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Breast Fibroadenoma in a Transgender Woman Following Hormone Therapy

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Background	Transgender individuals experience a gender identity that differs from their sex assigned at birth. While this population has historically faced discrimination and disparities in healthcare, there is increasing recognition and acceptance of transgender health needs. Transitioning to their identified gender may involve social affirmation, hormone therapy (HT), or surgical procedures. Male-to-female transgender individuals (transgender women) often receive lifelong exogenous estrogen and antiandrogens to develop female secondary sex characteristics. Long-term HT has been associated with breast cancer in other populations, but most literature on transgender women focuses on malignant breast tumors rather than benign lesions.
Summary	We present the case of a transgender woman who initiated HT at 31 years old and subsequently underwent several surgical interventions to achieve a female phenotype. After four years of HT, she developed a hard mass in her left breast, which was found to be a 1.5 cm, smooth, well-circumscribed nodule. Breast ultrasound and mammography suggested a benign lesion, and core biopsy confirmed a fibroadenoma. Given the limited evidence on managing fibroadenomas in transgender women receiving long-term HT, conservative management with regular surveillance was chosen. However, the patient continued her HT regimen.
Conclusion	Breast lesions, including benign tumors, are increasingly encountered in transgender individuals. However, only three prior cases of fibroadenoma in transgender women have been reported. Increased reporting of benign breast tumors in transgender women is needed to enhance our understanding and management of these cases.
Key Words	fibroadenoma; breast diseases; transgender persons; hormone replacement therapy

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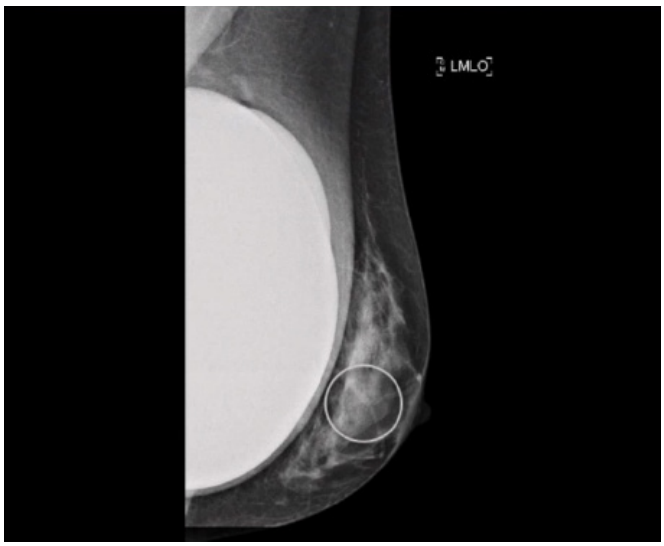
Case Description

The patient, a 37-year-old transgender woman, initiated gender-affirming hormone therapy (HT) with estradiol and spironolactone at age 31, followed by progesterone for breast development. At age 32, the patient underwent facial feminization surgery and received submuscular breast implants one year later. Finasteride was added to her regimen to promote hair growth. She reported satisfaction with HT and experienced no significant adverse effects.

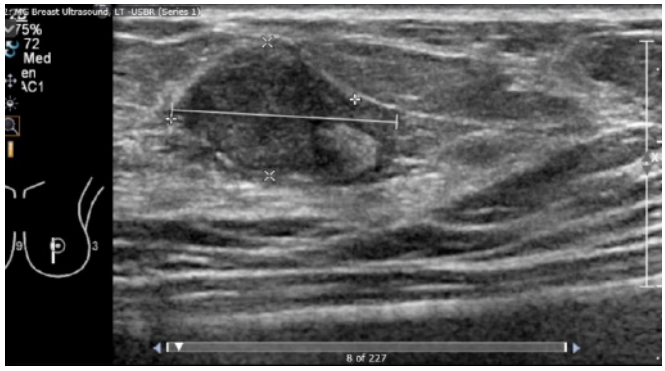
At age 35, she presented with a 1.5 cm, smooth, well-circumscribed left breast nodule at the nine o'clock position, just lateral to the areola, which persisted despite pectoral flexion. Both breasts had well-healed scars from the augmentation surgery and appeared symmetrical. There were no abnormalities in the right breast, such as a dominant palpable mass, tethering, dimpling, pagetoid change, or "peau d'orange" texture. Based on clinical presentation, the mass was suspected to be a fibroadenoma.

Figure 1. Mammogram Demonstrating Ovoid, 13 mm Nodule in Left Breast (BI-RADS Category 4A). Published with Permission



During HT workup, a mammogram identified a nodule less than 2 cm in size (Figure 1). Ultrasound examination supported the diagnosis of a fibroadenoma (Figure 2). Based on these findings, the patient opted for conservative management with regular mammographic follow-up rather than surgical intervention. Her HT regimen with estradiol and spironolactone was continued.

