Oncological Mastectomy in the Context of Reaffirmation of Sex in a Male Transgender Patient: Case Report and Literature Review

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ABSTRACT

**Background:** Breast cancer in the male transgender patient is a great challenge for the medical team, because it is completely different from the usual clinical scenario and there is a lack of scientific knowledge and protocols for managing this special medical situation.

**Case presentation:** We present a 32-year-old transmasculine patient, who developed a palpable nodule on the left breast during the androgen hormonal treatment. Imaging showed a BIRADS5 nodule and core biopsy detected a luminal B breast invasive carcinoma (IDC) with androgen receptor expression. He underwent a gender reaffirmation oncological mastectomy, chemotherapy and hormonal therapy.

**Conclusion:** In the transgender male scenario, the surgical technique should take into consideration the patient’s aesthetical desire and the oncological result. In this context, it is controversial if the hormonal and oncological therapies should also be changed.

INTRODUCTION

A transgender man is a biological female that identifies herself as a male. There are between 8 and 25 million transgender people in the world. In the United States there are 1.5 million transgender people, and this figure is increasing every year.\textsuperscript{1,2} In Uruguay in 2016, there were 853 transgender people, 10% of whom were transgender men. In our country, there are around 1900 new cases per year. There are no records of breast cancer in transgender people.

The increase in the transgender population reveals the necessity to modify the classical approach for cis women to satisfy the special requirements involved.

CASE REPORT

The patient was a 32-year-old trans male patient who initiated a treatment with testosterone 5mg per day for 45 days before consulting. Family records were unavailable. He had a 3cm hard lump in the 4 o’clock radius of left breast and no palpable lymph nodes. Ultrasound, mammography and breast magnetic nuclear resonance (MRI) (Figure 1) reported a BIRADS5 nodule with normal axilla.

Core biopsy showed an infiltrating ductal carcinoma (IDC), final histological grade II, positive estrogen receptor (ER), negative progesterone receptors (PR), positive HER 2 neu (FISH amplified) and Ki67 70%.

To achieve the patient’s aesthetic desires, bilateral total mastectomy with a free graft of the nipple areolar complex (NAC) and a sentinel node biopsy were performed without any incidents.

In the frozen section, we evaluated 4 sentinel lymph node that were negative. The patient had good immediate post-operative evolution (Figure 2).

Drains were removed on the 6th postoperative day. As a complication, he presented necrosis of the left nipple areolar complex (NAC) graft.
Figure 1. Axial DCE-MRI subtracted image. There is an irregular enhancement in distal 4 o’clock radius of the left breast that was confirmed as carcinoma by biopsy. There are no other pathological images in this or the contralateral breast.

Figure 2. Before (A) and after (B) oncological mastectomy with a NAC free graft.

The final pathological report showed IDC (score 9), final histological grade 3 and 1% of high grade in situ ductal carcinoma (DCIS) with free margins, lymphatic emboli present. The 4 lymph nodes were negative. pT1c N0sn. Androgen receptors (RA) were positive (Figure 3).

He received adriamycin and cyclophosphamide x 4, paclitaxel weekly for 12 weeks plus Trastazumab and Tamoxifen. There was no indication for radiotherapy. After discussing with the patient and the transgender health team, we decided to continue the testosterone treatment for gender reaffirmation.

DISCUSSION

Breast cancer is the most common cancer in biological female, but its incidence in transgender men remains unknown. Treating breast cancer in transgender patients is a completely different scenario than treating a cis woman, and as the transgender population increases, understanding it becomes essential, as mentioned by the World Professional Association for Transgender Health (WPATH).3

Besides the classical risk factors, in trans male patients we must also consider at least two different situations.4 Firstly, we must consider the hormonal treatment for masculinization, because there is contradictory evidence about its proliferative effect in the mammary gland. Secondly, we must address the risk reduction effect of sex affirming mastectomy.

In the literature, we found three population studies and five systematic reviews and case reports. Taking all the cases into account, there were only 24 cases of breast cancer in transgender men by 2020.3–11

It is important to emphasize that these papers show a substantial heterogeneity regarding histological diagnosis (DCIS, IDC and grade), biological profile (ER, PR, HER2 neu, AR), stage and sequence between the appearance of breast cancer and mastectomy. These is an important bias for an incidence analysis (Table 1). Available data show that the incidence of breast cancer in transgender men is significantly lower than that in general population.

Most authors attribute this lower risk to the low levels of estrogens induced by testosterone therapy added to the risk-reducing effect of mastectomies.

