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Case report

A rare case of breast cancer in a transgender woman ☆

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ABSTRACT

We report a case of breast cancer in a transgender woman (assigned male sex at birth, gender identity female) of Ashkenazi Jewish descent with BRCA2 mutation who had been taking cross-sex hormone therapy for 2 years. In addition to demonstrating breast cancer imaging findings and risk factors, this case draws attention to the paucity of research and data regarding breast cancer in transgender women and exemplifies the need for evidence-based consensus breast cancer screening recommendations for transgender women.

Case summary

A 70-year-old transgender woman presented to our institution with breast asymmetry and right-sided nipple inversion. Her past medical history was relevant for breast cancer in her maternal grandmother diagnosed in her late 60s, maternal and paternal Ashkenazi Jewish descent, and 2 years of treatment with cross-sex hormone (CSH) therapy for gender dysphoria. At the age of 68 she began CSH therapy with estradiol and monitored her breast development with serial photographs. She noticed breast asymmetry and mild right-sided nipple inversion in these photographs, which prompted her to seek medical attention.

Physical examination revealed a nontender, mobile, palpable retroareolar mass. The left breast and bilateral axillae were clinically unremarkable. Review of systems was negative for night sweats, weight loss, nipple discharge, and pain.

Imaging findings and diagnosis

Diagnostic mammography demonstrated extremely dense parenchyma and a 1.8 cm spiculated mass in her right

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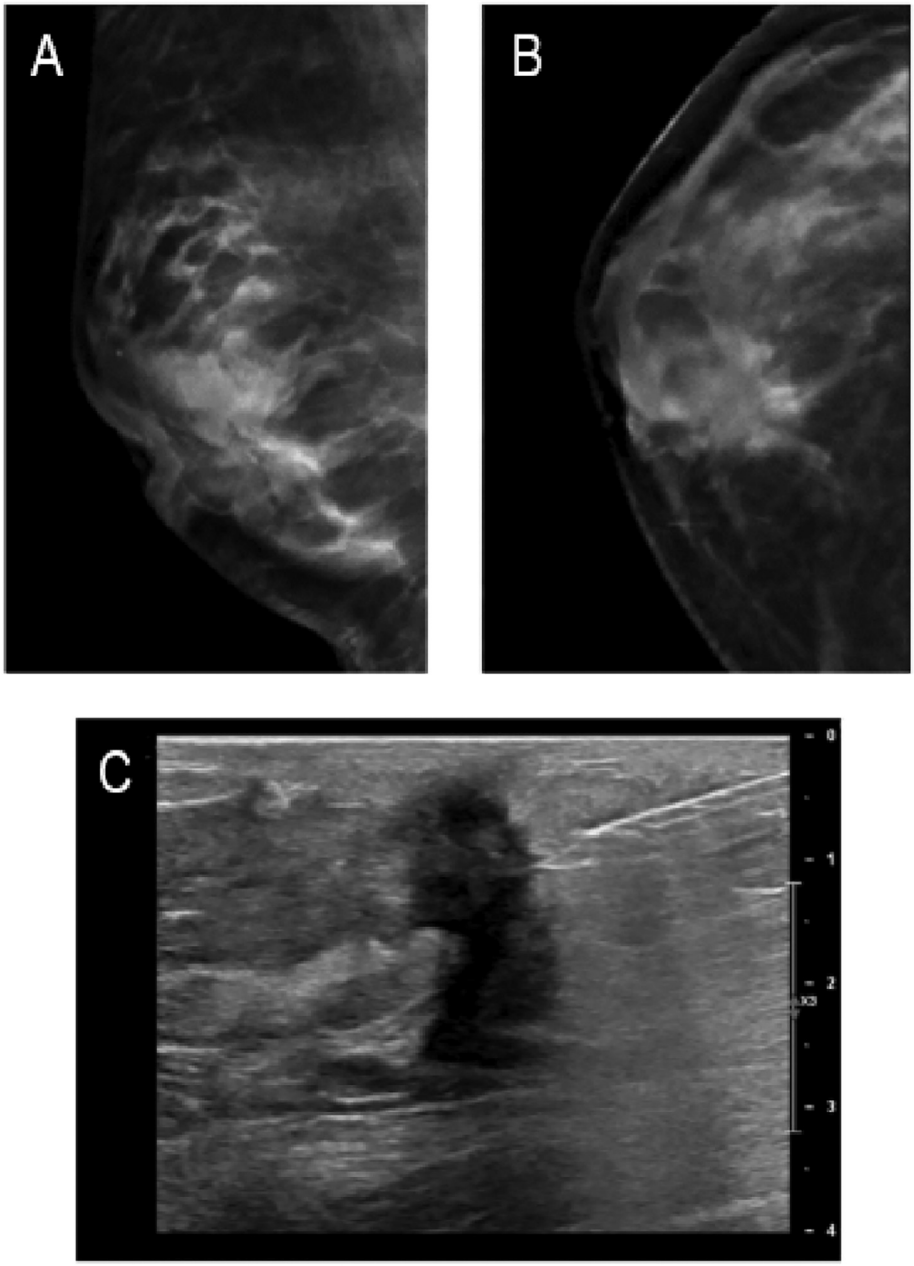

Fig. 1 – (A and B) MLO and CC digital breast tomosynthesis and (C) Core biopsy pre-fire ultrasound of the retroareolar mass.

retroareolar area with associated nipple inversion and overlying skin retraction. No axillary adenopathy was present sonographically. Directed ultrasound confirmed a 1.8 cm spiculated, non-parallel, hypoechoic mass at the retroareolar 3 o'clock radian, 1.5 cm from the nipple.