Figure 2. Breast Ultrasound Demonstrating 16 mm Abnormal Intramammary Lymph Node with Features Suggestive of Benign Etiology. Published with Permission



At age 37, she underwent orchiectomy, and spironolactone was discontinued. Her last follow-up showed no change in the breast mass. Her current medications include estradiol 3 mg twice daily, finasteride 2.5 mg nightly, and progesterone 100 mg daily.

Discussion

Fibroadenomas are the most common benign breast tumors,[1–3] and while benign, they are associated with an increased risk of future breast cancer.[3] Complex fibroadenomas carry a two- to three-fold increase in breast cancer risk.[3,4] While men rarely develop fibroadenomas due to a lack of fibroglandular tissue,[5] male-to-female transgender individuals receiving HT experience estrogen-induced development of breast ducts, lobules, and acini in a manner akin histologically to cisgender women.[5]

HT is a fundamental component of transgender health, promoting secondary sex characteristics and improving mental well-being.[6,7] However, long-term HT in transgender women is estimated to increase breast tumor risk 33- to 46-fold compared to cisgender men.[6,7] The exact duration of HT therapy linked to a higher risk of breast tumors in transgender women remains unclear.

Our patient's case highlights this uncertainty. Their fibroadenoma was detected after only four years of HT, while documented cases in other transgender women describe fibroadenomas diagnosed 7-19 years after starting HT.[5,9,10] Additionally, while fibroadenomas in cisgender women typically present before age 30,[11] the three reported cases in transgender women show a delayed presentation, with diagnoses occurring between 34 and 41 years of age (Table 1).[5,9,10]

Table 1. Cases of Fibroadenoma in Transgender Women.

Case	Age at Feminizing Surgery (years)	Age at Initiation of HT (years)	HT Regimen	Age at Presentation of Fibroadenoma (years)	Clinical Presentation
Kanhai (1999)	22 (Orchiectomy, vaginoplasty, augmentation mammoplasty	22	Cyproterone acetate 50 mg po daily Ethinyl estradiol 100 µg po daily	41	1.5 × 1.5 cm firm, smooth mass in medial upper quadrant of the right breast
Lemmo (2002)	34 (Augmentation mammoplasty)	22	Cyproterone acetate (dose unknown) Ethinyl estradiol (dose unknown)	34	1.5 cm, round, smooth, mobile, painless, well-defined mass in the upper outer quadrant of the right breast (detected on mammography)
De Faria (2019)	35 (Orchiectomy, feminizing genitoplasty)	29	Ethinyl estradiol 125 µg po daily	36	1 cm, mobile, fibroelastic, retroareolar nodule

The overall prevalence of benign breast tumors like fibroadenomas in transgender women on long-term HT is unknown, although it is possible their risk may resemble that of cisgender females. A retrospective study on transgender women receiving HT found a similar benign-to-malignant tumor ratio as seen in cisgender women.[12] Notably, fibroadenomas were the most frequent diagnosis, representing 33% of all breast tumors in this study.[12]

Although the prevalence of fibroadenoma in cisgender women is 10%,[11] its prevalence in transgender women is likely comparable but under-detected. This under-diagnosis may stem from transgender women often being grouped with cisgender men in healthcare settings, where breast cancer screening is less common due to societal stigma.[13]

Increased education and awareness regarding breast tumors associated with long-term HT, their management, and screening recommendations are needed for transgender individuals and their healthcare providers. Despite the elevated breast cancer risk in transgender women on long-term HT, there is a lack of clear screening guidelines for this population.[14] Current Canadian guidelines, for example, do not specifically address transgender women.[14] While some international guidelines, like the conjoint Endocrine Society guidelines, suggest following cisgender female screening protocols for transgender women with no additional risk factors, the evidence base for this recom-mendation is considered low-quality.[16]

Further research is needed to better characterize the relationship between HT duration and breast tumor incidence in transgender women. Long-term primary data are crucial to inform the risks and benefits of continuing HT in transgender women diagnosed with fibroadenoma, enabling informed, patient-centered treatment decisions.

Conclusion

The growing visibility a nd earlier m edical interventions for transgender individuals will likely lead to a rise in presentations of breast lesions in transgender individuals. While research on breast cancer in transgender women is emerging, there is a paucity of research reporting benign breast tumor cases and their management. This case highlights the diagnosis and management of a fibroadenoma in a transgender woman receiving HT, emphasizing the increasing clinical relevance of this presentation. Greater awareness and further research are needed to characterize the epidemiology and optimal management of benign breast lesions in this population.

Lessons Learned

Transgender women receiving HT are at increased risk for developing breast lesions, including fibroadenomas, which may be associated with an elevated risk of future breast cancer. These lesions can occur even after a relatively short duration of HT. Conservative management with close surveillance is a viable option for fibroadenomas in transgender women receiving HT, and continuation of HT may be safe. Further research is needed to establish evidence-based guidelines for screening, detection, and management of these tumors in transgender women. Additionally, investigating the relationship between HT duration and the incidence of new breast tumors will inform optimal surveillance strategies.

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