Subcutaneous mastectomy implies a risk reduction of around 90%, but this depends on how much glandular tissue is preserved. Therefore, transferring these findings to a sex affirming mastectomy surgery that leaves a higher percentage of glandular tissue is not possible.12
<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th>Age (in years) at diagnosis</th>
<th>Mastectomy prior to diagnosis</th>
<th>Family history</th>
<th>Testosterone use in years</th>
<th>Tumor type</th>
<th>BRCA status</th>
<th>Receptor status</th>
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</thead>
<tbody>
<tr>
<td>Burcombe et al. (2003)</td>
<td>Case report</td>
<td>33</td>
<td>Yes (10 years after mastectomy)</td>
<td>Negative</td>
<td>13</td>
<td>Ductal Carcinoma</td>
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<td>ER+, PR+</td>
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<td>Shao et al. (2011)</td>
<td>Case report</td>
<td>27</td>
<td>No*</td>
<td>Positive</td>
<td>6</td>
<td>Invasive ductal carcinoma grade 3</td>
<td>Negative</td>
<td>ER+, PR+, HER2+</td>
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<td>Case report</td>
<td>53</td>
<td>No*</td>
<td>Positive</td>
<td>5</td>
<td>Invasive ductal carcinoma grade 2</td>
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<td>ER+, PR-, HER2+</td>
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<tr>
<td>Nikolic et al. (2012)</td>
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<td>Yes (1 year after mastectomy)</td>
<td>Negative</td>
<td>2.5</td>
<td>Invasive ductal carcinoma</td>
<td>Not Tested</td>
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<td>3</td>
<td>Tubular adenocarcinoma</td>
<td>Unknown</td>
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<tr>
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<td>Infiltrative ductal carcinoma</td>
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<td>Katayama et al. (2016)</td>
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<td>15</td>
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<td>Barghouthi et al. (2018)</td>
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<td>Invasive ductal carcinoma</td>
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<td>Van Renterghem et al. (2018)</td>
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<td>Yes, incidental finding</td>
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<td>1.3</td>
<td>Moderately differentiated invasive carcinoma</td>
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<tr>
<td>Chotai et al. (2019)</td>
<td>Case report</td>
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<td>Yes (20 years after mastectomy)</td>
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<td>10</td>
<td>Invasive ductal carcinoma grade 3</td>
<td>Unknown</td>
<td>ER+, PR+, HER2+</td>
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<tr>
<td>De Blok et al. (2019)</td>
<td>Retrospective cohort study</td>
<td>30-50 (n=2), 60 (n=1)</td>
<td>Yes (n=3) (several years after mastectomy)</td>
<td>Unknown</td>
<td>Median 15; range 2-17</td>
<td>Ductal origin (n=3)</td>
<td>Unknown</td>
<td>ER+ (n=2), PR+</td>
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</table>
We have not found cases where the patient has been diagnosed with breast cancer at the beginning of his hormonal treatment and wanted a sex affirming mastectomy. Given the size of the breasts, we opted for a mastectomy with a NAC free graft, plus a sentinel node biopsy to achieve oncologically effective treatment and masculinization of the torso. It was very important to preserve a flap thickness that ensured viability without leaving too much glandular tissue, especially in the tale of Spence.

In this context, ensuring free margins and a complete removal of the gland was a priority. Other key points were converting the submammary groove into a submuscular groove, not leaving dog ears and finally relocating the areolar nipple complex.\textsuperscript{13-15}

The patient had necrosis of the left PDA graft in the pathological breast in the evolution, probably, due to the need for finer dermo-fat flaps, but despite this, the aesthetic result was satisfactory (Figure 5).

Figure 5. 2 months after oncological mastectomy with CAP-free graft.
Finally, the data about the role of androgens in the development of breast cancer are conflicting and there are no data about the effect of androgens on AR positive breast cancer, so the best adjuvant endocrine therapy is not known. Also, 72% of all breast cancers express androgen receptor and it is generally considered a good prognostic factor, especially in luminal tumors, but none of these aspects has been analyzed in the context of androgen hormone therapy.16

Some authors recommend stopping androgen therapy, but this can contradict the patient’s will. Regarding the peripheral androgen-to-estrogen conversion, some authors recommend aromatase inhibitors and others lowering the androgen dose or switching to dihydrotestosterone, which is non-aromatizable.11,12,17

Taking this into consideration, the detection of AR should become a standard for this population, although the effects of stimulating or blocking the AR are unknown, and even less frequently observed, in an androgen therapy context.

CONCLUSION
This article makes a contribution to the scarce literature on a sensitive topic that affects a socially vulnerable population that is growing by raising awareness about this problem, with the hope that protocols or treatment guidelines are developed to provide quality care to this population.

ETHICAL CONSIDERATIONS
The patient signed up an informed consent to publish his information and images within this case report.

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None.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interests related to the publication of this manuscript.

REFERENCES