Figure 1

The mass was biopsied under ultrasound guidance. Biopsy pathology reported concordant strongly ER/PR+ and HER2- invasive ductal carcinoma. She was referred to the multidisciplinary breast clinic for subsequent evaluation and treatment. She discontinued CSH therapy and began neoadjuvant tamoxifen 20 mg qd. She underwent bilateral mastectomies with immediate expander reconstruction and right sentinel lymph node sampling.

Surgical specimen pathology revealed a strongly ER/PR+ and HER2- grade 3 tumor measuring 1.8 cm with lymphovascular invasion. No treatment effect was observed in the tumor. Her Oncotype DX score was 28 and the tumor Ki-67 proliferation index was 37%. She declined recommended adjuvant chemotherapy with docetaxel and cyclophosphamide but elected to undergo adjuvant radiation therapy. Subsequent genetic testing was positive for BRCA2 mutation.

She plans for gender-affirming vaginal reconstruction but has encountered logistical and financial barriers.

Furthermore, surgical expertise in gender-affirming vaginal reconstruction is not currently available in this region.

Discussion

Breast cancer is the leading cause of cancer in women [1]. Cisgender women carry a 12% lifetime risk of breast cancer, while cisgender men carry only a 0.1% lifetime risk of breast cancer [2]. However, there is limited data and research regarding the risk and pathogenesis of breast cancer in transgender women undergoing CSH therapy [3]. This paucity of data is at least in part due to a lack of evidence-based consensus breast cancer screening recommendations offered to transgender women, poor subject follow-up, as well as barriers to care faced by the community, which include historical marginalization, reluctance to disclose, and lack of provider experience and resources [4,5]. These factors often lead to late diagnosis and advanced stage of invasive breast cancer at the time of diagnosis [6].

Evidence regarding breast cancer risk in transgender women is mixed [2,7]. However, a recent large retrospective study conducted in the Netherlands using electronic medical data from 2260 adult transgender women found a statistically significant 46-fold increased lifetime risk of breast cancer in transgender women as compared to cisgender men. In the same study, transgender women were found to be at a 70% lower lifetime risk of breast cancer than cisgender women [2].

"Transgender" refers to a person who identifies as the gender opposite to that assigned at birth, which may cause a dissonance referred to as "gender dysphoria". As part of treatment for this dissonance, a transgender woman often elects to undergo exogenous estrogen therapy with or without gender-affirming breast and reconstructive vaginal surgery. In cisgender men, most estrogen is created from the peripheral aromatization of androgens in the fat, brain, skin, and bone tissues. Supplemental exogenous estrogen leads to the development of breast tissue in transgender women and is central to CSH therapy [8]. The association of ER+ tumors with estrogen dose and exposure length in postmenopausal cisgender women has long been established [9]. While incompletely understood, the suggested increased risk of breast cancer in transgender women may follow this same association, especially taking into consideration that approximately 90% of male breast cancers are ER+ [10]. Thus, breast cancer screening is generally recommended for transgender women at the age of 50 after 5 years of CSH therapy [11]. The woman discussed in this case may have benefited from screening but would not have met these criteria, as she was 70 years old but had only taken CSH therapy for 2 years.

The woman discussed in this case eventually tested positive for a BRCA2 mutation. Mutations to this tumor suppressor gene are transmitted in an autosomal dominant fashion and are associated with increased breast cancer risk. Cisgender women carrying a BRCA2 mutation have a greater than 50% lifetime risk of developing breast cancer. Transgender women carrying a BRCA2 mutation have a greater than 80-fold increased lifetime risk of developing breast cancer as compared to the general male population. BRCA2 mutations are associated with up to 20% of male breast cancer cases [12]. In this patient, it is unclear if prior knowledge of her BRCA2 mutation would have affected her decision to initiate CSH therapy. However, such knowledge may have led to an important conversation between her and her physician regarding her genetic predisposition to breast cancer that may have been compounded by CSH therapy. Considering her family history of breast cancer and maternal and paternal Ashkenazi Jewish descent, it may have been reasonable to perform genetic testing prior to beginning CSH therapy.

Many different institutional and organizational transgender breast cancer screening recommendations have been proposed but vary based on length of CSH therapy and patient age. For example, the Endocrine Society generally recommends adherence to the same screening guidelines for cisgender women, while the UCSF guidelines generally recommend screening at the age of 50 after 5 years of hormonal therapy [13,14]. The differences in screening recommendations are mostly due to the limited relevant epidemiological data. As transgender breast health research increases and multifactorial barriers to care faced by the transgender community are addressed, our hope is for progress toward evidence-based consensus breast cancer screening recommendations for transgender women.

In conclusion, we present a case of breast cancer in a transgender woman. This case contributes to the published data in this area and draws attention to the need for evidence-based consensus breast cancer screening recommendations and increased access to care for transgender women.

Patient consent

The patient consented to the publication of this case report.

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