

BRCA2-associated Breast Cancer in Transgender Women: Reconstructive Challenges and Literature Review

Naomi A. Cole, BS*
 Libby R. Copeland-Halperin MD†
 Nina Shank, MD†
 Vidya Shankaran, MD*,†

Summary: Breast cancer in trans women is rare. Only 21 cases have been reported worldwide. Multidisciplinary teams must balance oncologic treatment with patient goals. Here we describe a case of invasive ductal carcinoma in a transgender woman who was found to have a *BRCA2* gene mutation. A shared decision-making process led to the patient undergoing bilateral nipple-sparing mastectomy with immediate tissue expander placement. Later findings prompted discussions about adjuvant chemotherapy and radiation. Additionally, we discuss the complexities associated with reconstructing a transfeminine chest. (*Plast Reconstr Surg Glob Open* 2022;10:e4059; doi: 10.1097/GOX.0000000000004059; Published online 22 April 2022.)

Gender-affirming care 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.¹ 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.

From the *Dartmouth Geisel School of Medicine, Lebanon, NH; and †Dartmouth-Hitchcock Medical Center, Division of Plastic Surgery, Lebanon, NH.

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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.²

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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Fig. 1. Preoperative clinical photograph of the patient after 2 years of estrogen therapy. There is significant ptosis of the right breast and asymmetry of the right nipple as compared with the left.

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 cases^{1,3-17} 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 2cm, 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 less¹⁹ 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

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	Symmers ³
2	30	Infiltrating adenocarcinoma	At least 7 y	Not reported	Symmers ³
3	45	High-grade IDC	11 y	ER-, PR+	Pritchard et al ⁴
4	50	IDC	14 y	ER-, PR not reported	Ganly and Taylor ⁵
5	46	Secretory carcinoma	About 8 y	ER-, PR-, HER2-	Grabellus et al ⁶
6	58	Adenocarcinoma	About 11 y	ER+, PR+	Dhand and Dhaliwal ⁷
7	43	IDC	At least 13 y	ER-, PR-, HER2-	Pattison and McLaren ⁹
8	57	Ductal carcinoma	About 36 y	ER+, PR-, HER2-	Gooren et al ⁸
9	56	Poorly-differentiated carcinoma with probable breast origin (unconfirmed)	About 17 y	Not reported	Gooren et al ⁸
10	71	Not reported	Not reported	ER+, PR-	Brown and Jones ¹¹
11	54	Not reported	Not reported	ER-, PR-	Brown and Jones ¹¹
12	55	Poorly differentiated IDC	At least 30 y	ER-, PR-, HER2+	Maglione et al ¹⁰
13	65	DCIS ²	About 13 y	ER+, PR+	Maglione et al ¹⁰
14	60	IDC	About 8 y	ER+, PR+, HER2-	Sattari ¹³
15	52	Adenocarcinoma	30 y	ER+, PR-	Gooren et al ¹²
16	46	IDC	At least 16 y	ER+, PR+, HER2+	Gooren et al ¹²
17	51	IDC	About 37 y	ER-, PR-, HER2-	Gondusky et al ¹⁶
18	41	IDC	14 y	ER-, PR-, HER2-	Teoh et al ¹⁴
19	53	Focally undifferentiated ductal carcinoma	7 y	ER+, PR+, HER2-	Corman et al ¹⁵
20	74	IDC	At least 40 y	ER+, PR+, HER2-	Lienhoop et al ¹
21	70	IDC	2 y	ER+, PR+, HER2-	This study

DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.



Fig. 2. Three months post tissue expander replacement with permanent prosthesis (bilateral 535 cm³ high profile smooth gel implants).

smaller and more laterally displaced.^{23,24} With NSM and prosthetic implantation, the lateral displacement appears more pronounced (Fig. 2). This is an outcome that must be addressed with patients before proceeding with nipple-sparing procedures, as they may elect to undergo nipple reconstruction in lieu of laterally displaced nipples. Despite estrogen therapy, trans women generally have a more restricted skin envelope than cis women due to less breast tissue. The restrictive skin envelope may lead to difficulty creating a natural appearing breast mound.

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.

Vidya Shankaran, MD

Division of Plastic Surgery
1 Medical Center Drive
Lebanon, NH 03756

E-mail: vidya.shankaran@hitchcock.org

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