is a valuable adjunct to improve the upper pole appearance. Additionally, trans-female nipples are generally...

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**Table 1. Nonimplant-associated Breast Cancer Cases in Transgender Female Patients**

| Case | Age (y) | Cancer Type | Years on Hormone Therapy | Immunohistochemistry | Reference |
|------|---------|-------------|--------------------------|----------------------|-----------|
| 1    | 30      | Poorly-differentiated adenocarcinoma | At least 6 y | Not reported | Symmers1 |
| 2    | 30      | Infiltrating adenocarcinoma | At least 7 y | Not reported | Symmers1 |
| 3    | 45      | High-grade IDC | 11 y | ER-, PR+ | Pritchard et al11 |
| 4    | 50      | IDC | 14 y | ER-, PR not reported | Ganly and Taylor2 |
| 5    | 46      | Secretory carcinoma | About 8 y | ER+, PR+, HER2- | Grabellus et al20 |
| 6    | 58      | Adenocarcinoma | About 11 y | ER+, PR, HER2- | Dhand and Dhaliwal19 |
| 7    | 43      | IDC | At least 13 y | ER+, PR, HER2- | Pattison and McLaren17 |
| 8    | 57      | Ductal carcinoma | About 36 y | ER+, PR, HER2- | Gooren et al10 |
| 9    | 56      | Poorly-differentiated carcinoma with probable breast origin (unconfirmed) | About 17 y | Not reported | Gooren et al10 |
| 10   | 71      | Not reported | Not reported | ER+, PR+ | Brown and Jones15 |
| 11   | 54      | Not reported | Not reported | ER-, PR- | Brown and Jones15 |
| 12   | 55      | Poorly differentiated IDC | At least 30 y | ER-, PR-, HER2- | Maglione et al27 |
| 13   | 65      | DCIS2 | About 13 y | ER+, PR+ | Maglione et al27 |
| 14   | 60      | IDC | About 8 y | ER+, PR+, HER2- | Sattari18 |
| 15   | 52      | Adenocarcinoma | 30 y | ER+, PR, HER2- | Gooren et al27 |
| 16   | 46      | IDC | At least 16 y | ER+, PR+, HER2- | Gooren et al27 |
| 17   | 51      | IDC | About 37 y | ER+, PR+, HER2- | Gondusky et al26 |
| 18   | 41      | IDC | 14 y | ER+, PR, HER2- | Teoh et al14 |
| 19   | 53      | Focally undifferentiated ductal carcinoma | 7 y | ER+, PR+, HER2- | Corman et al23 |
| 20   | 74      | IDC | At least 40 y | ER+, PR+, HER2- | Lienhoop et al23 |
| 21   | 70      | IDC | 2 y | ER+, PR+, HER2- | This study |

DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.
patients as cancer screening guidelines continue to evolve. Risks of developing breast cancer in transgender female with the psychological implications of disrupting the gen-
ment and reconstruction in transgender women. The risk of breast cancer recurrence must be carefully balanced smaller and more laterally displaced. With NSM and three months post tissue expander replacement with permanent prosthesis (bilateral 535 cm³ high profile smooth gel implants).

CONCLUSIONS Our case outlines the complexity of breast cancer treatment and reconstruction in transgender women. The risk of breast cancer recurrence must be carefully balanced with the psychological implications of disrupting the gender-affirmation process. Future studies should explore the risks of developing breast cancer in transgender female patients as cancer screening guidelines continue to evolve.

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