Androgen Receptor Positive Breast Cancer in a Female-to-Male Transgender Individual

K. Wilson[1], F. Raza[2], K. Donthireddy[1]

[1]Hematology/Medical Oncology, UT Health Science Center Tyler, Tyler, TX, [2]Internal Medicine, UT Health Science Center Tyler, Tyler, TX

Background

Limited guidelines exist regarding breast health in the transgender population. The method of gender-affirming transition undergone by a transgender individual has been shown to influence the risk of developing breast cancer [1]. The role between exogenous testosterone and the pathogenesis of breast cancer remains unclear. Here, we report a case of invasive ductal carcinoma of the breast in a female-to-male transgender patient after receiving gender-affirming hormonal therapy.

Case Presentation

A 36-year-old female-to-male transgender individual presented with a palpable left breast mass for evaluation.

- The patient began testosterone and aromatase inhibitor for transitioning six years prior under the care of endocrinologist.
- Menarche at age 12. The patient continued monthly menstrual cycles after initiation of gender-affirming hormonal therapy.
- Past Family history was significant for multiple family members with breast cancer and colon cancer.
- Clinical exam was significant for 3cm mobile mass at 6 o'clock position and matted level one lymph node.
- Diagnostic mammogram and biopsy was performed and confirmed a 3.8 cm mass in the lower inner left breast.
- Pathological exam of the biopsy revealed invasive ductal carcinoma, grade 3.
- Hormone receptor status: estrogen receptor positive (39%), progesterone receptor negative (0%), human epidermal growth factor receptor 2 negative (0%), with Ki67 85%. Androgen receptor was positive (34%).
- PET scan confirmed locally advanced disease with 4.1cm left breast mass with left axillary adenopathy.
- Genetic testing was obtained that was negative for BRCA 1/2 but identified a PALB2 VUS.

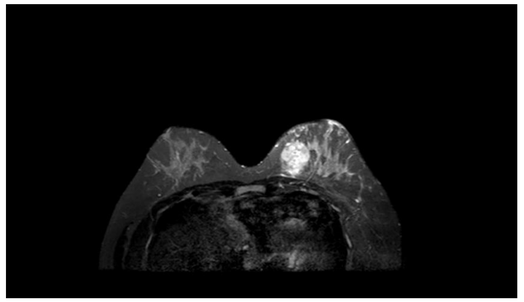


Figure 1. 3.8 x 3.5 x 3.1 cm heterogeneously enhancing mass

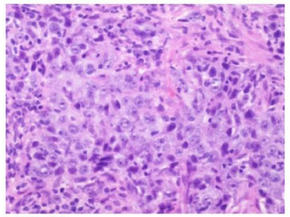


Figure 2. Left axillary lymph node, metastatic poorly differentiated adenocarcinoma

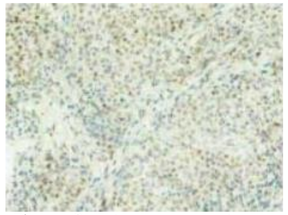


Figure 3. Estrogen receptor staining positive, 39%.

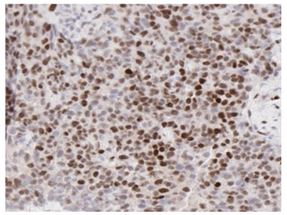


Figure 4. Androgen receptor staining positive 34%.

Management

1. Completed neoadjuvant chemotherapy with dose-dense doxorubicin, cyclophosphamide and paclitaxel regime.
2. The patient was advised to discontinue testosterone therapy as androgen receptor staining was positive.
3. Completed bilateral mastectomy. Surgical pathology showed complete response.
4. Referred for adjuvant radiation.
5. Planned to start ovarian suppression in combination with aromatase inhibitor therapy and CDK4/6 inhibitor.
6. Planned for hysterectomy with bilateral salpingo-oophorectomy.

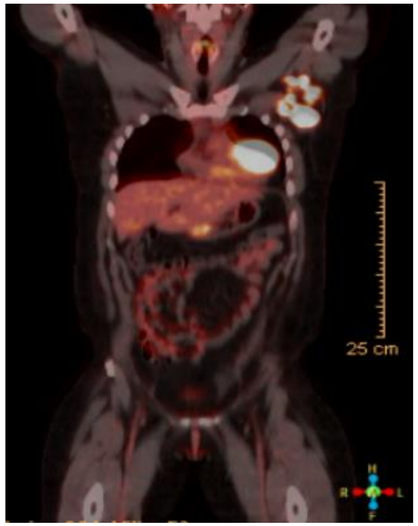


Figure 5. PET scan highlighting 4.1 cm FDG avid left breast mass, with left axillary adenopathy.

Discussion

- Female-to-male individuals who have undergone chest reconstruction surgery to remove breast tissue have significantly reduced risk of breast cancer [2,3].
- They face higher breast cancer risk compared to cisgender men but lower than cisgender women [4].
- The use of testosterone therapy and effects on breast cancer are controversial, with two theories reported:
  - Protective by decreasing glandular tissues, ultimately reducing the amount of tissue susceptible to cancer [5,6].
  - Causative in that testosterone is aromatized to estradiol leading to increased proliferation and breast cancer risk [7,8].
- **Our case illustrates the potential risk of inadequate estrogen suppression combined with prolonged androgen stimulation contributing to the development of breast cancer in a female-to-male transgender patient. A systematic review identified 26 similar cases of transgender patients who developed breast cancer post gender-affirming testosterone therapy [9].**

Conclusion

Our case highlights two key points:

- The importance of identifying personal risk factors for breast cancer, such as family history, genetic predisposition, and prior surgical procedures within this patient population.
- The need for further research on the impact of gender-affirming hormonal therapy on breast cancer risk to better inform clinicians in screening and clinical recommendations for this population.

Further research, including randomized controlled trials, is necessary to clarify the overall effect on individual patient risk and to ensure clinicians that are prescribing these hormonal therapies for medical transition can engage in open, informed risk-versus-benefit discussions with their patients.

Contact

Kendra Wilson
The University of Texas at Tyler Health Science Center
Kendra.Wilson@uttyler.edu
405-740-4056

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